THE PHOTOCHEMICAL SYNTHESIS OF 2-AZETIN-4-ONES
AND 2-AZETINES

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by
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I declare that the work described in this thesis is my own,
except where the work of others is specifically acknowledged.

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AUTHOR'S STATEMENT

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[Signature]
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The photochemical precursors, (I) and (II) of N-methyl-2-azetin-4-one have been synthesised and their stereochemistries established by spectral and chemical studies. The transient synthesis of 2-azetin-4-ones by means of the 1,2-photoaromatisation reaction has been achieved. Under the conditions employed, these compounds undergo facile photochemical ring opening to imino ketenes which have been trapped as adducts with methanol and methylamine.

The thermal decarbonylation of the exo,anti-(I) and endo,anti-(II) isomers has been investigated. The decarbonylation of (I) has been found to be assisted by cyclobutyl edge participation but does not involve simultaneous cyclobutyl sigma bond cleavage. The reaction of 2-pyrone with 2-azabicyclo[2.2.0]hex-5-en-3-one has been examined. Subsequent thermal decarboxylation of the adducts thus obtained has proven a convenient synthesis of 9-azabicyclo[6.2.0]deca-2,4,6-trien-10-one, a compound which readily undergoes thermal bond reorganisation.

N-Carbomethoxy-2-azetine and N-(p-toluenesulphonyl)-2-azetine have been synthesised by the 1,2-photoaromatisation reaction. The former compound is very susceptible to photochemical addition of hydroxylic compounds and readily undergoes [4 + 2]π addition to 3,6-di(2'-pyridyl)-s-tetrazine. The application of the same reaction to the synthesis of N-methyl-2-azetine was not successful.

Preliminary attempts have been made to generate and trap azetine by base-catalysed elimination of p-toluenesulphinic acid from N-tosyl-2-azetine but have also proved unsuccessful to date.
INTRODUCTION

1. SYNTHETIC ROUTES

The most commonly exploited entry to compounds (1), (2) and (3) has been by the thermal addition of a heterocyclic 5 component to a suitably activated alkyne (see Scheme 1.1). Addition of phenylacetylene to ethoxyacetylene under mild conditions yielded the oxa (5). Additional syntheses have been found to readily undergo (7 + 2) addition. Aube and Shoemier found that addition of (4) to disopropylacetylene provided both oxetane (8) and cyclobutene (9). Similarly, reaction with benzylsulphenylsulphenylsulphone gave thiebin-1,1-dioxide (10). 4-Dehydrobenzofuran (11) were isolated from the addition of phenyl isocyanate, the initially formed 2-azetidiones (12) having undergone facile ring opening and subsequent cyclization. Reaction with the 2-enamine (13) yielded the 2-azetine (14) amongst other products. In each case the diastereoselectivity of addition is that expected by consideration of the lone polarities. The bonds trifluoroketone catalysed reaction of oximes with cyano compounds and their joined to give oximes and enolised via associated intermediate oximes and 2-enynes has been reviewed. The addition of benzyl isocyanate to
1. MONOHETERO ANALOGUES OF CYCLOBUTENE

This section aims to discuss the synthesis and chemistry of derivatives of 2-azetine (1), oxete (2), thiete (3) and, to a lesser extent, the related 1-azetine (4). It is not a comprehensive review of the field; rather, an attempt to systematise the work of relevance to that contained in this thesis and to emphasise the synthetic strategies and properties common to compounds of this class.

1.1 Synthetic Routes

The most commonly exploited entry to compounds (1), (2) and (3) has been by the thermal addition of a heterocyclic II component to a suitably activated alkyne (see Scheme 1.1). Addition of hexafluoroacetone to ethoxyacetylene under mild conditions yielded the oxete (5). 1 Ynamines have been found to readily undergo [2 + 2] addition. Kuehne and Sheeran found that addition of (6) to diphenylketene yielded both oxetes (8) and cyclobutenones (7). Similarly, reaction with transient sulphenes gave thiete-1,1-dioxides (9). 4-Quinolones (11) were isolated from the addition of phenyl isocyanate, the initially formed 2-azetin-4-ones (10) having undergone facile ring opening and subsequent cyclisation. 2 Reaction with the ketenimine (12) yielded the 2-azetine (13) amongst other products. 3 In each case the regioselectivity of addition is that expected by consideration of the bond polarities. The boron trifluoride catalysed reaction of ynamines with carbonyl compounds and their imines to give enones and enimines via postulated intermediate oxetes and 2-azetines has been reviewed. 4 The addition of benzoyl isocyanate to
several substituted alkynes was found to give 2-azetin-4-ones (14) in yields ranging from 0.5% to 85% (Scheme 1.2). However claims of the isolation of a 2-azetin-4-one and an oxete from the reaction of chlorosulphonyl isocyanate with substituted alkynes have been disproved. The products obtained were in fact 6-chloro-1,2,3-oxathiazine-2,2-dioxides (16), the initially formed 2-azetin-4-ones (15) undergoing thermal ring opening to imino ketenes, followed by rearrangement and cyclisation in all cases.

Another successful approach to the synthesis of compounds (1), (2) and (3) has been introduction of the double bond into an already
formed ring by an elimination procedure (see Scheme 1.3). Thiete (3) (and similarly four simple alkyl derivatives) has been synthesised from the quaternary amino thietane (17) by a low temperature Hofmann elimination.\(^9\),\(^{10}\),\(^{11}\) Thiete-1,1-dioxide (19) was similarly prepared by dehydrochlorination of the saturated precursor (18, \(X = \text{Cl}\))\(^{12}\) or by a Hofmann elimination 18, \(X = \text{NMe}^3\))\(^{13}\). The perhalo-oxetane (20),
synthesised by the cycloaddition of hexafluoroacetone to 1,2-dichloro-1,2-difluoroethane, was dechlorinated to yield the oxete (20). The 2-azetines (27), formed by spontaneous amine elimination from the intermediate azetidines (26), were isolated from the reaction of the enediamines (24) with N-sulphonylimines (25). The first 2-azetin-4-one to be synthesised and adequately characterised, 1,2-diphenyl-2-azetin-4-one (23), was obtained by cleavage of the azo compound (22) with boron trifluoride etherate. The structure was confirmed by catalytic hydrogenation to the known 1,4-diphenyl-2-azetidine.

1-Azetines (29) are much more readily available, since O-alkylation of the corresponding azetidinones (28) (readily synthesised by addition of chlorosulphonyl isocyanate to olefins, followed by basic hydrolysis) has proved a versatile route to these compounds. 1-Azetines have also been prepared by the pyrolysis of cyclopropyl azides, the simplest 1-azetine to date, 2-phenyl-1-azetine, having been synthesised by this method.

Synthesis of aromatic fused 2-azetines and 2-azetin-4-ones is generally achieved by either thermal or photochemical elimination of nitrogen from the corresponding triazines. Scheme 1.4 presents compounds that have been synthesised by this approach. Recently Olofson and coworkers reported an elegant synthesis of N-alkylbenzoazetinones (33c-e) by reaction of the corresponding benzisoxazolium salts (36) with triethylamine.
1.2 Thermal Stability

The dominant factor in any discussion of the reactivity of these compounds is the ease with which they undergo ring cleavage to give acyclic derivatives. The energy release in so doing is considerable; cyclobutene has been estimated to have a strain energy of 30.6 kcal mol\(^{-1}\) and compounds (1), (2) and (3) are similarly strained. In comparison to cyclobutene, 2-azetine (1) and thiete (3) should undergo ring opening more readily because C-N and C-S single bonds are considerably weaker than C-C single bonds (Table 1.1). Oxete (2), which has a
strong C-O bond, and 1-azetine (4), for which we are concerned with C-C bond breaking, should undergo ring opening with comparable facility. However, in addition to the simple thermochemical data, any comparison must consider the susceptibility of any strained heterocyclic ring to ionic attack due both to the polarisation of the ring hetero-bonds and the ability of the heteroatom non-bonding electrons to assist in any ionic cleavage.

In the absence of any ionic catalysis, ring opening occurs by a
FIGURE 1.1 Orbital correlation diagram for the thermal opening of 2-azetine to 2-azabutadiene.

FIGURE 1.2 Orbital correlation diagram for the thermal opening of 1-azetine to 1-azabutadiene.
thermally allowed conrotary electrocyclic process analogous to the opening of cyclobutene. In an attempt to assess the perturbation induced on the system by the introduction of a nitrogen atom into the 2- and 1-positions of cyclobutene we have constructed orbital correlation diagrams for the 2-azetine and 1-azetine ring openings.†

The correlation diagram for 2-azetine ((1) → (39) in Scheme 1.5) is shown in Figure 1.1. The σ MO is essentially unchanged because it is at right angles to the n orbital; however interaction between the n orbital and the π MO leads to an increase in the π MO energy, as depicted in Figure 1.3. In 1-azabutadiene (39) the n orbital is at right angles to the π orbitals and cannot interact but it follows from simple PMO theory that the replacement of a carbon atom by a nitrogen atom causes both bonding molecular orbitals to be lowered in energy.

It is clear then that electrocyclic ring opening of 2-azetine is energetically more favourable than the opening of cyclobutene. This contrasts to the conrotary opening to 1-azetine to 2-azabutadiene (40) (refer to Scheme 1.5 and Figure 1.2). In this case the n orbital cannot conjugate with the π MO's of either molecule and it lowers the MO's of each to a similar extent. Therefore the ease of ring opening of 1-azetine will closely resemble that of cyclobutene.

There are few experimental data to test these speculations. A kinetic study of the vapour phase pyrolysis of substituted 1-azetines†

† The assistance of Dr. M. N. Paddon-Row is gratefully acknowledged.
confirmed that the rates of ring openings of these compounds are nearly the same as those for the analogous cyclobutenes, but an earlier stereochemical study of the reaction could draw no definite conclusions about the mechanism of ring opening, the results being accounted for equally well by a stepwise reaction leading to intermediate (41) or by conrotatory ring opening to give the vinyl imine (42) directly. Solution thermolysis of 2-alkoxy-1-azetines gave the corresponding 1-alkyl-2-azetidinones by intermolecular rearrangement rather than ring opened products.

The thermal stability of 2-azetines and 2-azetin-4-ones is largely unknown. Ring-fused 2-azetines (44a) and (44b) (formed by photolysis of diazepine ketones (43a) and (43b) rapidly reverted to the
monocyclic form at room temperature but (42c) was much more stable. Studies indicated that the ring opening went via the dipolar transition state (45), rather than by simple electrocyclic opening of the 2-azetine ring. The similar 2-azetine (48) was thermally stable, heating to 195° being required to effect reversion to diazanorcaradiene (46) via diazepine (47). The only benzazetine synthesised to date is very stable thermally. 1-Phenylbenzazetine (31) ring opened to the vinyl imine (49) (trapped as the N-phenylmaleimide adduct (50)) when heated at 200°. This example of course, has little bearing on the simple 2-azetines, since formation of (49) demands loss of the benzene ring resonance energy.

Photolysis of 3,4-dimethylpent-3-en-2-one (51) was found to give 2,3,4,4-tetramethyloxete (52). The thermal reversion of oxete (52) to enone (51) was studied by Friedrich and Schuster; these workers concluded that oxetes rearrange faster by a factor of $10^7$ than their corresponding cyclobutenes. This figure was obtained by comparing extrapolated solution data with gas phase data for 1,2,3,3-tetramethylcyclobutene and may not be quantitatively accurate but it does establish a large rate enhancement. Solvent studies were consistent with a simple electrocyclic rearrangement with little charge separation. The reaction was also found to be strongly catalysed by small amounts of acid.

Pyrolysis of thiete-1,1-dioxide (19) in both gas and liquid
phases led to high yields of the cyclic sulphinate (54), believed to be

\[
\begin{align*}
(19) & \xrightarrow{\text{hv disrotatory}} (56) \xrightarrow{\text{hv disrotatory}} (57) \\
(53) & \text{PhOH} \\
(55) & \text{SO}_2\text{Ph}
\end{align*}
\]

formed by the intermediacy of vinyl sulphone (53). Attempts to trap the sulphone (53) with a variety of reagents succeeded only in the case of phenol, for which the expected adduct (55) was obtained in 15% yield. 39,40,41

1.3 Photochemistry

There is a dearth of information about the photochemistry of these compounds. Since disrotatory ring opening is a photochemically allowed process, an equilibrium between photo-excited (56) and (57) will be set up, but the position of the equilibrium is variable and photo-products derived from either (56) or (57) may be expected.

The photolysis of a series of thiete-1,1-dioxides (58 a-e) led to the formation of unsaturated ketones (60 a-e) by immediate loss of sulphur monoxide from the initially formed vinyl sulphenes (59 a-e). The intermediacy of the sulphone (59) was established by its quantitative trapping as the sulphonic ester (62) when the thiete (56f) was photolysed in methanol. A minor fragmentation pathway exhibited by (58a) was the loss of sulphur dioxide and dimerisation to give the diene (61). 42 An earlier attempt to observe the sulphone (59f) directly was unsuccessful;
irradiation of (56f) at 77°K led to formation of the cyclic sulphinate (63) with no evidence of an intermediate. 43

The photolysis of benzazetinones (33) leads to rapid equilibration with the isomeric imino ketenes (64), 26,27,44 a reaction which is discussed in detail in Chapter 2. 1-Phenylbenzazetine (31) also readily undergoes similar reaction. 25,45

1.4 Cycloaddition Reactions

The ability of the hetero-cyclobutenes to undergo cycloaddition reactions, and particularly their dienophilicity with regard to Diels-Alder reactions is of considerable interest. Cyclobutene itself is an electron rich dienophile by virtue of the ring strain associated with its double bond, and hence reacts with inverse demand dienes, such as 3,6-dicarbomethoxy-α-tetrazine. 46 2-Azetine, oxete and thiete might be expected to exhibit considerably different behavior to cyclobutene due to the interaction of the heteroatom lone pair electrons with the double...
bond but, as yet, the dienophilicity of thiete-1,1-dioxide (19) only has
been studied in any detail.

Compound (19) gives Diels-Alder adducts with 1,3-diphenylisobenzofur-an at 80°,48 with butadiene, furan and 2,5-dimethylfuran at 110°,49
and with anthracene at 147°.50 Few stereochemical assignments have been
made, but on the basis of their pmr spectra the 1,3-diphenylisobenzofuran
and isobenzofuran adducts (65) of 2,2-dimethylthiete-1,1-dioxide have been
assigned \textit{exo} stereochemistry.51 The reaction of tetracyclone (66) with (19) gave
cycloheptatriene (68) (65%) and ketone (67) (15%). The mechanisms for
product formation are shown in Scheme 1.6.49 The cycloaddition of (19)

\[
\begin{align*}
\text{(19)} & \quad \text{+} \quad \text{(66)} \\
\Delta & \quad \rightarrow \quad \text{(67)}
\end{align*}
\]

to tetraphenylcyclopentadiene gave approximately equal amounts of \textit{endo}
and \textit{exo} adducts, (70) and (71) respectively.49 2-Pyrone reacted with
(19) to give benzyl α-toluenethiosulphonate (74) and benzylsulphonic acid (75). Both products could be explained by cheletropic elimination of carbon dioxide from the initially formed Diels-Alder adducts (72), followed by ring cleavage and disproportionation of the resulting benzyl sulphinic acid (73). 51

\[
\begin{align*}
\text{SO}_2^- + \text{O} & \rightarrow \left[ \begin{array}{c}
\text{CO}_2 \end{array} \right] \\
\text{(19)} & \rightarrow \left[ \begin{array}{c}
\text{CO}_2 \text{SO}_2^- \\
\text{(72)}
\end{array} \right]
\end{align*}
\]

\[
\begin{align*}
\text{PhCH}_2\text{SO}_2\text{SCH}_2\text{Ph} & + \frac{1}{3}\text{PhCH}_2\text{SO}_2\text{H} + \frac{1}{3}\text{H}_2\text{O} \\
\text{(74)} & \rightarrow \text{(75)}
\end{align*}
\]

The exocyclic double bond of methylenethiete sulphone (76) was more reactive than the endocyclic double bond. Thus (76) gave spiro adduct (77) with 1,3-diphenylisobenzofuran and photolysis gave the \textit{trans}-1,2-dimer (78) as the only product. 52
2. THE 1,2-PHOTOAROMATISATION REACTION

Warrener and coworkers have defined the 1,2-photoaromatisation reaction to be the "ultraviolet irradiation induced fragmentation where a portion (containing the energy absorbing chromophore) is converted to an aromatic hydrocarbon and the other fragment remains structurally intact," the prefix numbers representing "the relative positions of the two $\sigma$ bonds involved in the fragmentation." The reaction, represented diagramatically below, is a $[\pi^2S + \pi^2S + \sigma^2S + \sigma^2S]$ pericyclic reaction and hence photochemically allowed by simple application of the Woodward-Hoffmann rules. That the reaction is in fact concerted remains in some doubt however, since Caldwell found that photosensitised irradiation of (E)-7,8-diacetoxybicyclo[4.2.0]octa-2,4-diene (79) led to the formation of both (E)- and (Z)-1,2-diacetoxyethylenes (80a and b) as primary photoproducts. Two mechanisms could be proposed to account for this.

Loss of stereochemistry could be due to rotation about a single bond in the diradical intermediate (81) or, alternatively, because 1,2-diacetoxyethylene is initially formed as an olefin triplet with twisted geometry which then decays to both (Z)- and (E)-isomers.

In practice the 1,2-photoaromatisation reaction is most useful
when the two participating sigma bonds form part of a fused cyclobutane ring, as in (82). This enables the formation of unsaturated cyclic compounds not readily accessible by more conventional methods. The synthetic potential of this reaction is apparent in Schröder's synthesis of bullvalene (84) by irradiation of the cyclooctatetraene dimer (83). The reaction has also been used successfully to regenerate a very unstable species under conditions much more favourable for its isolation or direct observation. In this manner, Diels-Alder addition of transiently generated cyclobutadiene to 3,6-dihydropthalic anhydride (85) gave the adduct (86) which was converted in seven steps to the triene (87).

Irradiation of (87) in a glass of 98°K enabled the low temperature generation of cyclobutadiene to be achieved. The same procedure

\[ \text{Irradiation of (87) in a glass of 98°K enabled the low temperature generation of cyclobutadiene to be achieved.} \]
was used by Maier and coworkers to generate tetramethylcyclobutadiene at 77°K. 57

A general procedure for the synthesis of cyclic olefins via the 1,2-photoaromatisation reaction has been developed by Warrener and coworkers. 53,58 Synthesis of the bicyclo[4.2.0]octa-2,4-diene precursor (91) is achieved by Diels-Alder reaction of a potential diene (88) with a fused cyclobutene to give an adduct (90), which can subsequently undergo photoinduced cheletropic elimination of X to generate diene (91) in situ. Further photofragmentation of (91) affords the aromatic

\[
\begin{align*}
\text{(88)} & \quad \text{(89)} & \quad \text{(90)} & \quad \text{(91)} \\
R_1 & \quad R_2 & \quad X & \quad \text{hv} & \quad \text{hv} \\
& \quad R_3 & \quad R_4 & \quad -X & \quad \text{hv} \\
& \quad R_5 & \quad R_6 & \\
& \quad R_7 & \quad R_8 & \\
\end{align*}
\]

\(X = \text{CO, COCO}\)

hydrocarbon (92) and the cyclic olefin (93). 2,5-Dimethyl-3,4-diphenyl-cyclopenta-2,4-dienone, which exists as its dimer at room temperature (approximately 5% monomer is in equilibrium with the dimer at 80°59) has been found to be a particularly suitable diene. Tetrachloro-o-benzoquinone has also been employed, but the use of this diene is subject to complicating side reactions. 58 Overall then, the procedure involves the removal of a cyclobutene unit in two steps. Some successful applications of this sequence are presented in Table 1.2.

3. THE PHOTOCHEMISTRY OF HETERO 1,3-CYCLOHEXADIENES

The previous section developed the concept of the 1,2-photoaromatisation reaction as part of a sequence for the conversion of fused
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**TABLE 1.2**
cyclobutenes (89) to cyclic olefins (93). For this method to have applicability to the synthesis of unsaturated four membered heterocycles, the precursors (95) must be readily attainable themselves. The preferred method of synthesis of these compounds would appear to be by photochemically allowed disrotatory ring closure of dienes (94). Once formed, cyclobutenes (95) might be expected to show good thermal stability since symmetry allowed thermal ring opening is conrotatory and hence leads to energetically unfavourable \((Z, E)\) dienes (96). However, photochemically allowed conrotatory ring opening to \((E, Z, Z)\)-hexatrienes is a competitive process. The relative efficiencies of the pathways are highly dependent on molecular structure and photolysis conditions. A striking example is afforded by the photochemistry of the \(\Delta_5^5,7^7\) steroidal dienes. The photolysis of ergosterol (97) and lumisterol (99), in which the 9- and 10-substituents are \(\text{trans}\) leads to the formation of precalciferol (98) which subsequently thermally rearranges. In contrast, pyrocalciferol (100) and isopyrocalciferol undergo ring closure to give the cyclobutene derivatives (101) and (103) respectively when photolysed.\(^{65}\) The simple diene (104) is intermediate in behavior, giving both the cyclobutene (106) and the triene (105).\(^{66}\)

Dimerisation is another complicating side reaction, \(1,3\)-cyclohexadiene itself readily undergoing photosensitised dimerisation to yield a series of \([2 + 2]\) and \([4 + 2]\) dimers.\(^{67}\) In view of this diversity
of reaction pathways a brief review of the photochemistry of hetero-1,3-cyclohexadienes is presented.

The photochemistry of 2-pyrone (107) and its derivatives has been studied in detail by several groups. Most important, in the context of this work, was the reported formation of bicyclic lactone (109) in high yield by the photolysis through Corex of dilute ethereal solutions of 2-pyrone. A large number of mechanistic studies of the photolysis of (107) in nucleophilic solvents gave confusing results. Recent work by Chapman and coworkers has done much to clarify the situation. The photolysis of (107), matrix isolated in argon at 8°K, gave rapid formation of the ketene (108) which established a photo-equilibrium with (107). Continued irradiation led to the disappearance of (107) and (108), the ultimate product being the bicyclic lactone (109).
A reinvestigation of the photolysis of 4,6-dimethyl-2-pyrone (110) in methanol by the same workers demonstrated that the crotonic esters (113) previously obtained were derived, not from a ketene intermediate, but from acid-catalysed cleavage of the lactones (111) and (112) formed by photochemical addition of methanol to (110).\textsuperscript{75}

\[
\begin{align*}
\text{MeCONHCHMe} &= \text{CHO}_2\text{Me} \\
(114) &\quad \text{(112)}
\end{align*}
\]

Photoexcited 2-pyrones readily dimerise in concentrated solution. Irradiation of 4,6-dimethyl-2-pyrone (110) in saturated benzene solution gave rise to two \([4 + 4]\) dimers (thermal cheletropic elimination of 2 moles of carbon dioxide from these giving good yields of 1,3,5,7-tetramethylcyclooctatetraene) and a \([2 + 2]\) dimer.\textsuperscript{76} Similar irradiation of 2-pyrone gave an inseparable dimer mixture which yielded only 2.4% of cyclooctatetraene when pyrolysed, suggesting that \([2 + 2]\) and \([4 + 2]\) dimers were present rather than \([4 + 4]\) dimers.\textsuperscript{72} Sensitised irradiation of 2-pyrone gave a 50:50 mixture of \([4 + 2]\) dimers.\textsuperscript{70}

After some incorrect early reports, 2-pyridones (114)\textsuperscript{75,78,79,80,81} and 2-aminopyridines (117)\textsuperscript{79,81} were established to give \([4 + 4]\) dimers
having structures (115) and (116) respectively. Subsequently, the irradiation of dilute solutions of 1-methyl-2-pyridone (114, R = Me) was reported to give the bicyclic lactam (118, R = Me). Two detailed studies have been made of the photochemistry of 2-pyridones, both of which implicate a singlet state mechanism for both isomerisation and dimerisation. The photoisomerisation of substituted 2-pyridones to their corresponding cyclobutenes has proved a general reaction and a large number of compounds have now been synthesised by this method.

Apart from these two well studied systems, the photolysis of few other monohetero-1,3-cyclohexadienes has been studied. This is primarily due to the difficulty in synthesising these generally unstable compounds: 1,2-dihydropyridines have only recently become easily available, whilst 2H-pyran and 2H-thiapyran remain little known compounds. Irradiation of 1-carbomethoxy-1,2-dihydropyridine (119) has been reported to give the bicyclic azetidine (120) in 85% yield. In contrast, photolysis of the highly substituted 2H-pyran (121a) and 2H-thiapyran (121b) gave the ring opened products (122a) and (122b).

Photolysis of pyrazinone (123) gave the unstable azetine (124), which was isolated as its reduced derivative (125).
In a few cases, the photolysis of pyridines has enabled the isolation of Dewar type valence isomers. These compounds hold particular interest as synthetic precursors to azetidinones. Irradiation of solutions of pyridine in acetonitrile or n-butane at low temperatures gave moderate quantities of the Dewar valence isomer (126), which was found to have a half-life of 2.5 minutes at 25°C. Photolysis in aqueous sodium borohydride gave the bicyclic azetidine (127). 5-Amino-2,4-pentadienal (128), previously observed in the aqueous photolysis of pyridine, was considered to be formed by hydration of (126).

Pentakis(pentafluoroethyl)pyridine (129) gave almost quantitative yields of the valence isomer (130) when irradiated through pyrex for long periods. Isomer (130) afforded a dramatic example of the stability...
engendered by electron-withdrawing fluorine substituents, having a half-life of 104 hours at 170°. Recently, small amounts of the valence isomer (132) (in addition to prismane isomers) have been obtained from the photolysis of the perfluoroalkyl pyridine (131). Dewar type

\[
\begin{align*}
\text{(129)} & \quad \text{hv} \quad \Delta \\
\text{(130)} & \\
\text{(131)} & \quad \text{hv} \\
\text{(132)} & \\
\end{align*}
\]

valence isomers have also been isolated as stable intermediates in the photochemical conversion of perfluoroalkyl pyridazines to the corresponding perfluoroalkylpyrazines. \textsuperscript{93,94}
CHAPTER 2

2-AZETIN-4-ONES

Prior to the work presented here, no theoretical or spectroscopic studies had been made of azetinones (132) or their derivatives. However, its saturated analogue 2-azetidinone (138) and derivatives of (136) have been the subject of considerable investigation. Barrow and Spedding analysed the p.m.r. spectra of 14 azetidinones and concluded, on the basis of long range couplings to the protons of the nitrogen substituent, that the N-substituent lay out of the plane of the ring with the hybridisation of the ring nitrogen being somewhere between sp² and sp³. On the basis of the observed upfield shifts in its p.m.r. spectrum when solutions were diluted with benzene, and comparison of the C13-H coupling constants of the methyl group with that of N,N-dimethylacetamide, Moriarty and Xilagoras concluded that the amido C=N bond of N-aryl-2-azetidinone has about 40% double bond character. The ultraviolet spectra of non-stERICALLY hindered N-arylazetidinones suggest that they have a completely planar structure. X-ray analysis of compounds (135) and (136) proves that the ring atoms and the carbonyl
2.1 Theoretical Studies

Any speculative consideration of the inherent molecular properties of 2-azetin-4-one (133) must address itself primarily to the extent of electron delocalisation present in the potentially extended \( \pi \) system of this molecule. Any appreciable contribution from the canonical structure (133b) will cause the ring to have considerable antiaromatic character thus distortion from coplanarity to reduce the overlap of the nitrogen p orbital with the p orbitals of the carbons can be expected.

Prior to the work presented here, no theoretical or spectroscopic studies had been made of azetinone (133) or its derivatives. However, its saturated analogue 2-azetidinone (134) and derivatives of (134) have been the subject of considerable investigation. Barrow and Spotswood analysed the p.m.r. spectra of 14 azetidinones and concluded, on the basis of long range couplings to the protons of the nitrogen substituent, that the N-substituent lay out of the plane of the ring with the hybridisation of the ring nitrogen being somewhere between sp\(^3\) and sp\(^2\). On the basis of the observed upfield shifts in its p.m.r. spectrum when solutions were diluted with benzene, and comparison of the O13-H coupling constants of the methyl group with that of N,N-dimethylacetamide, Moriarty and Kliegman concluded that the amido C-N bond of N-methyl-2-azetidinone has about 40% double bond character. The ultraviolet spectra of non-sterically hindered N-phenylazetidinones suggest that they have a completely planar structure. X-ray analysis of compounds (135) and (136) proved that the ring atoms and the carbonyl
oxygen were coplanar and, in the case of (136) that the N-substituent was only nine degrees out of the ring plane. Although the N-arylazetidinones mentioned above gain more delocalisation energy than N-alkyl or N-unsubstituted compounds, the conclusion must be drawn that, in the absence of unfavourable steric interactions, non-fused azetidinones adopt as a structure in which the ring atoms and the nitrogen substituent all lie in the same plane. As a consequence, the ring C-N bond has appreciable double bond character.

To assess the effects of amide resonance on 2-azetinone a study of the energy changes involved in wagging the N-H bond was undertaken, the total energies being computed using a CND0/2 program\textsuperscript{t}. Calculations of energy changes involving changing bond lengths are not particularly reliable using this method, since the errors introduced by the neglect of differential overlap are themselves sharp functions of internuclear distances. However, calculations of energy changes involving only changing bond angles are much more successful and generally reproduce stereochemistries correctly.\textsuperscript{101,102} To test the sensitivity of the procedure to the problem in hand, the ground state energy of formamide (137) was calculated using experimental bond lengths\textsuperscript{103} and a planar ground state configuration. The energy change caused by wagging the N-H(1) and N-H(2) bonds in phase was then computed. The results show a distinct minimum present at about 5° (Figure 2.1).
This initially surprising result is in fact accurate. A study of formamide using microwave spectroscopy by Costain and Dowling showed that the H₂N-C group does form a shallow pyramid with H(1) 12 degrees out of the H(3)CON plane and H(2) seven degrees out of plane.¹⁰⁴

A planar ground state geometry for azetinone (133) was computed by beginning with standard bond lengths and optimising the C-O and amido C-N bond lengths. The geometrical parameters of the final structure are presented in Table 2.1. The C-O bond length is long compared to that of formamide (1.19Å) and the amide C-N bond also long (1.40Å compared to 1.376Å). These figures probably reflect the crude nature of the optimisation and the limitations of the calculation procedure rather than having any physical significance. Wagging the N-H bond out of the plane of the ring caused considerable lowering of energy of the ground state. As shown in Figure 2.2, a minimum occurred with the N-H bond 55 degrees out of plane, this conformation being a significant 19.75 kJ mol⁻¹
FIGURE 2.1 Energy profile for wagging of the N-H bonds of formamide

FIGURE 2.2 Energy profile for wagging of the N-H bond of azetinone
lower in energy than the all planar configuration. The calculations, then, support the contention that the N-substituent of these compounds will be well out of the ring plane so that the molecule has little 4π "antiaromatic" character.

1.2 Synthesis of Photochemical Precursors to Azetinones: Stereochemical Studies

The 1,2-photoaromatization reaction appeared to hold considerable promise as an efficient route to the synthesis of 2-azetin-4-ones. Initial effort was directed to the synthesis of 1-methyl-2-azetin-4-one (166), since the N-methyl signal would provide a useful "handle" in studies using p.m.r. spectroscopy and also because of the known availability of the cyclobutene precursor (118a).

Irradiation of dilute solutions of 1-methyl-2-pyridone (114a) with a medium pressure mercury lamp through a Corex filter (λ > 250 nm) gave high yields of the internal photoaddition product, 2-methyl-2-azabicyclo[2.2.0]hex-5-en-3-one (118a) in accordance with previous reports. 68,82 Initially ether was used as solvent for all photolyses but was later replaced with ethanol to avoid the problems of dimeric and polymeric side products coating the lamp immersion well. The conversion of (114a)
to (118a) was slow; about 60 hours irradiation being required for 30 mmol scale reactions. However the high thermal stability of (118a) (prolonged heating under reflux in chloroform did not effect cycloreversion), coupled with its high dienophilic reactivity ensured the viability of the approach.

Reaction of (118a) with 2,5-dimethyl-3,4-diphenylcyclopenta-2,4-dienone (138) in refluxing chloroform gave two adducts in a 4:1 ratio. Complete reaction took only three hours which demonstrates the enhanced dienophilic reactivity of (118a) compared with (Z)-3,4-dichlorocyclobutene (142), the latter requiring two weeks for complete reaction under the same conditions. The major isomer, which could be isolated pure by fractional crystallisation was assigned exo, anti stereochemistry (see Scheme 2.1). The minor isomer could not be obtained pure by fractional crystallisation or by chromatography, but a pure sample was obtained by Jones oxidation of the corresponding bridgehead alcohol (described in detail later). It was assigned endo, anti stereochemistry (Scheme 2.1).

The stereochemistries of the adducts of the dienone (138) and two cyclobutenes have been definitely assigned. Reaction with the dichlorocyclobutene (142) yields a mixture of the exo, anti-isomer (143) and the endo, anti-isomer (144) in the ratio 4:1. This is the kinetic ratio since no interconversion of (143) and (144) has been observed under the reaction conditions. The cyclobutene (145) adds to the dienone (138)
to give the *exo*, *anti*-isomer (146) and the *endo*, *anti*-isomer (147) in the ratio 6:1.\textsuperscript{105} In the present case, the assignment of *exo*, *anti* stereochemistry to the major isomer and *endo*, *anti* stereochemistry to the minor is supported by several observations. The minor isomer undergoes facile thermal decarbonylation, in contrast to the major isomer, supporting *endo* stereochemistry of the cyclobutyl ring for the former and *exo* stereochemistry for the latter. This result is discussed more fully later.

Photochemical decarbonylation of both isomers proceeds at the same rate, and both isomers give rise to the same diene intermediate: thus they have the same stereochemistry about the cyclobutyl ring. That the disposition about this ring is in fact *anti* rather than *syn* is supported by examination of the p.m.r. spectra of *exo*, *anti* and *endo*, *anti*-(139a) (Figures 2.3 and 2.4 respectively). The assignments shown are consistent with the protons proximal to the nitrogen being at lower field. This has been established unambiguously by Eu(fod\textsubscript{3})\textsubscript{3} shift studies on bicyclic lactam (118b) and is in agreement with the observations of Paquette and coworkers.\textsuperscript{106} However Eu(fod\textsubscript{3})\textsubscript{3} studies on related compounds (see later) make the C-methyl assignments uncertain since the low field methyl is seen to move slightly faster than the high field methyl.

The use of coupling constants for the assignment of stereochemistries of four-membered rings has been the subject of some discussion. Generally *cis* vicinal coupling constants are larger than *trans* coupling constants in cyclobutanes, but the extreme limits observed (J\textsubscript{*cis*} = 4.5 to 12.0 Hz and J\textsubscript{*trans*} = 2.0 to 10.5 Hz)\textsuperscript{107,108} have meant that assignments on this basis alone cannot be made with any great assurance. Gamba and Mondelli have reported that four-bond couplings (\(4J\)) across a cyclobutyl ring provide the best means of determining stereochemistry: \(4J\) is positive when the two interacting protons are *cis* and negative when *trans*.\textsuperscript{109,110} However the sophisticated techniques these assignments require make this method of limited utility in routine work.
In the case of the cyclobutyl derivatives (140a) and (141a), vicinal coupling constants may be used with more confidence for stereochemical assignments. The wide range of values for the vicinal couplings in cyclobutyl rings is due to a large extent to the mobility of the ring and its common preference for high energy conformations. In (140a) and (141a), the cyclobutyl ring is forced to a nearly planar conformation due to both the conformationally rigid nature of the pyridine system and the 6-endo ring. Consequently, despite the overlap of the positive and negative limits of the vicinal coupling constants, cited earlier as a general rule, in (140a) and (141a), the coupling constants will be considerably larger for the proton-proton coupling constant. In both endo and exo structures, however, the H4 and H6 protons are very small and, in particular, is a sharp example, demonstrating that the stereochemistry of the cyclobutyl ring is exo. The bread sequences of the C3 and C6 protons are less informative but, significantly, they differ little in appearance from those for the same protons in the photopyridone (118a), again indicating that the H2a and H2c coupling constants are small. Although only a reduction in the coupling between the C3 and C6 protons because of the electro-negative nature of the whole nitro group might be expected, the vicinal coupling for substituted pyridones are in the range of 4-6. The small splitting between the C3 and C6 protons is evidently a function of the proton positions as the strained bridged residues of the four-membered ring.

Support for the stereochemistry of the cyclobutyl ring comes from the chemical shifts of 8.26 and 8.29 ppm for the protons of the C3 and C6 protons, respectively. These differences are too small to measure, the vicinal coupling constants.

FIGURE 2.3 P.m.r. spectrum of the exo,anti-ketone (140a)

FIGURE 2.4 P.m.r. spectrum of the endo,anti-ketone (141a)
In the case of the cyclobutyl derivatives (140a) and (141a), vicinal coupling constants may be used with more confidence for stereochemical assignments. The wide range of values for the vicinal couplings in cyclobutyl rings is due to a large extent to the mobility of this ring and its common preference for a puckered conformation.\textsuperscript{111} In (140a) and (141a) the cyclobutyl ring is constrained to planarity by its cis fusion to both the conformationally rigid bicyclo [2.2.1]heptane system and the $\beta$-lactam ring. Consequently, despite the overlap of the absolute limits of cis and trans coupling constants cited above, for compounds (140a) and (141a) cis coupling constants will be considerably larger than trans coupling constants. In both endo and exo isomers $J_{H2,H7}$ is ca 6.5 Hz whereas $J_{H3,H6}$ is smaller (the H3 and H6 resonances have a width at half peak height of ca 6 Hz). However, the couplings $J_{H2,H3}$ and $J_{H6,H7}$ are very small (H7, in particular, is a sharp doublet), demonstrating that the stereochemistry of the cyclobutyl ring is trans. The broad resonances of the C3 and C6 protons are less informative but, significantly, they differ little in appearance from those for the same protons in the photopyridone (118a), again indicating that the H2, H3 and H6, H7 coupling constants are small. Although a reduction in the coupling between the C3 and C6 protons because of the electronegative nature of the amide moiety might be expected, the vicinal cis couplings for substituted $\beta$-lactams are in the range of 4.9-5.9 Hz. Hence the small coupling between the C3 and C6 protons is evidently a function of the protons' positions at the strained bridgeheads of two four-membered rings.

Support for anti stereochemistry about the cyclobutyl ring also comes from the downfield shifts of 0.15 and 0.28 p.p.m., respectively, of the C3 and C6 protons of the endo isomer relative to the exo isomer. These differences in chemical shifts can be attributed to shielding by the carbonyl group in the exo, anti-isomer and to deshielding by the
phenyl rings in (141a).† Shifts of this magnitude would not be observed for the syn isomers (148) and (149) since the C3 and C6 protons are well removed from both the carbonyl and phenyl groups in these molecules.

Lanthanide shift reagent studies were made in an attempt to confirm the stereochemical assignments. For useful information to be obtained, the site of co-ordination needed to be at the C11 bridgehead, a position which must lead to notably different shift patterns for the exo, anti and endo, anti isomers (Figure 2.5), in addition to those for the syn isomers. Since lanthanide shift reagents are known to co-ordinate very weakly to the sterically hindered ketone bridge of adducts of 2,5-dimethyl-3,4-diphenyl-cyclopentadienone (138),¹¹²,¹¹³ the ketones (140a) and (141a) were considered unlikely to be suitable. In fact Eu(fod)₃ did complex quite strongly with these compounds, but the site of co-ordination was the lactam moiety rather than the ketone bridge (as evidenced by the difference in the rate of shift of the C-methyl substituents).

† The effect of the phenyl rings on the C3 and C6 protons of the endo, anti isomer (141) is difficult to assess since the extent to which they are out-of-plane is uncertain. Comparison of the ultraviolet spectra of adducts of the dienone (138) (λ_max 258,233 nm) with that of (Z)-stilbene (λ_max 276,231 nm) suggests that considerable orbital overlap is still present, but examination of molecular models indicates that they are ca 45° out-of-plane.
The stereochemistry of the cyclopropyl adduct (150) has been assigned by a lanthanide induced shift analysis of the alcohol derivative (151) and since alcohols are generally regarded as stronger coordinating sites for l.s.r.'s than amides it was hoped that preferential hydroxyl complexation might occur for the alcohols derived from the ketones (140a) and (141a). Reduction of isomerically pure (140a) with either sodium borohydride or lithium aluminium hydride at room temperature gave a single alcohol (152). This is consistent with exo stereochemistry for the cyclobutyl ring since it has been consistently observed that steric hindrance in exo-fused derivatives of the dienone (138) prevents attack on the carbonyl from that side. The alcohol (152) can be assigned syn, exo, anti-stereochemistry.\textsuperscript{+}

\textsuperscript{+} In the nomenclature used here the first stereochemical prefix refers to the disposition of the hydroxyl towards the cyclobutyl ring as shown below.
The p.m.r. spectrum of (152) is depicted in Figure 2.6. The assignments shown are based on the nitrogen side of the molecule generally being at lower field. The sharpening of the signal at 63.52 upon addition of D₂O to the sample solution confirmed that it was the C11 proton. The shape of the hydroxyl peak was variable: in one sample coupling (J \( \approx 3.5 \text{ Hz} \)) with the C11 proton was observed along with a corresponding broadening of the coupled proton. It is notable that, relative to the ketone (140a), the C3 and C6 protons of (152) are downfield by 0.39 and 0.32 ppm respectively, suggesting that, in (140a), these protons are considerably shielded due to their proximity to the carbonyl group. No "W" coupling between the C2 and C11 protons is observable.

FIGURE 2.6 P.m.r. spectrum of the \( \text{exo,anti-} \text{alcohol(152)} \)
The results of the addition of Eu(fod)₃ to the alcohol (152) are shown in Figure 2.7. The slow rate of shift of the hydroxyl proton indicates negligible coordination to this site and consequently the results are of little value. The chemo-structural assignments made previously to acids is shown to occur preferentially at the oxygen atom by the relative shifts we confine the proton assignments to alcohols. Although two alcohols shift reagents generally complex with alcohols, the use of a reference to acids, it is evident in this case that the spectrally unfavourable orientation of the hydroxyl hydrogen to outweighs this consideration.

The reduction of the ketone by the sodium borohydride (151) of compound (150) is in agreement with the reported formation of two alcohols in the ratio 2:1 by sodium borohydride reduction of the keto-ketone (155). The relative intensity of the CH₃ at C8 and C1 methyl groups of (153) and (154) were in keeping with the mono-ketone NHMe group of (152) and the alkyl groups of (152) and (155) were minor. The formation of Eu(fod)₃ adducts to the two alcohols could not be made.

FIGURE 2.7 Addition of Eu(fod)₃ to the exo,anti-alcohol (152)
The results of the addition of Eu(fod)$_3$ to the alcohol (152) are shown in Figure 2.7. The slow rate of shift of the hydroxyl proton indicates negligible co-ordination to this site and consequently the results are of little value for stereochemical assignment. Since co-ordination to amides is known to occur preferentially at the oxygen atom, the relative shifts do confirm the proton assignments previously made and enable assignment of the C-methyl groups. Although lanthanide shift reagents generally complex with alcohols in preference to amides, it is evident in this case that the sterically unfavourable disposition of the hydroxyl function in (152) outweighs this consideration.

The reduction of a mixture of the isomeric ketones (140a) and (141a) gave, in addition to the syn, exo, anti-alcohol (152) derived from (140a), two other alcohols (153) and (154). Preparative layer chromatography of the reduction product gave (152) pure but did not separate (153) and (154). The p.m.r. signals of (153) and (154) were almost coincident, but the addition of Eu(fod)$_3$ confirmed that two compounds were in fact present, since they shifted at considerably different rates. Comparison of the shifts of those signals which could be identified showed clearly that, for both compounds, complexation was occurring at both the hydroxyl and amide carbonyl. The complexity was such that assignments to the two epimers could not be made. The formation of two alcohols from the endo-ketone (141a) is in agreement with the reported formation of two alcohols in the ratio 1:1 by sodium borohydride reduction of the endo-ketone (155). The oxidation of a mixture of (153) and (154) with Jones' reagent gave a pure sample of the endo, anti-ketone (141a) which confirmed that these two alcohols were in fact syn- and anti-alcohols derived from the same ketone. This procedure

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† The Eu(fod)$_3$ studies were carried out on a recrystallised sample which comprised a 2:1 ratio of epimers, with the major isomer having the larger C-methyl and N-methyl shifts. The ratio in which (151) and (152) were originally formed was not determined.
of chromatographic separation of the \textit{exo}- and \textit{endo}-alcohols and re-oxidation of the \textit{endo}-alcohol mixture constitutes the only means of obtaining pure (141a).

The N-H and N-phenyl ketones, (139b) and (139c) have also been prepared by the route shown in Scheme 2.1. Photolysis of 2-pyridone (114b) has been reported to give a 15\% yield of 2-azabicyclo[2.2.0]hex-5-en-3-one (118b) when a pyrex filter is employed,\textsuperscript{85} but it has been found that a Corex filter gives much better yields (60-70\%), with reduced irradiation time. As mentioned previously, the proton assignments in the p.m.r. spectrum of the photo-pyridone (118b) were established by Eu(fod)\textsubscript{3} studies. The upfield bridgehead and olefinic resonances were found to have the higher \textit{AEu} values, identifying them as the C4 and C5 protons respectively (Figure 2.8).

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure2.8.png}
\caption{The addition of photo-pyridone (118b) to the dienone (138) was less stereospecific than that of the corresponding N-methyl compound (118a), giving the \textit{exo}, \textit{anti}- and \textit{endo}, \textit{anti}-adducts (140b) and (141b) in the ratio 2:1. The p.m.r. spectra of (140b) and (141b) closely resembled those of the N-methyl adducts (140a) and (141a). The formation of (140a) by methylation of (140b) with sodium hydride and dimethyl sulphate in dimethylformamide confirmed that these compounds had the same stereochemistry.}
\end{figure}
1-Phenyl-2-pyridone (114c) had been reported to be formed when the sodium salt of 2-pyridone, iodobenzene and activated copper catalyst were heated together in a Wood's metal bath, but this procedure proved unsatisfactory. A better method involved refluxing the same materials in dimethylformamide which gave a 33% yield of product. Photolysis of the pyridone (114c) gave only low yields of the photoisomer (118c) which reacted with the dienone (138) to give the exo, anti- and endo, anti-adducts (140c) and (141c). These isomers could not be separated and photochemical experiments were carried out using a 1:1 mixture of (140c) and (141c). Comparison of samples with different isomer ratios enabled full p.m.r. assignments to both compounds to be made.

Warrener has argued that the preferential exo addition of 2,5-dimethyl-3,4-diphenylcyclopenta-2,4-dienone (138) to (Z)-3,4-dichlorocyclobutene (142) is due to the secondary orbital stabilisation arising from interaction with the non-bonding orbitals of the chlorine atom being insufficient to overcome the unfavourable steric interaction of the 3,4-substituents in the dienone (138). Recently Jones demonstrated the effect that the out-of-plane phenyls of (138) have on the stereochemistry of addition by comparison with the fused dienone (156), in which the phenyl groups are constrained to planarity. Addition of (156) to the cyclobutene (145) gave an exo:endo ratio of ca 2:1 in comparison to the 6:1 ratio previously observed for the addition of (138) to the same dienophile. These results stand in contrast to the assertions of Houk that only secondary orbital interactions between unsaturated centres and van der Waals repulsions between saturated
centres are of general significance in determining the stereoselectivity of Diels-Alder reactions.  

The additions of 2-azabicyclo[2.2.0]hex-5-en-3-one derivatives reinforce the importance of consideration of steric interactions in the addition of dienophiles to the dienone (138). The orbitals of the amide moiety of the cyclobutene lactams (118a-c) have the capacity for strong secondary interaction, yet *endo* addition is strongly disfavoured for steric reasons. If the four possible modes of attack, presented in Scheme 2.2, are considered, it can be seen that attack on the more hindered face of the cyclobutene is sterically unfavourable, particularly in the *endo, syn* case, although this orientation allows maximum orbital overlap. That the *endo, anti* orientation, although preferred to the *syn* orientations, is still much less favourable than the *exo, anti* reiterates that mere consideration of secondary orbital interactions in the reactions of the dienone (138) is insufficient.
The desirability of obtaining azetinone precursors with a chromophore absorbing appreciably at wavelengths greater than 300 nm in order that a pyrex filter might be employed in photolyses led to an attempt to synthesise compounds (157) and (160) in the manner depicted in Scheme 2.3. The reaction of (118a) with tetrachloro-\(o\)-benzoquinone

\[
\text{Cl} \quad \text{Cl} \quad \text{Cl} \quad \text{Cl} \quad + \quad \begin{array}{c}
\text{Cl} \\
\text{Cl}
\end{array} \quad \begin{array}{c}
\text{R} = \text{Me}
\end{array}
\]

(118)

(157)

\[
\text{Cl} \quad \text{Cl} \quad \text{Cl} \quad \text{Cl} \quad \text{Me}
\]

(118a) (159a)

\[
\text{Cl} \quad \text{Cl} \quad \text{Cl} \quad \text{Cl} \quad \text{H}
\]

(118b) (159b)

\[
\text{Cl} \quad \text{Cl} \quad \text{Cl} \quad \text{Cl}
\]

(161)

\[
\text{Cl} \quad \text{Cl} \quad \text{Cl} \quad \text{Cl}
\]

(163)

\[
\text{Cl} \quad \text{Cl} \quad \text{Cl} \quad \text{Cl}
\]

(162)

\[
\text{Cl} \quad \text{Cl} \quad \text{Cl} \quad \text{Cl}
\]

(164)

\[
\begin{array}{c}
\text{MeO} \quad \text{OMe}
\end{array}
\]

\[
\begin{array}{c}
\text{MeO} \quad \text{OMe}
\end{array}
\]

\[
\begin{array}{c}
\text{MeO} \quad \text{OMe}
\end{array}
\]

\[
\begin{array}{c}
\text{MeO} \quad \text{OMe}
\end{array}
\]

in refluxing benzene gave 1-methyl-2-pyridone, formed by thermal ring opening of (118a), as the only detectable product. Both (118a) and (118b) added readily to the diene (158) with complete stereospecificity to give adducts (159a) and (159b) which have been assigned \textit{endo,anti} stereochemistry. This is consistent with the reported formation of the \textit{endo,anti-}

adduct (161) by the reaction of the cyclobutene (145) with (158).

Nenitzescu and coworkers reported that (Z)-3,4-dichlorocyclobutene (142) gave the \textit{endo, syn}-adduct (162) by analogy with the reaction of (142) with cyclopentadiene to give the \textit{endo, syn}-adduct (164). A later report claimed the \textit{endo, anti} structure (163) for the same product. No arguments in favour of this stereochemistry were presented but, by consideration of the very unfavourable steric approach giving rise to (162), (163) is almost certainly the correct structure.
Mechanistically, *exo* approach to the dimethoxy diene (158) can be ruled out by the unfavourable steric interaction with the lower bridge methoxyl (see Scheme 2.2; R₁ = OMe, R₂ = R₃ = Cl). Steric interaction between the β-chloro substituents and the amide make *endo*,*syn-* less favoured than *endo*,*anti-* approach. Again the *anti* disposition about the cyclobutyl ring is supported by the p.m.r. spectra of the adducts (159a) and (159b). The C2 and C7 protons are strongly coupled (J ca 6.5 Hz) but there is little or no vicinal coupling between the C2, C3 and C6, C7 proton pairs.

The formation of (160b) by deketalisation of (159b) was not successful. When a two phase system of concentrated sulphuric acid and dichloromethane¹²⁵ was employed an unidentified ketal, believed to be derived from acid-catalysed hydrolysis of the β-lactam ring during workup, was obtained, whilst less acidic conditions, including glacial acetic acid, resulted in the quantitative recovery of (159b).

2.3 Photochemistry

Photolysis of the ketone (139a) gave clean decarbonylation resulting in a small steady state concentration of the intermediate diene (165). The diene photoaromatised at a comparable rate to give near quantitative yields of 1,4-dimethyl-2,3-diphenylbenzene (92) and, presumably, the azetinone fragment (166). The results of a low temperature photolysis of (139a) in deuteriochloroform as solvent using a vycor filtered low pressure mercury lamp are shown in Figure 2.9. The solution, in a sealed vycor nmr tube insert, was maintained below -30°. The singlet at δ 1.54 was assigned to the C-methyls of the diene (165) which are
coincidentally equivalent. This compound could be isolated by preparative layer chromatography of incomplete photolysis mixtures and was characterised fully as its N-phenyltriazolinedione adduct (209). The reaction proceeded smoothly but no signals attributable to 1-methyl-2-azetin-4-one (166) or products derived therefrom could be observed. Particularly, the complete absence of signals in the $\delta$ 5.0 to $\delta$ 6.6 region indicated that (166) was not stable under these conditions.

![FIGURE 2.9 Low temperature photolysis of (139a)](image)

Attempts were made to trap the azetinone by cycloaddition reactions. Photolysis of the ketone (139a) in furan at temperatures ranging from $-30^\circ$ to $10^\circ$ led to clean 1,2-photoaromatisation, but only low yields of azetinone derived products were obtained. The major photolysis product was unstable under the chromatography conditions employed and could not be isolated. The presence of an N-methyl doublet ($J\alpha 4$ Hz) at $\delta$ 2.92 and a broad singlet at $\alpha\delta 5.7$ in the p.m.r. spectrum of the crude photolysate indicated that the product forming was the 3-substituted furan (169), rather than either of the anticipated Diels-Alder adducts (167)
and (168). The formation of (169) is consistent with the observation of

(167)

Burgess and Milne that the photochemical generation of N-phenylbenzazetin-
one (33a) in furan leads to the formation of the analogous substituted
furan (170).

The reported trapping of the thermally unstable oxete (171) by

[2 + 2] cycloaddition of benzaldehyde triplet to give the fused oxetane
(172) prompted us to attempt a similar trapping of the azetinone (166).

Photolysis of the ketone (139a) and a slight excess of benzaldehyde in
tetrahydrofuran at -65° gave complete consumption of both compounds and
produced a complex mixture of at least nine compounds as judged by t.l.c.
analysis. Since the quantities involved were prohibitively small, this
approach was not pursued further.

These results led us to suspect that the azetinone (166) was
undergoing a very facile \([2 + 2]\) ring opening to the reactive imino
ketene (182) (Scheme 2.5). The loss of signals in the low temperature
deuteriochloroform photolysis, best explained by polymerisation of this
intermediate under the high concentrations required for p.m.r. work, and
the failure to trap (166) both support this view. This behaviour
parallels that of closely related compounds. The cyclobutenones (173a) and (173b)
undergo facile photochemical ring opening to the vinyl
ketenes (174a and b), the former ketene being trapped as the methanol
adduct (175a). The photolysis of N-substituted benzo-1,2,3-triazinones,
particularly the N-phenyl compound (32a), has been studied in detail. Both Burgess and Milne\textsuperscript{26} and Ege\textsuperscript{44} found independently that the photolysis of (32a) led to acridone in neutral solution and anthranilic acid derivatives (179) in the presence of nucleophiles. One important difference was in the mechanisms proposed by the two groups. Burgess and Milne proposed initial cleavage A (Scheme 2.4) to give the intermediate (177) based on the small amount of ester (178) they obtained by rapid quenching of a photolysate with methanol. They then proposed loss of nitrogen to give the ketene (64a) which is in rapid equilibrium with the benzazetinone (33a). Infrared spectroscopy studies led these workers to conclude that the formation of acridone (180) was slow in comparison to the rate of equilibration of (33a) and 64a) in which the azetinone (33a) was predominant at room temperature. However, the N-N bond cleavage (cleavage B) proposed by Ege, and subsequently proven correct by $^{15}$N
labelling studies\textsuperscript{129} establishes the azetinone (33a) as the primary product which then undergoes rapid photochemical cleavage to give the tautomeric ketene (64a). This distinction is important because it implicates (33a) as an intermediate which rapidly ring opens. The thermally stable naphthazetinone (35a) underwent photochemical ring opening and cyclisation to benzo[\textit{d}]acridone (181).\textsuperscript{28}

\[
\begin{align*}
\text{(35a)} & \xrightarrow{hv} \text{(64a)} \\
\text{(181)}
\end{align*}
\]

As anticipated then, photolysis of the ketone (139a) in methanol or methanol-tetrahydrofuran mixtures over a temperature range of $-60^\circ$ to $0^\circ$ led to the formation of the ($\text{E}$)- and ($\text{Z}$)-3-methylaminoacrylic acid methyl esters, (183) and (184) respectively, in the ratio 1.2:1.

\[
\begin{align*}
\text{(166)} & \xrightarrow{MeOH} \text{MeOH} \quad + \\
\text{(182)} & \quad \text{(183)} \quad \text{(184)}
\end{align*}
\]

Mechanism 1

\[
\begin{align*}
\text{(186)} & \xrightarrow{H-tN} \text{1,3 H shift} \quad \text{(187)} \\
\end{align*}
\]

Mechanism 3

However, when a solution of the ketone (139a) in tetrahydrofuran was
irradiated at -60°, and then quenched with a large excess of methanol and allowed to warm to room temperature no detectable amounts of the esters (183) and (184) were formed. Clearly then, methanol is adding to a species unstable even at -60°.

Three mechanisms which can account for the products observed are shown in Scheme 2.5. Direct addition of methanol to the azetinone (166) (Mechanism 1) must be considered since there are precedents for this. The benzazetinones (33) are both thermally stable at room temperature, but are very reactive towards nucleophiles.³⁰,²⁹ Both Mechanism 1 and 

Mechanism 2, which involves a one-step addition to the imino ketene (182), are not favoured because they lead to the (Z)-isomer (183) as the only primary product. The stepwise addition of methanol to the ketene (182) to give the imine (187), followed by a 1,3 hydrogen shift, either as a photochemically allowed 1,3-sigmatropic shift or by radical abstraction (Mechanism 3), gives an equimolar mixture of (Z) and (E) isomers and is therefore the favoured mechanism.

That the (Z):(E) ratio observed was not a photostationary state obtained by photochemical isomerisation of the initially formed (Z)-ester (183) was confirmed by photolysis of an almost pure sample of (183) ((Z):(E) = 11:1) in perdeuteriomethanol at -30°. After two hours (the usual photolysis time for small scale irradiations of the ketone (139a)) the (Z):(E) ratio was still 3:1 and the photoequilibrium of 2.3:1 was only achieved after 4.5 hours irradiation. Olefin (Z)-(E) isomerisations are known to be triplet sensitised¹³⁰ and the possibility that the o-terphenyl (92) acts as a sensitiser in this case has not been investigated. However the consistency with which the same isomer ratio was
obtained renders this unlikely. Although the \((z)\)-isomer (183) slowly isomerised to the \((E)\)-isomer at room temperature the rate of conversion was much too slow to be significant in this work.

The samples of \((z)\) and \((E)\) acrylic esters (183) and (184) used in these experiments were obtained by the Michael addition of methylamine to methyl propiolate at room temperature. A pure sample of the \((z)\)-isomer was obtained by distillation of the crude isomer mixture. Pure \((E)\)-isomer was obtained by letting isomer mixtures stand for prolonged periods, complete conversion being noted after four months.

Photolysis at \(-10^\circ\) of the ketone (139a) in tetrahydrofuran saturated with methylamine led to the formation of \((z)\)- and \((E)\)-3-methylamino-N-methylacrylamide (185) and (186) in the same ratio as the isomers derived from the addition of methanol \((z):(E) = 1.2:1\). The isomer ratios were readily obtained from the relative peak heights of the C2 proton doublets at \(\delta 4.24\) (\(J = 7.5\) Hz) and \(\delta 4.55\) (\(J = 13.0\) Hz) respectively, in the pmr spectrum. The structures were confirmed by unambiguous synthesis. The low temperature reaction of methylamine with methyl propiolate (188) gave N-methylpropiolamide (189),\(^{131}\) (in contrast to the room temperature reaction which gives exclusively the Michael addition product) which reacted slowly at room temperature with excess methylamine to yield an isomeric mixture of acrylamides (185) and (186). The photolysis of (139a) in the presence of methylamine also yielded appreciable quantities of an unidentified product which was isolated partly pure by preparative layer chromatography. Its p.m.r. spectrum indicated that it was derived from methylamine attack on (139a) since the slightly resolved singlets at \(\delta 1.21\) were characteristic of the
general structure (190). No attempt was made to purify and characterise the compound but it is notable that this is the only instance for the reactions studied in which quantitative decarbonylation and photo-aromatisation does not occur.

2-Azetin-4-one (191) exhibited a similar propensity to undergo facile ring opening. No products apart from the aromatic fragment (92) could be observed upon irradiation of solutions of the ketone (139b) in non-nucleophilic media. However, the photolysis of (139b) in methanol

$$\text{HC} = \text{C}-\text{CO}_2\text{Me} + \text{NH}_3$$

(188)

tetrahydrofuran solution gave high yields of (E)- and (Z)-3-aminoacrylic acid methyl esters, (193) and (194). These compounds were not isolated pure from the small scale experiments performed, but structural confirmation came from their p.m.r. spectra which were indistinguishable from those of the isomers prepared by the addition of ammonia to methyl propiolate (188).

The imino ketene (64a) tautomeric with N-phenylbenzazetinone (33a) has been implicated in a number of thermal and photochemical reactions. In the absence of nucleophiles this species generally undergoes rearrangement to acridone (180). It was anticipated, therefore, that photolysis of the N-phenyl ketone (139c) should result in the formation of 4-quinolone (197) by cyclisation of the transient N-phenyl ketene (196). However, no (197), nor any other azetinone derived product was observed by p.m.r. spectroscopy when a deuteriochloroform solution of (139c) in a quartz tube was irradiated, although the formation
of the aromatic fragment (92) indicated that clean 1,2-photoaromatisation was proceeding. It seems likely that the high concentrations necessary for direct monitoring of the reaction by p.m.r. spectroscopy led to intermolecular reaction of the intermediate ketene (196) and subsequent polymerisation.

These results leave little doubt that the 2-azetinone (198) is forming and rapidly ring opening to the tautomeric imino ketene (199). The possibility that the ring opening proceeds thermally is unlikely in view of the previously mentioned failure to trap adducts derived from either N-methylazetinone (166) or its ring-opened tautomer (182) by methanol quenching at -60°. Ring opening then, can be assumed to be photochemical, and probably a concerted conrotatory process. Although only polymeric products are obtained in the absence of an efficient trapping agent, the mechanism for their formation remains unknown. Polymerisation of (199) may occur directly, but the possibility still exists for the rapid establishment of an equilibrium between (198) and (199), with a further slow irreversible elimination of carbon monoxide, either from (198) to yield the diradical species (200), or from (199) to give the carbene (201). Both (200) and (201) could then cyclise to the azirine (202), a "hot" molecule which would rapidly undergo further reaction.
There are some precedents for this behaviour; for example, low yields of 3,3-dichloro-1,2-diphenylcyclopropenone (204) are formed by photolysis of the cyclobutenone (203). However, in contrast to cyclobutanone, for which cycloreversion, decarbonylation and cyclo-expansion have been observed, the photolysis of 1-aryl-2-azetidinones (205) gives only cycloreversion products, as shown in Scheme 2.6. Similarly the photolysis of azetidin-2,4-diones generally did not give products derived from the loss of carbon monoxide. These results...
suggest that photodecarbonylation is not a favoured process for β-lactams.

In view of the difficulty of resolving the ultimate fate of the azetinones, it was decided that further study of the photochemistry of these compounds should await the completion of the matrix photolysis facilities currently being developed in these laboratories. The generation of 2-azetin-4-one under these conditions will be free from the complications of thermal reactions and should enable the direct observation of both azetinone and its ring-opened tautomer. Further, any loss of carbon monoxide under these conditions would produce azirine (202), a molecule long sought because of its potential anti-aromatic character.

2.4 Thermal Studies

Introduction

In addition to the stereochemical and mechanistic insights gained from a study of the thermal decarbonylation of 1,4,8-trimethyl-9,10-
diphenyl-4-azatetracyclo[6.2.1.0²⁷.0³.⁶]undec-9-ene-5,11-dione (139a), results in this area suggested that compounds derived from the Diels-Alder addition of potential dienes to 2-azabicyclo[2.2.0]hex-5-enes could provide a novel entry to the aza-(CH)₁₀ energy surface. By 1972 20 (CH)₁₀ isomers had been characterised;¹³⁷ apart from the intrinsic interest many of these compounds hold, their multitudinous thermal and photochemical rearrangements (which have been the subject of two comprehensive reviews¹³⁷,¹³⁸) have provided a stimulating area for new mechanistic insights.† In contrast, study of the aza analogues of these compounds has languished despite Paquette's synthesis of the azabullvalene (206) by the sequence shown in Scheme 2.7¹⁴⁰,¹⁴¹ and the discovery that this compound, like bullvalene itself, undergoes facile degenerate rearrangement.¹⁴⁰,¹⁴² Hence the work presented in the latter part of this section represents only a brief

![Scheme 2.7](image)

start towards an area strictly beyond the confines of this thesis.

Results and Discussion

The pyrolysis of melts of the αααα, anti-ketone (140a) or a

† See, for example, ref. 139.
mixture of the isomers (140a) and (141a) gave, not only the anticipated diene (165), but also the isomeric triene (207) in the ratio 1:4 (Scheme 2.8). The thermally produced diene (165) had an identical p.m.r. spectrum to that of the diene intermediate in photolyses of (140a) and (141a). The isomers (165) and (207) could not be separated by chromatographic methods, but the addition of N-phenyltriazolinedione (208) at 0° to mixtures of the two led to the formation of the Diels-Alder adduct (209) from (165) but not from (207). This confirmed that (165) and (207) were not in equilibrium at this temperature. The structure of the adduct (209) followed from its p.m.r. spectrum, which showed the cyclobutyl proton pattern characteristic of these systems, and its infrared spectrum, which had a strong carbonyl absorption at 1752 cm⁻¹ confirming that the β-lactam ring was still intact. The triene (207) was obtained by preparative layer chromatography of the residue after the diene (165) had been converted to the adduct (209). It could not be induced to crystallise and an analytically pure sample could not be obtained. The structural assignment followed from the infrared spectrum (carbonyl absorption at (1746 cm⁻¹) and the p.m.r. spectrum. The C-methyls, which were shifted downfield relative to their positions in the diene (165), appeared as doublets of doublets due to allylic coupling with the C2 and C7 protons (present as broadened quartets) and homoallylic coupling with the C1 and C8 bridgehead protons. The proton assignments were confirmed by lanthanide
induced shift studies, the relative shifts being shown in Figure 2.10. Like the alcohol (152), the downfield C-methyl was the faster moving, suggesting that it is the C3-methyl rather than the C6-methyl as might be expected from their relative proximities to the nitrogen atom.

![Chemical Shift Graph](image)

**FIGURE 2.10**

The results of the thermolysis of a 1:1 mixture of the isomers (140a) and (141a) in dimethyl sulphoxide-\(d_6\) at 160° are shown in Figure 2.11. If the DMSO-\(d_5\) absorption is used as an internal marker, it can be seen that even after 15 minutes 50% decomposition of the *endo* isomer (141a) had occurred, whilst almost none of the *exo* isomer (140a) had decomposed. After 45 minutes decarbonylation of the *endo*-isomer was complete whilst even after 165 minutes the *exo*-isomer was less than 50% decomposed. Significantly, after 15 minutes, the diene (165) was the major product with only a small amount of the triene (207) present. After 45 minutes the proportions were reversed with (207) present as the major product. These results establish definitely that the diene (165) is the primary product which then undergoes disrotatory ring opening to (207).
These observations pertain directly to the question of edge participation of small rings. The thermal elimination of carbon monoxide from systems containing a proximate cyclopropyl group is much faster than in analogous non-fused systems or those containing an enone-fused group. For example, the exo-anti isomer (210) has a half-life of 82 min at 150°, while the endo-anti isomer (211) has a half-life of only 57 min at 150°. This marked difference is not explained by the favourable overlap present between the Walsh orbitals of the cyclopropyl ring and the sigma bonds attached to the leaving group in a concerted process involving the 144° of carbon monoxide and leaving group. The cyclopropyl bond, resulting in the scission of the cyclopropyl ring, is not involved in the process. However, in the endo-anti isomer, the 144° overlap does not occur. The effective overlap is 144° and the isomer is probably eliminated by an alternative process. The isomer (211) probably involves intermediate formation of aziridines (213), which then decompose to (214). Similar results have been obtained in the rate of cyclopropyl nitrene elimination (144, 145). An endo-anti isomer of a system of the type in (215) may be eliminated by a concerted process involving conjugation of the exo-anti isomer at the developing carbon-nitrogen centre.

Although the bent bond character of cyclopropane is considerably less than cyclopropane (146, 147) edge participation is still observed in such cyclopropyl systems, both in solvolysis (146, 148, 155) and thermal elimination (156, 157, 158, 192, 193). However, the question of whether cyclopropyl participation is necessary to the elimination of the aziridine (215) decomposed factum is still open. If this aziridine decomposed factum is still open. If this aziridine is eliminated, it must be eliminated by simultaneous sigma bond cleavage, i.e., cyclopropene (216), and to the conclusion that elimination of nitrogen was occurring by a radical.

**FIGURE 2.11** Thermolysis of _exo,anti_-isomer (140a) and _endo,anti_-isomer (141a) at 160°
These observations pertain directly to the question of edge participation of small rings. The rate of thermal elimination of carbon monoxide from systems containing a proximate endo cyclopropyl group is much greater than from non-fused systems or those containing an exo fused group. For example the exo-ketone (210) has a half-life of 82 minutes at 150°, whilst the endo-isomer (211) has a half-life of only 89 minutes at 35°. The enhancements observed are explained by the favourable overlap present between the Walsh orbitals of the cyclopropyl ring and the sigma bonds attached to the leaving group. Thus a concerted process involving simultaneous loss of carbon monoxide and breaking of the cyclopropyl bond, resulting in direct formation of cycloheptatriene (213), is implicated. No participation in systems with exo stereochemistry is noted because the orbitals do not overlap. The less favourable process of decarbonylation of (210) probably involves intermediate formation of norcaradiene (212) which then opens to (213).

Similar dramatic enhancements in the rate of cheletropic nitrogen elimination and of solvolysis of systems of the type (214) with the leaving group anti to the cyclopropyl ring have been observed. The latter is attributed to cyclopropyl edge participation at the developing carbonium ion centre.

Although the bent bonding character of cyclobutane is considerably less than cyclopropane edge participation is still observed in endo cyclobutyl systems, both in solvolyses and thermal eliminations. However the question of whether cyclobutyl participation involves necessary simultaneous sigma bond cleavage has remained contentious. The azo compound (215) decomposed faster than (219) by a factor of 10^4 but the detection of small amounts of tricyclooctane (217), in addition to the product which would be formed by simultaneous sigma bond cleavage, 1,5-cyclooctadiene (218), led to the conclusion that elimination of nitrogen was occurring by a radical
mechanism and that the observed acceleration was due to relief of steric strain. However Berson and coworkers have demonstrated that the loss of nitrogen from isomers (220) and (221) is stereospecific in the mode of an allowed concerted reaction. Further, no ring closed products were observed. The solvolysis of both the brosylate (222) and the tosylate (223) led to extensively rearranged products indicative of concomitant cyclobutyl sigma bond cleavage. In contrast, the carbonium ion (224), although considerably stabilised by interaction between the cyclobutyl sigma orbitals and the orbitals of the bridge carbon, formed the unrearranged ketal (225) upon addition of ethanol.

Isolated examples of cyclobutyl edge participation in the elimination of carbon monoxide are known. Battiste and coworkers reported that the endo-ketone (226) decarbonylated at 90-100° whilst the exo-isomer (227) required heating to 150°. McCay and Warrener found that the endo-isomer (144) decarbonylated to give the diene (231) at 135°, in comparison to the exo-isomer (143) which was stable at that temperature. However, as pointed out by McCay, this result still left open the question of whether cyclobutyl participation in decarbonylation...
tion involves sigma bond cleavage, since the facile isomerisation of triene (230) to diene (231) would preclude its observation even if it were the primary product. Similarly, the diene (229) would not be observed if formed in the thermolysis of (226).

The results of the thermolysis of ketones (140a) and (141a) are unique in that both products formed by the two possible modes of cleavage are sufficiently stable under the reaction conditions to make possible the unequivocal assignment of the primary thermolysis product. Significantly then, elimination of carbon monoxide from the endo-isomer (141a) is assisted by cyclobutyl sigma orbital interaction but this does not involve breakage of the sigma bond.

The results obtained with the tetrasubstituted ring system (165) prompted attempts to synthesise precursors to the unsubstituted diene (237), in order that the thermal rearrangements of this compound and its isomers might be further studied. This was conveniently achieved by the addition of 2-pyrone to photopyridone (118b) and subsequent decarboxylation of the lactone adducts (235) and (236).

2-Pyrone (232) was chosen as diene in preference to cyclopentadienone\textsuperscript{157} and its diethyl ketal\textsuperscript{158} because of its relative stability and ease of preparation.\textsuperscript{159} Adducts of (232) are known to decarboxylate smoothly at 160°C to give the corresponding dienes\textsuperscript{160,161} and the addition of 2-pyrone to the cyclobutene (233) had been reported.\textsuperscript{161} The adduct (234)
presumably having the stereochemistry depicted.

As expected then, 2-pyrone reacted with photopyridone (118b), although complete reaction at 60° required three days. The reaction was remarkable for the lack of either regioselectivity or stereoselectivity governing product formation and yielded a complex mixture of products. Combined preparative layer chromatography and column chromatography afforded five isomers out of the eight possible (see Scheme 2.9) either fully or partially separated. The p.m.r. spectra of these isomers are presented in Figure 2.12. The only proton assignments that could be

+ The numbering of the isomers refers to their order of chromatographic eluted. Thus, isomer 1 was eluted first and isomer 5 last.
FIGURE 2.12  P.m.r. spectra of isomers of 4-aza-9(10)-oxatetra-cyclo[6.2.2.0^2,7.0^3,6]dodec-11-ene-5,10(9)-dione [(235) and (236)]

2.12(a) Isomers 1 and 2

2.12(b) Isomer 2
2.12(c) Isomer \( \delta \)

2.12(d) Isomer \( \delta \)

FIGURE 2.12 (Continued)
Support for the gross structures of the mixture of isomers X and Y comes from the following spectroscopic data. The ultraviolet spectrum shows an absorption at 293 nm (ε = 1400) only, consistent with the absence of conjugation, whereas the infrared spectrum shows a broad absorption at 3205 cm⁻¹ (N-H stretching) and a strong, complex absorption at 1690 cm⁻¹ (γ-lactam and γ-lactone). In the nmr spectrum, a weak multiplet is seen at δ 1.51, in addition to the usual bands for the tetracyclic system.

FIGURE 2.12 (Continued)

2.12(e) Isomer 5

FIGURE 2.13 P.m.r. spectrum of 9-azabicyclo[6.2.0]deca-2,4,6-trien-10-one (238)
made with certainty were the broad singlets at $\delta$ 7.0-7.2 to the proton attached to nitrogen, the multiplet at $\alpha\alpha$ $\delta$ 6.6 to the vinyl protons and the multiplet at $\alpha\alpha$ $\delta$ 5.4 to the proton alpha to the lactone oxygen. Support for the gross structures of the mixture of isomers 1 and 2 came from the following spectral data. The ultraviolet spectrum showed end absorption ($\lambda_{\text{max}}$ 210 nm, $\varepsilon$ 1450) only, consistent with the absence of conjugation, whilst the infrared spectrum showed a broad absorption at 3205 cm$^{-1}$ (N-H stretch) and a strong carbonyl absorption at 1755 cm$^{-1}$ ($\beta$-lactam and $\delta$-lactone). The mass spectrum showed a weak molecular ion at m/e 191, in addition to strong peaks at 78 (benzene), 104 (cyclooctatetraene) and 69 (azetinone).

No assignments of either structure or stereochemistry have been made to any of the adducts due to the difficulty of completely analysing the p.m.r. spectra of these compounds. At this stage, confident assignments would appear to demand X-ray crystallography.

Both steric factors and the secondary orbital interaction possible between the amide orbitals and the diene molecular orbitals suggest that endo addition of photopyridone (118b) to the diene (232) should be favoured over exo addition. Further, the rather rare phenomenon of syn addition (approach at the more hindered face of the cyclobutene) could also be favoured here because of the better orbital mixing it allows. This is consistent with the observation of Nenitzescu and coworkers$^{123}$ that the addition of (Z)-3,4-dichlorocyclobutene (142) to cyclopentadiene gives the endo, syn isomer (164).

The decomposition of a mixture of isomers 1 and 2 in vacuo at 175°C gave, after chromatography, what appeared to be a mixture of the diene...
(237) and the triene (238) in the ratio 1:3. The triene (238) was obtained pure from this mixture by recrystallisation. The structure of this compound was established definitely by the following data. The ultraviolet spectrum ($\lambda_{\text{max}}$ 243 nm, $\epsilon$ 1700) compared closely to that of (239) ($\lambda_{\text{max}}$ 250 nm, $\epsilon$ 2090)$^{162}$ and the carbonyl absorption at 1742 cm$^{-1}$ in the infrared spectrum confirmed the presence of the $\beta$-lactam ring. The p.m.r. spectrum, which is depicted in Figure 2.13, and the mass spectrum were also in agreement with the assigned structure. Attempts to trap the diene (237) as its N-phenyltriazolinedione adduct were not successful, but the presence of (237) in the mixture was inferred by multiplets at $\delta$ 3.22, 3.64 and 5.64 in the p.m.r. spectrum. The upfield signals can be attributed to three of the cyclobutyl protons, whilst the other proton is obscured by the triene resonance at $\delta$ 3.96. However, definite confirmation still awaits the isolation of this compound.

Some preliminary solution thermolysis studies were carried out on a mixture of isomers 1 and 2 in DMSO-$d_6$ solution. Some typical results are depicted in Figure 2.14. Decarbonylation occurred to yield the triene (238) at temperatures as low as 100°. At higher temperatures both the lactones and the initially formed triene (238) decomposed rapidly to give unidentified products.

The facile loss of carbon dioxide from isomers 1 and 2 suggests that they may be endo-isomers in which cyclobutyl edge participation is occurring but, from consideration of the orbital diagrams in Figure 2.15, it is likely that the cyclobutyl sigma orbitals are not favourably disposed for overlap with the breaking sigma bonds. The results obtained do not allow any definite conclusions to be drawn concerning the timing
Attempts were made to prepare either the endo isomer (249) or exo isomer (241) model of 1,2-cyclopentanedione (250) and the enantiomers (182) to a suitable model compound for the study. But these were illustrated by the failure of the same isolation attempts as noted when a mixture of the trans isomers 1 and 2 was heated under reflux in a dilute solution of anthracene (251) in benzene. In the present case, the melting points and spectral data of this compound positively identified it as being a trans-cyclopentane-1,2-dione (252). The other products were not isolated, and no related isomeric reactions are known in these F2C. One of the most interesting ones obviously was to obtain one of the 1,2-cyclopentane-1,2-diones (253) or 2,3-diones (254), followed by separation of the isomers of 1,2-cyclopentane-1,2-dione (255) or 2,3-dione (256) by virtue of their differing melting points and spectral properties.

**FIGURE 2.14** Thermolysis of isomers 1 and 2
of cleavage of the sigma bond. However it seems likely that, as previously observed for decarbonylation, elimination of carbon dioxide is assisted by cyclobutyl sigma bond interaction but does not involve simultaneous cleavage of the sigma bond.

Attempts were made to prepare either the *endo*, *anti*- (240) or *endo*, *syn*- (241) adduct of 2-pyrone (232) and the cyclobutene (142) as a suitable model compound for further study in this area, but these were frustrated by the failure of (232) to add to (142).

When a mixture of the lactone isomers (235) or (236) was heated under reflux in triethylene glycol for a short period a mixture of at least ten products (by tlc analysis) was obtained. The mixture was not examined in detail but preparative layer chromatography enabled an 8% yield of a crystalline product to be isolated. The melting point and spectral data of this compound positively identified it as a 1-isoquinolone (248). The other products have not yet been isolated and identified but this single result allows for some speculation. Some possible mechanisms are shown in Scheme 2.10. The isoquinolone (248) is obviously derived from either (E)- (246) or (Z)-9,10-dihydroisoquinolone (247). The most likely pathway is conrotatory ring opening of (238) to give (Z,Z,Z,E)-azacyclodeca-3,5,7,9-tetraen-2-one (243) or the (E,Z,Z,Z)-isomer (244), followed by disrotatory closure of (243) or (244) and dehydrogena-
tion of the resultant dihydroisoquinolone (246). All the steps described conserve orbital symmetry and this result parallels the thermolysis of the triene (239), which yields the tetrahydronaphthalene (250) via the (2,2,2,2E)-cyclodecatetraene (249).163

If the (E)-isomer (246) is the penultimate thermolysis product,
the conversion of (246) to (248) represents the first observed aromatisation of an (E)-9,10-dihydronaphthalene derivative. The frequently observed dehydrogenation (either by disproportionation or loss of hydrogen) of (Z)-9,10-dihydronaphthalene appears to be a concerted reaction since it is stereospecific. However, the thermal loss of hydrogen from 1,3-cyclohexadiene is non-stereospecific, suggesting a radical-chain process, and it seems reasonable to propose stepwise loss of hydrogen from (246).

A less likely mechanism involves Cope rearrangement of (238) to the cyclobutene (242), which then undergoes a "forbidden" ring opening to the (Z,Z,Z,Z)-tetraene (245), closure to the (Z)-dihydro isomer (247) and concerted elimination of hydrogen. This mechanism parallels that proposed by Baldwin and coworkers to explain the thermal formation of (Z)-dihydroindene (254) from the triene (251), a process which violates the conservation of orbital symmetry. Baldwin et al. have used configuration interaction to construct a state correlation diagram for the isomerisation of (252) to (253) and found it to be concerted and energetically favourable. Although this conversion and the related epimerisation of 9-substituted-bicyclo[6.1.0]nona-2,3,6-trienes remain controversial, recent results tend to rule out diradical intermediates and the Baldwin proposal remains the most feasible.
In the light of the above results, it will be of interest to further investigate this thermolysis; particularly to determine the stereochemistry of the dihydroisoquinolone intermediate and to investigate the preferred modes of closure of the possible unsymmetrical decatetraenes (243) and (244). The low temperature photolysis of the triene (238) should be of interest in the light of the discovery by Staley and Henry that irradiation of the triene (239) gives a rapidly equilibrating mixture of the valence isomers (255) and (256). Further, the conversion of (238) to the azatetraene (257) should provide a facile entry to the synthesis of azacyclodecapentaenes as shown in Scheme 2.11.

\[ \text{Scheme 2.11} \]
CHAPTER 3

2-AZETINES

3.1 Introduction

Efforts towards the synthesis of 2-azetines had a manifold purpose. The first was to synthesise and investigate the properties of small examples of this little known ring system, in line with interests in the continuing interest of this group in unsaturated small ring heterocycles. The few non-fused 2-azetines reported to date have all been highly substituted and have yielded little insight into the thermal stability of this ring, which has been described in Chapter 1, and its susceptibility to ionic cleavage. Further, these compounds are of particular interest because of their potential they hold as precursors to the elusive molecule azetin; the latter was a long term synthetic goal of this work.

3.2 The Synthesis of 2-Azetine Precursors

The synthesis of the desired photochemical precursors was achieved successfully by the preparation of 2-azabicyclo[2.2.2]octan-6-yne (260) and their subsequent addition to 2,3-dichloro-3,4-dihydrocyclopenta-2,4-
diene (298). Two other methods (shown in Scheme 3.1) which were investigated without success were the reduction of the readily prepared 6-lactam (298) and a sequence involving formation of the bicyclic-3-enone rings by nitrogen elimination from an adduct (264). The latter approach has been successfully employed in the synthesis of the fused-cyclohexenes (269) and (268).[12]

As mentioned in Chapter 1, the synthesis of 2-azabicyclo[2.2.2]octan-6-yne (260b) by an olefin metathesis route followed by treatment with the Hamme was later reported. Compound (230b) appeared to be the ideal solution for this study, but attempts to
3.1 Introduction

Efforts towards the synthesis of 2-azetines had a manifold purpose. The first was to synthesise and investigate the properties of simple examples of this little known ring system, an aim consistent with the continuing interest of this group in unsaturated small ring heterocycles. The few non-fused 2-azetines reported to date have all been highly substituted and have yielded little insight into the thermal stability of this ring, which has been discussed in Chapter 1, and its susceptibility to ionic cleavage. Further, these compounds are of particular interest because of the potential they hold as precursors to the elusive molecule, azete: the latter was a long term synthetic goal of this work.

3.2 The Synthesis of 2-Azetine Precursors

The synthesis of the desired photochemical precursors was achieved successfully by the preparation of 2-azabicyclo[2.2.0]hex-5-enes (260) and their subsequent addition to 2,5-dimethyl-3,4-diphenylcyclopenta-2,4-dienone (138). Two other methods (shown in Scheme 3.1) which were investigated without success were the reduction of the readily prepared β-lactam (139b) and a sequence involving formation of the four-membered rings by nitrogen elimination from an adduct (264). The latter approach has been successfully employed in the synthesis of the fused cyclopropanes (265)\(^{114}\) and (266).\(^{171}\)

As mentioned in Chapter 1, the synthesis of 2-azabicyclo[2.2.0]hex-5-ene (260b) by \textit{in situ} sodium borohydride reduction of transient 2-azabicyclo[2.2.0]hexa-2,5-diene (126) has been reported. Compound (260b) appeared to be the ideal synthon for this study, but attempts to
repeat the work were unsuccessful. However, the previously reported N-carbomethoxy cyclobutene (260a) was also suitable since the urethane moiety possessed the potential for considerable synthetic modification.

The reported conversion of N-carbomethoxy-1,2-dihydropyridine (259a) to its bicyclic isomer (260a) using a 300 nm light source was found to proceed at an unacceptably slow rate. The use of a 450W medium pressure mercury lamp and a pyrex filter gave similar results but the substitution of a Corex filter led to acceptable yields (ca 40%) of (260a), in addition to a large number of unidentified products. The cyclobutene could not be purified by chromatography, since other urethane byproducts co-chromatographed with it, and the total photolysate was used for all synthetic work. Compound (260a) added readily to the dienone (138) to give two isomers in the ratio of ca 2.5:1, which were assigned
exo, anti (267) and endo, anti (268) stereochemistries respectively. The isomers could not be separated by chromatography, but crystallisation from methanol gave the pure major isomer. All experiments involving compound (261a), then, were performed using the exo, anti-isomer (267). The endo, anti-isomer was not isolated, but the C-methyl singlets at δ 1.34 and δ 1.39 present in the p.m.r. spectrum of the adduct mixture (261a) before recrystallisation were indicative of its presence.

The p.m.r. spectrum of (267) was consistent with the assigned structure. The C5 proton anti to the cyclobutyl ring appeared as an overlapping doublet of doublets at δ 4.39 with a geminal coupling constant of 9.0 Hz and a vicinal cis coupling of 7.1 Hz. The C5 proton syn to the cyclobutyl ring (δ 4.04) had a much smaller vicinal trans coupling of 2.2 Hz. The C3 proton was well downfield as an unresolvable multiplet at δ 4.28 whilst the C6 proton also appeared as a broad multiplet at δ 2.59. The C2 and C7 protons, which normally exhibit a simple AB pattern in these systems, appeared as a broad singlet and a slightly broadened doublet as shown in Figure 3.1. The conformational nature of this broadening was confirmed by recording the spectrum at higher temperatures whereupon the C2 and C7 protons resolved into an AB system (J 6.8 Hz). Some sharpening of the downfield azetidine protons was also evident. When the spectrum of (267) was recorded in perdeuteromethanol at room temperature the AB system collapsed into a broad singlet and broadening of the C1-methyl singlet was also noted.
The rigidity of the azetidine ring in (267) and the observed low barrier to rotation about the N-ester bond of N-carbomethoxyaziridine lead to the conclusion that the broadening is due to slow inversion of the nitrogen atom. On the basis of previously observed high rates of nitrogen inversion in azetidine rings, this behaviour is remarkable. In general, the rate of inversion in these compounds is only slightly less than acyclic tertiary amines. Although some slowing in (267) may be due to the increased rigidity of the fused azetidine ring, no broadening occurs in the spectra of the corresponding N-tosyl (271) and N-methyl (274) compounds. Even at -50°, the spectrum of (274) showed no more broadening than would be expected as a consequence of increased solvent viscosity. A tentative explanation is that hydrogen

+ The rate of nitrogen inversion is increased by the carbomethoxy group by virtue of the enhanced conjugative interaction and reduced steric compression on passing from a pyramidal ground state to a trigonal transition state. The p-toluenesulphonyl group also causes rate enhancement, although it seems unlikely that this enhancement arises by d orbital overlap.
bonding between the C2 proton and the ester group is responsible for the slow inversion. Hydrogen bonding between hydroxylic solvents and the nitrogen atom is known to slow inversion and it is possible that intramolecular hydrogen bonding may also be of importance in (267).

The \textit{exo} stereochemistry of the cyclobutyl ring of the major isomer (267) was confirmed by the failure of (267) to decarbonylate at 160° in dimethyl sulfoxide solution. Reduction of (267) with sodium borohydride gave a single alcohol (269) which was assigned \textit{syn}, \textit{exo}, \textit{anti} stereochemistry.

The p.m.r. spectrum of the alcohol (269) was similar to that of the ketone (267). The C3 and C6 proton resonances were downfield by 0.40 p.p.m. relative to their chemical shifts in (267), indicating that these protons are shielded by the carbonyl bridge in (267). Again, this is consistent only with \textit{exo}, \textit{anti} stereochemistry. The C5 protons showed the same pattern as for the ketone (267). The observed coupling constants were 9.0 Hz (geminal), 7.1 Hz (\textit{cis} vicinal) and 2.7 Hz (\textit{trans} vicinal). Conformational broadening similar to that in (267) was observed for the C2 proton and some broadening of the C1 methyl was also evident.

The lanthanide shift reagent Eu(fod)$_3$ complexed strongly with both (267) and (269), but, for both compounds, the major site of complexation was the urethan moiety, as evidenced by the large difference in the rates of shift of the two C-methyl resonances. In both cases, addition of Eu(fod)$_3$ also led to extreme broadening of all but the C8 methyl and aromatic resonances, due to europium complexation further slowing the rate of nitrogen inversion.

Removal of the N-carbomethoxy group from the ketone (267) required prolonged reflux with potassium hydroxide in aqueous methanol but proceeded reasonably cleanly to give the azetidine (270) as the only
product, as evidenced by t.l.c. analysis. Attempts to purify (270) by chromatography on both silica and alumina were largely unsuccessful and the compound could only be obtained as a slightly impure and rather unstable brown oil. The p.m.r. spectrum of (270) showed the C-methyl groups almost coincident at δ 1.20 and a characteristic phenyl proton pattern but the signals for the other protons, which appeared at δ 2.2-3.0 and δ 3.4-4.4 were extensively broadened. A variable temperature study of the p.m.r. spectrum of this compound was not made and it is not known whether the broadening observed is a consequence of nitrogen inversion or proton exchange.

The instability of (270) is similar to that observed for other fused azetidines lacking a nitrogen substituent; for example the azetidine (272) decomposes even on standing under nitrogen. Since azetidine itself is reasonably stable this instability seems to be a consequence of the increased ring strain concomitant with ring fusion. It has been observed in the course of this work that the presence of an electron-withdrawing substituent on the nitrogen atom leads to a dramatic increase in the stability of these fused azetidines, suggesting that decomposition occurs by acid-catalysed ring cleavage and subsequent polymerisation.

The azetidine (270) was readily converted to the corresponding N-tosyl compound (271) by treatment with p-toluenesulphonyl chloride and
pyridine. The structure of (271) was fully confirmed by its analytical and spectral data. In particular, the mass spectrum had a molecular ion at 495 and a breakdown pattern consistent with decarbonylation and aromatisation. The p.m.r. spectrum showed a multiplet at $\delta$ 4.04-4.17 which was assigned to the three protons alpha to the nitrogen atom and a broad singlet coincident with the aromatic methyl resonance at $\delta$ 2.44 which was assigned to the C6 bridgehead proton. In contrast to the N-carbomethoxy compound (267), no collapse of the C2, C7 proton AB system was observed, the protons being present as a pair of doublets, J 7 Hz, at $\delta$ 2.76 and $\delta$ 3.16.

Preparation of the N-methyl compound (261d) was attempted by all the routes shown in Scheme 3.2. Lithium aluminium hydride reduction of the N-carbomethoxy ketone (261a) gave the N-methyl alcohol (273) in 82% yield. The structure of this compound was confirmed by analytical and spectral data. The oxidation of (273) with Jones reagent gave only a 5% yield of the N-methyl ketone (261d). Although amines are stable to Jones reagent, the acidic conditions evidently effect cleavage of the azetidine ring. This oxidation was not pursued since the alternative synthesis described below proved convenient but it is likely that yields could be much improved by reagents which can be employed under neutral conditions, such as the recently described pyridinium chlorochromate.
The sequence finally employed for the synthesis of (261d) involved lithium aluminium hydride reduction of the N-carbomethoxy bicyclic amine (260a) to the corresponding N-methyl compound (260d) and subsequent Diels-Alder addition to the dienone (138). The reduction of crude (ca 40%) (260a) resulted in conversion to (260d) in good yield, as inferred by the p.m.r. spectrum of the crude product. The presence of (260d) was readily confirmed by the multiplets at δ 6.38 and δ 6.69 assignable to the olefinic protons, a multiplet at δ 4.46 (bridgehead proton alpha to the nitrogen atom), and a singlet for the N-methyl at δ 2.32. No attempt was made to isolate the rather labile product, which was immediately reacted with (138) to give a mixture of the exo, anti- (274) and endo, anti-adducts (275) in the ratio of ca 4:1. This method afforded (261d) in an overall yield of 6% for the three steps from 1-carbomethoxy-1,2-dihydropyridine (259a). Compound (261d) was obtained as a yellow gum which could not be induced to crystallise and decomposed gradually on standing. The only spectral datum available for the endo-isomer (275) was the singlet attributable to the coincident C-methyl groups at δ 1.36 in the p.m.r. spectrum. The p.m.r. spectrum of the exo, anti-isomer (274) showed the C-methyls coincident at δ 1.19 and a singlet for the N-methyl at δ 2.43. The C2 and C7 protons appeared as an AB pair, J 6.7 Hz, at δ 3.03 and 2.70. The C7 doublet was slightly broadened by additional fine coupling. The C5 protons appeared as doublets of doublets with geminal coupling of 8.3 Hz, vicinal cis coupling of ca 7 Hz and vicinal trans coupling of 3.2 Hz.

In order that the N-carbomethoxy sequence might be repeated with more easily removed protecting groups on the nitrogen atom, both 1-carbobenzoxy-1,2-dihydropyridine (259e) and 1-methanesulphonyl-1,2-dihydropyridine (259f) were synthesised in similar fashion to that

† Only very low yields of (260d) resulted from photolysis of the unstable 1,2-dihydropyridine (259d).

* This is also noticeable in the spectra of the N-carbomethoxy (267) and N-tosyl (271) compounds.
employed for the carboxetylxy compound (259a). Photolysis of (259f) did not result in the formation of any of the N-methanesulphonyl bicyclic isomer (260f) and the N-carbobenzoxy compound (259e) gave only very low yields of the bicyclic isomer (260e). The formation of (260e) was inferred by the following p.m.r. data: a multiplet at $\delta 6.48$ assigned to the olefinic protons and a multiplet at $\delta 4.84$ which could be assigned to the bridgehead alpha to the nitrogen atom. Absorptions corresponding to the shifts expected for the other protons were present but definite assignments could not be made.

The attempted synthesis of compounds (263) (see Scheme 3.1) was not successful. N-Phenyltriazolinedione (208) added smoothly to N-carboxetylxy-1,2-dihydropyridine to give the adduct (262), but none of the desired adduct (263) was obtained when (262) was heated under reflux with the dienone (138) in either benzene or chlorobenzene.

Attempts to synthesise the fused azetidine (258) from the $\beta$-lactam (139b) also failed. The sterically hindered carbonyl of the exo, anti-isomer (140b) could not be ketalised by either conventional methods or by that of Andersen and Uh. Hence, it was decided to reduce both the ketone and amide functions of (140b), and then reoxidise the resultant
alcohol as the final step. The reduction of azetidinones with lithium aluminium hydride was originally reported to require mild conditions (0°) if ring cleavage were to be avoided, but the reduction of (140b) at room temperature gave only the alcohol (276). The fused azetidines (277) and (278) had been successfully prepared by lithium aluminium hydride reduction of the corresponding azetidinones using more vigorous conditions and, accordingly, reduction of (140b) in refluxing tetrahydrofuran was attempted. The product obtained was not the desired azetidine (258). Its mass spectrum had a strong molecular ion at m/e 343, confirming that it was isomeric with (258), but the primary fragmentation was loss of 28 (CO, C₂H₄?) to give a strong peak at m/e 315. The p.m.r. spectrum had a broadened doublet well downfield at δ 4.76 integrating for one proton, a broadened singlet at δ 3.32 (one proton), an AB pair at δ 3.12 and 2.85, J = 13 Hz, and a complex multiplet at δ 1.77-2.56 containing a small amount of impurity, since it integrated for more than the necessary five protons. The large coupling constant of the AB system indicated that the cyclobutyl ring was no longer intact but little more information could be gleaned. The compound was smoothly converted to its tosyl derivative by treatment with p-toluenesulphonyl chloride in pyridine. The tosyl derivative was quite dissimilar to the authentic syn, exo, anti-alcohol (279), prepared by sodium borohydride reduction of the ketone (271). Analytical and mass spectra data indicated that it was isomeric with (279) and, again, the mass spectrum showed loss of 28 as a strong primary fragmentation. The infrared spectrum showed an absence of alcohol or secondary amine functions in addition to a strong C-O stretch at 1150 cm⁻¹, indicative of an ether. The rearranged product is probably derived from the attack of an alkoxy anion generated
at the bridgehead on the 3- or 6-positions, as shown in Scheme 3.3. The most likely compound resulting from this mode of attack would be the ether (280), but this structure is incompatible with the p.m.r. spectrum which shows a very high field proton at $\delta$ 1.43 and a fairly unperturbed AB system at $\delta$ 3.06 and 3.33, J 12 Hz. The 270 MHz and 100 MHz spin-decoupled spectra of the tosyl derivative are currently being obtained and, hopefully, these additional data will enable the structure to be elucidated.

3.3 The Photosynthesis and Reactions of 2-Azetines

The photochemistry of the N-carbomethoxy ketone (267) was investigated under varying conditions. When $\alpha$ 0.25M solutions of (267) in deuteriochloroform were irradiated at -20° in a quartz n.m.r. tube, decarboxylation to the diene (281)$^+$ and subsequent 1,2-photoaromatisation, $^+$ No attempt was made to isolate and fully characterise the diene (281), but preparative layer chromatography of a photolysate resulting from incomplete reaction afforded a sample of (281) of moderate purity. The p.m.r. spectrum again showed conformational broadening. The C7 methyl appeared as a broadened singlet at 6 1.41 and the C10 methyl as a very broadened singlet at 6 1.52. The appearance of the C1 and C6 protons was difficult to determine because they were partially coincident with the carboxyl methyl group at 6 3.69.
as evidenced by the formation of the aromatic fragment (92), proceeded smoothly. Considerable polymerisation occurred under these conditions but the appearance of singlets at δ 5.58 and δ 6.61 in the p.m.r. spectrum suggested that the azetine (282) was forming. When more dilute conditions were employed clean formation of (92) and (282) occurred so long as moisture was rigorously excluded from the photolysis. Small quantities of the azetine (282) could be isolated almost pure by short-path vacuum distillation from the crude photolytate at 0°. Compound (282) was a colourless liquid which was readily hydrolysed but showed good stability in the absence of moisture. The structure was supported by the p.m.r. spectrum which was readily assigned as indicated in Figure 3.2. The most notable feature was the lack of vicinal coupling between the ring protons. In comparison, for cyclobutene derivatives the olefinic coupling constant varies over a range of 2.5 to 4.0 Hz, 188 and for thiete (3) it is 3 Hz. 11 Similarly, the very small coupling between the C3 and C4 protons is characteristic of unsaturated four-membered rings, the same coupling being 0.8 Hz for cyclobutene111b and 1 Hz for thiete.11 The chemical shifts were consistent with those observed for thiete which exhibited peaks at δ 6.50 (C2 proton), δ 5.60 (C3 proton) and δ 3.80 (C4 protons).11 The mass spectrum showed a strong molecular ion at m/e 113, † the dominant breakdown pattern being characteristic of ester cleavage with strong peaks at m/e 59 and m/e 31.

The photolysis of the ketone (267) in the presence of water gave a new product which could be isolated pure by short-path vacuum distilla-

† A small peak due to contamination by the hydrolysis product was present at m/e 131.
tion as a colourless liquid and was identified on the basis of its p.m.r.
and mass spectra as N-carbomethoxy-3-amino-1-propanal (287).

When (267) was photolyzed in dichloromethane which had not been
purified prior to use, in addition to small quantities of N-carbomethoxy-
2-azetine (282) and the aldehyde (287), appreciable yields were obtained
of a new product derived from the addition of traces of ethanol present
in the solvent. The compound was isolated pure in low yield by preparative
layer chromatography on silica gel and subsequent short-path distillation.
On the basis of its spectral data its structure was assigned as N-carbo-
methoxy-3-amino-1-propanal diethyl acetal (285). The structure of (285)
was confirmed by unambiguous synthesis, as depicted in Scheme 3.4. The
reaction of methyl chloroformate with 3-amino-1-propanal diethyl acetal
(284) prepared by literature methods,\textsuperscript{189,190} gave a product indistinguish-
able in all respects from that obtained from the photolysis.+

\[ \text{CH}_2=\text{CH}-\text{CHO} + \text{HCl} \rightarrow \text{CH}_2=\text{CH}-\text{CHO} + \text{H}^+ \rightarrow \text{CHO} + \text{H}_2\text{O} \]

**Scheme 3.4**

The formation of both the aldehyde (287) and its diethyl acetal (285) can be easily explained by acid catalysed addition of water or ethanol to the double bond of the azetine. As shown in Scheme 3.4, cleavage of the water addition product (286) leads to the aldehyde since the proton is an efficient leaving group. In the case of the ethanol addition product this pathway is not available so ring cleavage is

+ An attempt to prepare the aldehyde (287) by deketalisation of the acetal (285) with p-toluenesulphonic acid in acetone gave only polymeric product. Similarly the addition of acrolein to a suspension of the sodium salt of methyl urethane in benzene gave only polymer and some recovered methyl urethane.
assisted by the attack of another ethanol molecule. This mechanism is analogous to that proposed for the formation of the 2,4-dinitrophenylhydrazone of 3-thio-1-propanal (288) when thiete (3) was treated with acidic 2,4-dinitrophenylhydrazine (see Scheme 3.4).10

However further observations mitigated against this rationalisation. The photolysis of a dichloromethane solution of the ketone (261) in a quartz n.m.r. tube gave a clean solution of 2,3-dimethyl-1,4-diphenylbenzene (92) and the azetine (282). When a drop of 5% aqueous hydrochloric acid was added to the solution and the mixture shaken well, the formation of aldehyde was immediately discernible by p.m.r. spectroscopy. However the rate of formation was slow and after 18 hours at room temperature the conversion of azetine to aldehyde was only ca 50% complete. The same sample was then irradiated for 30 minutes at less than 0°. Re-examination of the spectrum showed almost complete conversion of azetine, whilst after a further 30 minutes irradiation the solution was a clean mixture of the aldehyde (287) and the aromatic compound (92). It is clear, then, that the hydrolysis and subsequent cleavage of the azetine is much faster in the presence of ultraviolet irradiation. Similar photolysis experiments conducted in deuteriochloroform containing a drop of water or a drop of 5% aqueous potassium carbonate established that the formation of the aldehyde (287) was rapid (continuous monitoring of the photolysis did not reveal any observable buildup in the concentration of the azetine) and not dependent on either acid or base catalysis.

The results lead to the conclusion that the azetine formed is undergoing rapid photochemical hydration and subsequent cleavage. Similar facile photochemical addition of water has been reported for closely related systems. The photolysis of the enamide (289) in benzene containing ca 0.03% water gave a 22% yield of the hydroxy compound (290), demonstrating that the photochemical addition of nucleophiles can be a very efficient process.
The photochemical addition of hydroxylic compounds to cycloalkenes has been studied in detail by Kropp and coworkers and found to be ionic in character. Kropp postulated that cyclohexenes, -heptenes and -octenes gave addition products via protonation of a highly strained ground state (E)-intermediate. Cyclopentenones and other highly constrained cyclic olefins gave addition products derived from a radical mechanism; for example, the photolysis of norbornene in xylene-methanol mixtures led to the products shown in Scheme 3.5. In contrast, large-ring cyclic or acyclic olefins, for which the (E)-isomer is not particularly strained exhibited only (E)-(Z) isomerisation under similar conditions.

Photochemical ionic addition has been observed in five-membered heterocyclic rings. Irradiation of the 2,3-dihydrofuran (291) in methanol gave the addition products shown in Scheme 3.6 by an ionic mechanism, whilst addition to the phosphine (292) gave the adduct (293) upon
sensitised irradiation in methanol. In the former case it was argued that the addition of methanol is permissible because interaction of the oxygen non-bonding electrons exerts a stabilising effect on the excited intermediate and in the latter that electron transfer from the phosphorus non-bonded orbital to the * orbital gives a polarised excited state which is readily protonated. Similarly, photochemical hydration of the double bond of uracil occurs by attack on an intermediate high energy species, either on the excited singlet or upper vibrationally excited ground state species formed by internal conversion.

Since no products suggesting a radical mechanism were obtained from the addition of ethanol and the hydration product is the same as that obtained thermally, the results for N-carbomethoxy-2-azetine (282) are best explained by attack of the hydroxylic reagent on an excited species. The hydroxyazetidine (286) thus obtained could be expected to rapidly undergo ring opening. A similar opening has been reported by Rees and coworkers, who found that the addition of diphenylketene to 2-phenylbenzazete (311) in moist ether at -20° gave the amidoketone (295) via the hydroxybenzazetine (294).

\[
\begin{align*}
\text{Ph} & \text{N} + \text{Ph}_2\text{C} = \text{C} = \text{O} \\
\text{(311)} & \rightarrow \text{Ph} \text{N} \text{Ph} \\
\text{Ph} & \text{N} \text{COCHPh}_2 \\
\text{(295)} & \rightarrow \text{Ph} \text{N} \text{OH} \\
\text{(294)} & \rightarrow \text{H}_2\text{O}
\end{align*}
\]

The initial hydration of (282) could occur via either a singlet or triplet state, since the o-terpheny (92) present could act as a sensitisier. In those cases where a "high" concentration of water was in excess of that required to saturate dichloromethane solutions at 20°. Thus a "high" concentration is in fact less than 0.1% v/v.
precludes observation of any buildup of the azetine, the possibility
exists that the initially formed electronically excited azetine decays
to a vibrationally excited ground state level which is immediately
hydrated; that is, that ground state (282) does not form at all. This
is unlikely though, since no products derived from solvent addition to
the double bond are observed in the photochemical formation of 2-azetin-
4-ones in methanol; in that case, at least, concerted ring opening is
evidently a much faster process than photoaddition.

The behaviour of N-carbomethoxy-2-azetine (282) contrasts to that
of N-phenylbenzazetine (31), which forms addition products (295) derived
from the ring-opened tautomer (49) when irradiated in hydroxylic sol-
vents.\(^{25,199}\) Although the enamine (296) is not trapped by hydroxylic
solvents (enamines (297) have not been observed) the photochemical
excitation of the azetine (282) must lead to an equilibrium concentration
of (296) being present. Attempts were made to trap (296) as the adduct
(298) by photolyzing the ketone (261a) in the presence of N-methylmale-
imide, but addition of the dienophile to the intermediate diene (281)
competed favourably with 1,2-photoaromatisation to give high yields of
the adduct (299). The stereochemistry depicted has not been definitely
confirmed, but is that derived from \textit{endo} addition to the less hindered
side of the diene. The steric bulk of the planar maleimide molecule
is sufficiently low to permit endo addition as evidenced by the formation of the endo-adduct (300) in the reaction of N-phenylmaleimide with tetracyclone. The p.m.r. spectrum of (299) showed the C9 and C13 protons well upfield at δ 2.75 and the N-methyl downfield at δ 3.10 in comparison with the adduct (301), in support of the stereochemistry depicted for (299). The C1 methyl singlet, C2 proton doublet and the four proton aromatic multiplet all exhibited broadening from conformational effects. Compound (299) was identical to the adduct obtained by heating the ketone (261a) with N-methylmaleimide at 200°.

N-Carbomethoxy-2-azetine (282) is thermally stable at room temperature but polymerises in deuteriochloroform solution at temperatures above ca 50°. It is evident that the electron-withdrawing group on the nitrogen atom confers the molecule with considerable stability. Tetracyanoethylene is known to react readily with similar cyclic enamines, but it failed to react with (282), as did the active diene 1,3-diphenyl-isobenzofuran. 3,6-Di(2'-pyridyl)-a-tetrazine (302) is an inverse electron demand diene which reacts readily with compounds containing ring strained double bonds and, as expected, (282) added readily to (302) at 0° to give two compounds. The major compound was confirmed as a 1:1 adduct by its analytical and mass spectral data. The presence of an NH stretch in the infrared spectrum and the strong ultraviolet absorption at 286 nm (ε 21700), which is indicative of the 3,6-di(2'-pyridyl)-pyridazine chromophore, suggested that this compound was N-carbomethoxy-[3,6-di(2'-pyridyl)pyridazinyl]methylamine (303). The p.m.r. spectrum was consistent with this assignment, showing nine aromatic protons, a sharp doublet 

† Both the UV and p.m.r. spectra of (303) closely resembled those of the pyridazine (304).
(J 6.5 Hz) at δ 4.75 for the methylene protons and a broad triplet (J 6.5 Hz) at δ 6.77 for the amino proton.

Compound (303) is clearly formed by cleavage of the aziridinyl ring of an initially formed \([\pi^4 + \pi^2]\) adduct. The mechanism shown in Scheme 3.7, wherein cleavage is initiated by abstraction of the C1 bridgehead proton by the adjacent pyridyl group is likely considering the facility of this opening.

It was anticipated that 1-methyl-2-azetine (306) would be considerably more reactive than the N-carbomethoxy compound (282). The substitution of an electron-donating group for the electron-withdrawing carbomethoxy substituent allows more overlap between the non-bonding nitrogen orbital and the π orbital. Consequently, as explained in Chapter 1, concerted thermal ring opening becomes more favoured. Acid-catalysed hydrolysis could also be expected to occur more readily because of increased stabilisation of the initially formed protonated species.

Attempts to date to synthesise 1-methyl-2-azetine (306) have been unsuccessful. To minimise the chances of thermal opening, the photolysis of the ketone (261d) and monitoring of the reaction by p.m.r. spectroscopy were performed at -50°. Irradiation of a \(\alpha\) 0.2M solution of (261d) in deuteriochloroform containing tetramethylsilane with a low pressure mercury lamp caused rapid consumption of the starting material but the reaction was complicated by other processes competing with
1,2-photoaromatisation. The p.m.r. spectrum indicated approximately 50% conversion to the aromatic compound (92), the balance being converted to two unidentified compounds, as judged by the C-methyl pairs at δ 1.19-1.22 and δ 1.41-1.47. The photostability of this mixture, and the observation that these peaks did not change upon addition of N-methylmaleimide to the solution, indicated that neither of these compounds was the intermediate diene (305). In those regions where the proton resonances of the azetine (306) might be expected, peaks developed at δ 6.79, 5.31 and 3.67, but these did not disappear either upon warming or addition of 3,6-di(2-pyridyl)-s-tetrazine (302) to the solution, indicating that they could not be attributed to (306). The photolysis of (261d) in dilute dichloromethane solution at -40° also failed to produce any evidence of the formation of (306).

3.4 N-(p-Toluenesulphonyl)-2-azetine: A Precursor to Azete

In recent years, intensive effort was made towards cyclobutadiene, which culminated in the successful formation and characterisation of this species by matrix photolysis of α-pyrone as shown in Scheme 3.8. However, attempts to extend this approach to the low temperature

\[
\begin{align*}
\text{(232)} & \xrightarrow{hv} \text{pyrex} \quad \text{(109)} \\
\text{(307)} & \xrightarrow{hv} \quad \text{(308)} \quad \text{(309)}
\end{align*}
\]

SCHMIE 3.8

generation of azete (309a) appear to have been less successful. Recently Krantz and Hoppe reported that matrix photolysis of (307a) led to the formation of hydrogen cyanide, acetylene and carbon dioxide, suggesting that azete had formed but was more readily photochemically cleaved than cyclobutadiene. Earlier, a preliminary report by Maier stated that
photolysis of (307b) led to the formation of the bicyclic intermediate (308b), followed by the desired cheletropic loss of carbon dioxide, but structural elucidation of the photoproducts was not complete at the time of writing.207

A resonance energy of -15.5 kcal mol\(^{-1}\) has been calculated for azete,208 compared with that of -18 kcal mol\(^{-1}\) for cyclobutadiene itself.209 Hence despite the small amount of stabilisation due to the nitrogen atom, azete can be predicted to be a very reactive, transient species.

The first reported azete derivative was 2-phenylbenzazete (311), which was formed as a bright red solid by the vapour phase pyrolysis of 4-phenyl-1,2,3-benzotriazine (310). The benzazete (311), which was stable at -80°, dimerised upon warming to room temperature and could be trapped as a variety of Diels-Alder adducts.210,211 Tris(dimethylamino)azete (313) was similarly prepared by vapour phase pyrolysis of tris(dimethylamino)-1,2,3-triazine (312). The azete (313) was found to possess remarkable thermal stability, with a half-life of 56 minutes at 30°.212 This stability may be attributed to push-pull substitution, an effect which has been demonstrated dramatically in the case of the cyclobutadiene (314) which is stable at 0° because of the strong contribution from the canonical structure (314c).213 In the case of the azete (313) the ring-nitrogen acts as an acceptor group; thus (313) is best described as the resonance hybrid (313 a-d), with structure (313d) being of especial significance.212,214
Although the instability of azete is certainly so great as to preclude direct observation under all but matrix isolated conditions, this species and simple derivatives of it should have sufficiently long lifetimes to be trapped by suitable dienes and dienophiles, or by dimerisation. In support of this, it has been reported that photolysis of the triazafulvenes (315) and (316) led to the same mixture of products, including the 1,5-diazocine (318). This compound was postulated to be formed via the intermediate azete (317) which subsequently dimerised and ring opened.\(^{215}\)

Paquette and coworkers attempted to synthesise 2-methoxyazete (320), together with the potential azete precursors (322) and (324), by retro Diels-Alder reaction of compounds (319), (321) and (323) but were unsuccessful in each case.\(^{186}\)

Similarly, an integral part of our interest in 2-azetines was to synthesise various N-substituted derivatives (325) which might be induced to undergo elimination to give azete (309a) under conditions...
suitable for its trapping. Initially, synthetic efforts were directed towards N-tosyl-2-azetine (326) which, it was hoped, would undergo base-induced elimination of p-toluenesulphinic acid to yield (309a).

The N-tosyl ketone (261c) was cleanly converted to the azetine (326) and the aromatic compound (92) when irradiated in dilute dichloromethane solution. Preparative layer chromatography of the crude photolysate gave a 33% yield of (326) as a slightly oily solid which showed good stability, although some decomposition did occur when samples were allowed to stand for prolonged periods. The mass spectrum (molecular ion at m/e 209 and a p-toluenesulphonyl cleavage pattern) and the p.m.r. spectrum, which is presented in Figure 3.3, confirmed
the structure of (326).

The photoinduced elimination of \( p \)-toluenesulphinic acid from the tetrahydroquinoline-N-tosylate (327) to give the 3,4-dihydroisoquinoline (328) has been reported\(^{216}\) but there was no evidence for similar behaviour in the photolysis of (261c). It is not certain whether this elimination

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FIGURE 3.3 P.m.r. spectrum of N-tosyl-2-azetine (326)

is a step-wise process which is promoted by solvent polarity. However, in view of the facile photoaddition of these solvents to N-carbomethoxy-2-azetine (282), the photochemistry of (326) in hydroxylic solvents was not investigated.

The base catalysed eliminations of \( p \)-toluenesulphinic acid and methanesulphinic acid have been employed successfully in the syntheses
shown in Scheme 3.9. Elimination from (329) was effected with sodium methoxide in benzene,\textsuperscript{217} and from (330) using potassium tert-butoxide in dimethyl sulphoxide.\textsuperscript{218}

Potassium tert-butoxide in dimethyl sulphoxide was employed in attempts to form azete. Addition of the base to a solution of N-tosyl-2-azetine led to the rapid consumption of starting material but both p.m.r. tube experiments and reaction in the presence of 1,3-diphenyliso-benzofuran failed to give an evidence for the trapping of azete either as dimers or the Diels-Alder adduct. The elimination has not been explored fully under a range of conditions and, hopefully, reaction at \(-70^\circ\) in tetrahydrofuran or other similar mild conditions may prove successful.
Melting points were determined on a Gallenkamp melting point apparatus, or a Recrystall Hot Stage microscope, and are uncorrected.

Microanalyses were performed by the A.N.U. Microanalytical Service under the direction of Max N. Streemann and Dr. J. J. Fildes. Ultraviolet spectra were recorded in 90% ethanolic solution on a Unicam SP 1800 instrument, using matched 0.5 cm or 1 cm silica cells. Unless otherwise specified, infrared spectra were recorded on a Unicam SP 2000 spectrophotometer. F.N.R. spectra were recorded at 100 MHz on a Varian EM-390 instrument; chemical shifts were measured on the 8 scale relative to tetramethylsilane as an internal standard. Low resolution mass spectra were measured on a Varian MAT CH4 spectrometer at 70 eV. The high resolution mass spectrum was recorded on an A.E.I. MS902 instrument.

Unless otherwise specified, preparative layer chromatograms were carried out on thick layer plates (100x20 cm, thickness 0.25 cm) using silica gel (Merck 9417, 254 + 366) as adsorbent. Bands were detected by exposure to short wavelength ultraviolet light.

Low temperature photolyses were carried out in either a vycor tube of 10 ml capacity or quartz u.v. tubes placed in the centre of a vycor filtered coil of low pressure mercury lamp (total arc length of 1 m, operated at about 0.25 amp and 1000 volts). The assembly was cooled by a stream of nitrogen, precipitated by passage through a carbon heat-exchange coil immersed in liquid nitrogen, maintained at a set constant temperature by a heater attached to an A.E.I. temperature control unit. In this fashion, temperatures as low as -90° could be achieved. Accurate temperature measurement was obtained by means of a series of thermocouples connected to a direct-reading electronic thermometer and applied chart recorder.

Other preparative photolyses were carried out using either American
General

Melting points were determined on a Gallenkamp melting point apparatus, or a Reichert hot-stage microscope, and are uncorrected. Microanalyses were performed by the A.N.U. Microanalytical Service under the direction of Miss B. Stevenson and Dr. J. E. Fildes. Ultraviolet spectra were recorded in 90% ethanol solution on a Unicam SP800 instrument, using matched 0.5 cm or 1 cm silica cells. Unless otherwise specified, infrared spectra were recorded as nujol mulls on a Unicam SP200G spectrophotometer. P.m.r. spectra were recorded at 100 MHz on a JEOL JNM-MH-100 instrument; chemical shifts were measured on the δ scale relative to tetramethyldisilane as an internal standard. Low resolution mass spectra were measured on a Varian MAT CH7 spectrometer at 70 eV. The single high resolution mass spectrum was recorded on an A.E.I. MS902 instrument.

Unless otherwise specified, preparative layer chromatograms were carried out on thick layer plates (100 x 20 cm, thickness 0.1 cm) using silica gel (Merck HF254 + 366) as adsorbent. Bands were detected by exposure to short wavelength ultraviolet light.

Low temperature photolyses were carried out in either a vycor tube of 10 ml capacity or quartz n.m.r. tubes placed in the centre of a vycor filtered coiled low pressure mercury lamp (total arc length of 1 m, operated at about 0.25 amp and 1000 volts). The assembly was cooled by a stream of nitrogen, precooled by passage through a copper heat-exchange coil immersed in liquid nitrogen, maintained at a set constant temperature by a heater attached to an A.E.I. temperature control unit. In this fashion, temperatures as low as -80° could be achieved. Accurate temperature measurement was obtained by means of a series of thermocouples connected to a direct-reading electronic thermometer and coupled chart recorder.

Other preparative photolyses were carried out using either American
or English Hanovia medium-pressure mercury lamps of nominal 450 watt output, and standard gas-lift circulation vessels. In all the photolyses described, a slow stream of dry oxygen-free nitrogen was passed through the circulator during irradiation to maintain circulation of the solution and oxygen-free conditions.

1-Methyl-2-pyridone (114a)

The title compound was prepared by the method of Prill and McElvain in 65% yield. B.p. 68-70°/0.1 mm (lit. b.p. 122-124°/11 mm).

\[ \lambda_{\text{max}} 334, 319, 307, 239, 234 \text{ nm; } \epsilon 1800, 3600, 3900, 3700, 4900 \].

P.m.r. (CDCl\textsubscript{3}): \( \delta 3.57 \text{ (singlet, 3H, N-methyl)} \), 6.20 (doublet of triplets, 1H, J 6.6, 1.8 Hz), 6.47-6.65 (multiplet, 1H), 7.20-7.55 (multiplet, 2H).

2-Methyl-2-azabicyclo[2.2.0]hex-5-en-3-one (118a)

A solution of 1-methyl-2-pyridone (114a) (2.0 g) in ethanol (commercial "absolute" grade, 1100 ml) was irradiated for 70h using a 450W American Hanovia lamp and Corex filter. The solvent was removed in vacuo at ca 40° and the residue purified by chromatography on silica gel (chloroform as eluting solvent) to give (118a) as a pale yellow liquid (0.72 g, 36%). P.m.r. (CDCl\textsubscript{3}): \( \delta 2.84 \text{ (singlet, 3H, N-methyl)} \), 4.21 (multiplet, 1H, C4 proton), 4.38 (multiplet, 1H, C1 proton), 6.68 (multiplet, 2H, olefinic protons).

exo,anti-1,4,8-Trimethyl-9,10-diphenyl-4-azatetracyclo[6.2.1.0\textsuperscript{2,7}.0\textsuperscript{3,6}]undec-9-en-5,11-dione (140a)

2-Methyl-2-azabicyclo[2.2.0]hex-5-en-3-one (118a) (0.45 g, 4.1 mmol) and 2,5-dimethyl-3,4-diphenylcyclopenta-2,4-dienone dimer (1220) (1.20 g, 2.3 mmol) were heated together under reflux in chloroform (15 ml) for 4h. The solvent was removed and the residue purified by chromatography on silica gel (chloroform as eluting solvent) to give a mixture of the
exo,anti- (140a) and endo,anti- (141a) adducts (0.96 g 60%). Two recrystallisations from benzene-petroleum spirit (b.p. 60-80°) gave pure (140a) as fine white crystals, m.p. 191-193° (dec.) (Found: C, 81.25; H, 6.33; N, 3.86. C25H23N02 requires C, 81.27; H, 6.27; N, 3.79%).

λ_max 233, 259 nm; ε 9500, 8700. ν_max 1768s, 1740s, 1270w, 1075w, 995w, 914w, 780m, 765m, 703m cm⁻¹. P.m.r. (CDCl₃): δ 1.02 (singlet, 3H, C-methyl), 1.06 (singlet, 3H, C-methyl), 2.75 (doublet, J 6.7 Hz, 1H, C7 proton), 2.89 (singlet, 3H, N-methyl), 2.98 (broadened doublet, J 6.7 Hz, 1H, C2 proton), 3.37 (multiplet, 1H, C6 proton), 3.70 (multiplet, 1H, C3 proton), 6.92-7.44 (multiplet, 10H, aromatic protons). Mass spectrum: m/e 369 (M⁺, 1.5%), 341 (loss of carbon monoxide, 1), 259(23), 258(100), 257(5), 243(16), 241(6), 228(7), 215(6), 165(5), 42(12); metastable ion at 229(258+243).

syn,exo,anti-11-Hydroxy-1,4,8-trimethyl-9,10-diphenyl-4-azatetracyclo-[6.2.1.0²,7.0³,6]undec-9-ene-5,11-dione (152)

exo,anti-9,10-Diphenyl-1,4,8-trimethyl-4-azatetracyclo-[6.2.1.0²,7.0³,6]undec-9-ene-5,11-dione (140a) (103 mg, 0.28 mmol) and sodium borohydride (100mg, 2.6 mmol) were stirred overnight in ethanol (3 ml) at room temperature. The mixture was added to water (50 ml) and extracted with chloroform (3 x 25 ml). The extracts were combined, dried and evaporated to give pure (152) (100 mg, 97%). Recrystallisation from ethanol gave an analytical sample as large colourless prisms, m.p. 226° (Found: C, 80.78; H, 6.59; N, 3.58. C25H25N02 requires C, 80.83; H, 6.78; N, 3.77%). λ_max 258, 232 nm; ε 7400, 7800. ν_max (CHCl₃) 3418s, 1825s cm⁻¹. P.m.r. (CDCl₃): δ 1.22 (singlet, 3H, C1 methyl), 1.25 (singlet, 3H, C8 methyl), 2.32 (broad singlet, 1H; removed by D₂O exchange; hydroxyl proton), 2.50 (doublet, J 5.5 Hz, 1H, C7 proton), 2.79 (singlet coincident with broadened doublet, separable by Eu(fod)₃ addition; 3 + 1H, N-methyl and C2 proton), 3.52 (singlet; sharpened by addition of D₂O; 1H, C11 proton), 3.67 (multiplet, 1H, C6 proton),
4.08 (multiplet, 1H, C3 proton), 6.88-7.34 (multiplet, 10H, aromatic protons).

Reduction of isomeric mixtures of 1,4,8-trimethyl-9,10-diphenyl-4-azatetracyclo[6.2.1.0^2.0^7.0^8]undeca-9-ene-5,11-dione (139a)

Isomeric mixtures of (139a) were reduced with sodium borohydride by the method described above for the pure exo,anti-isomer. Preparative layer chromatography (70% ethyl acetate-petroleum spirit (b.p. 60-80°) as the eluting solvent mixture) of the alcohol mixture obtained gave a band at R_f 0.6 which contained the syn,exo,anti-alcohol (152), identical to that obtained by the reduction of the exo,anti-ketone (140a), and a band at R_f 0.5 containing a mixture of the syn,endo,anti-alcohol (153) and the anti,endo,anti-alcohol (154). Recrystallisation from ethanol gave a sample m.p. 180-188°, containing (153) and (154) in the ratio 2:1. \( \lambda_{\text{max}} \) 273, 233 nm; \( \epsilon \) 6800, 8350. \( \nu_{\text{max}} \) 3500s, 1725s, 1421w, 1275m, 1155w, 1093m, 1075m, 743w, 705m cm\(^{-1}\). P.m.r. (CDCl\(_3\)): \( \delta \) 1.29-1.37 (overlapping C-methyl pairs), 2.04 (broad singlet, hydroxyl protons), 2.64 (doublet, \( J \approx 8 \text{ Hz} \)), 2.79 (overlapping N-methyls coincident with C2 protons), 3.25 (multiplet), 3.51 (multiplet), 3.76 (multiplet), 6.84-7.32 (aromatic protons). Mass spectrum: \( m/e \) 372 (22%), 371 (M^+), 73, 354 (loss of OH, 10), 314(34), 288(21), 273(23), 272(38), 263(24), 262(94), 260(25), 259(60), 258(100), 257(22), 255(22), 247(22), 244(25), 243(26), 241(21), 232(20), 229(25), 228(25), 215(28), 202(24), 184(26), 179(20), 178(34), 165(36), 152(20), 149(43), 141(20), 128(20), 115(36), 105(58), 91(46), 84(30), 77(43), 71(25), 57(40), 55(36), 43(54), 42(63), 41(33); all other peaks less than 20%.

endo,anti-1,4,8-Trimethyl-9,10-diphenyl-4-azatetracyclo[6.2.1.0^2.0^7.0^8]undeca-9-ene-5,11-dione (141a)

endo,anti-11-Hydroxy-1,4,8-trimethyl-9,10-diphenyl-4-azatetracyclo-
[6.2.1.0²,7.0³,6]undec-9-en-5-one (epimeric mixture of (153) and (154), 203 mg, 0.55 mmol) was dissolved in dry acetone (20 ml) and stirred with excess Jones reagent (2 ml of a solution of 1.4 g of chromium trioxide and 1.22 ml of concentrated sulphuric acid in 10 ml of water) for 10h at room temperature. Isopropanol (40 ml) and water (100 ml) were added and the solution stirred for a further 30 min. Chloroform extraction of the solution gave a solid which was purified by preparative layer chromatography (70% ethyl acetate-petroleum spirit (60-80°)) to give (141a) (151 mg, 75%). Recrystallisation from benzene-petroleum spirit (60-80°) gave rosettes of white needles, m.p. 192° (dec.). (Found: C, 81.25; H, 6.29; N, 3.68. C_{25}H_{23}NO_2 requires C, 81.27; H, 6.29; N, 3.79%).

P.m.r. (CDCl_3): δ 1.37 (singlet, 3H, C-methyl), 1.42 (singlet, 3H, C-methyl), 2.78 (doublet, J 6.3 Hz, 1H, C7 proton), 2.83 (singlet, 3H, N-methyl), 2.98 (doublet of triplets, J 6.3 and 1.2 Hz, 1H, C2 proton), 3.65 (multiplet, 1H, C6 proton), 3.85 (multiplet, 1H, C3 proton), 6.96-7.40 (multiplet, 10H, aromatic protons).

2-Azabicyclo[2.2.0]hex-5-en-3-one (118b)

A solution of 2-pyridone (5.0 g) in ethanol (1000 ml) was irradiated for 44 h with a 450 W medium pressure mercury lamp through a Corex filter. The solvent was removed in vacuo at 30° and the residue extracted with ether (2 x 75 ml). The ether extracts were combined and evaporated to give (118b) (3.6 g, 72%). Further purification could be effected by vacuum sublimation (ambient temperature, 0.05 mm) which gave a white solid, m.p. 60-63°, (lit. m.p. 65.5-66.5°85), which quickly discoloured upon atmospheric contact. \( \nu_{max} \) 3200, 1730brs, 1273m, 1141m, 1121m, 972m, 938m, 827w, 777m, 703m cm\(^{-1}\); (CHCl_3) 1755 cm\(^{-1}\) (C=O stretch). P.m.r. (CDCl_3): δ 4.17 (multiplet, 1H, C4 proton), 4.46 (multiplet, 1H, C1 proton), 6.60 (multiplet, 1H, C5 proton), 6.68 (multiplet, 1H, C6 proton). Mass spectrum: \( m/e \) 95 (M^+, 26%), 67(14), 53(6), 52(100), 51(20),
1,8-Dimethyl-9,10-diphenyl-4-azatetracyclo[6.2.1.02,7.03,0]undeca-8-ene-6,11-dione (139b)

2-Azabicyclo[2.2.0]hex-5-en-3-one (118b) (1.6g, 16.8 mmol) and 2,5-dimethyl-3,4-diphenylcyclopenta-2,4-dienone dimer (4.38 g, 16.8 mmol of monomer) were heated together under reflux in chloroform (10 ml) for 4h. The crystals which formed when the reaction mixture cooled were filtered off and washed with cold methanol to give pure exo,anti-isomer (140b) (1.3 g). The filtrate was evaporated and the residue purified by column chromatography (silica gel; 3% ethanol-chloroform as eluting solvent) to give a total yield of (139b) of 4.6 g (75%).

The (major) exo-anti-isomer (140b) crystallised preferentially from methanol as fine white needles, m.p. 253° (dec.). (Found: C, 81.09; H, 5.93; N, 3.82. C24H21NO2 requires C, 81.10; H, 5.96; N, 3.94%).

λmax 259, 227 nm; ε 7800, 10600. νmax 3170m, 1745s, 1710m, 1156m, 1005w, 778m, 760w, 703 s cm⁻¹. P.m.r. (CDCl₃): δ 1.21 (singlet, 6H, C-methyls), 2.79 (doublet, J 6.5 Hz, 1H, C7 proton), 2.98 (broadened doublet, J 6.5 Hz, 1H, C2 proton), 3.37 (multiplet, 1H, C6 proton), 3.77 (multiplet, 1H, C3 proton), 6.50 (multiplet, 1H, N-H), 6.90-7.32 (multiplet, 10H, aromatic protons). Mass spectrum: m/e 355(M⁺, 3%), 259(23), 258(100), 257(5), 243(14), 242(5), 241(6), 228(6), 215(6), 178(5), 165(6), 115(6).

The (minor) endo,anti-isomer (141b) could be obtained almost pure by fractional crystallisation of the isomer mixture from methanol. P.m.r. (CDCl₃): δ 1.40 (singlet, C-methyls), 2.84 (doublet, J 7.5 Hz, C7 proton), 2.99 (broadened doublet, J 7.5 Hz, C2 proton), 3.67 (multiplet, C6 proton), 4.00 (multiplet, C3 proton), 6.64 (multiplet, N-H), 6.92-7.38 (multiplet, aromatic protons).
1-Phenyl-2-pyridone (114c)

A mixture of 2-pyridone (23.75 g, 0.25 mol), sodium hydroxide (10.0 g, 0.25 mol), iodobenzene (60 g, 0.3 mol) and freshly activated copper bronze (5 g) was heated under reflux in dimethylformamide (100 ml) for 24h. The hot mixture was filtered and the filtrate concentrated in vacuo at 100° to a small volume. The resultant solution was added to water (500 ml) and extracted with chloroform (4 x 100 ml). The chloroform extracts were combined, dried and evaporated. Recrystallisation of the residue from ethanol gave 1-phenyl-2-pyridone (14 g, 33%) as large colourless prisms, m.p. 127-129° (lit. m.p. 128-118°). λ_max 311, 223 nm; ε 5200, 7500. ν_max 1660s, 1605m, 1530m, 1493m, 1276m, 1254m, 1142m, 1128w, 928w, 841m, 759s, 724ms, 696ms cm⁻¹. P.m.r. (CDCl₃): δ 6.13 (triplet, 1H), 6.54 (doublet, 1H), 7.30 (multiplet, 7H).

2-Phenyl-2-azabicyclo[2.2.0]hex-5-en-3-one (118c)

A solution of 1-phenyl-2-pyridone (114c) (2.0 g) in ethanol (1000 ml) was irradiated for 43h with a 450W medium pressure mercury lamp through a pyrex filter. The solvent was removed in vacuo and the residue extracted with ether (total of 300 ml). The extracts were combined and evaporated to give almost pure (118c) (310 mg, 5%). P.m.r. (CDCl₃): δ 4.10 (multiplet, 1H, C4 proton), 4.57 (multiplet, 1H, C1 proton), 6.45 (multiplet, 1H, C5 proton), 6.52 (multiplet, 1H, C6 proton), 7.22 (multiplet, 5H, aromatic protons).

1,8-Dimethyl-4,9,10-triphenyl-4-azatetracyclo[6.2.1.0²,⁷.0³,⁶]undeca-9-ene-5,11-dione (138c)

2-Phenyl-2-azabicyclo[2.2.0]hex-5-en-3-one (118c) (ca 250 mg, 1.46
mmol) and 2,5-dimethyl-3,4-diphenylcyclopenta-2,4-dienone dimer (380 mg, 1.46 mmol of monomer) were heated together under reflux in chloroform (10 ml) for 10h. The solvent was evaporated and preparative layer chromatography (15% ethyl acetate-petroleum spirit (60-80°) as eluting solvent) of the residue gave (139c) (390 mg, 62%) as a mixture of the exo,anti- (140c) and endo,anti-isomers (141c). Fractional crystallisation of this mixture gave samples enriched in (141c) (the minor isomer) but complete separation was not achieved. Two recrystallisations from ethanol gave (139c) (isomer ratio ca 1:1) as fine white needles, m.p. 196° (dec.). (Found: C, 83.56; H, 5.81; N, 3.12. C_{30}H_{25}N_{2}O_{2} requires C, 83.50; H, 5.84; N, 3.25%). λ_{max} 253, 233, 210 nm; ε 15500, 12900, 13400. v_{max} 1775s, 1751s, 1599m, 1495m, 1171w, 1108w, 1028w, 756m, 702m, 665w cm^{-1}. Mass spectrum: m/e 431(M^{+}, 8%), 403 (loss of carbon monoxide, 3), 284(8), 260(6), 259(13), 258(56), 243(9), 241(5), 228(5), 165(5), 146(20), 145(100), 117(17), 116(5), 104(8), 91(5), 77(17); metastable ions at 377(431-403) and 94.4(145-117).

Exo,anti-isomer (140c). P.m.r. (CDCl\textsubscript{3}): δ 1.29 (singlet, 3H, C-methyl), 1.41 (singlet, 3H, C-methyl), 2.86 (doublet, J \approx 6.5 Hz, 1H, C7 proton), 3.10 (broadened doublet, J \approx 6.5 Hz, C2 proton), 3.44 (multiplet, 1H, C6 proton), 4.14 (multiplet, 1H, C3 proton), 6.86-7.42 (multiplet, 15H, aromatic protons).

Endo,anti-isomer (141c). P.m.r. (CDCl\textsubscript{3}): δ 1.41 (singlet, 3H, C-methyl), 1.51 (singlet, 3H, C-methyl), 2.92 (doublet, J \approx 6.5 Hz, 1H, C7 proton), 3.10 (broadened doublet, J \approx 6.5 Hz, 1H, C2 proton), 3.74 (multiplet, 1H, C6 proton), 4.51 (multiplet, 1H, C3 proton), aromatic protons as for (140c).
**Attempted Reaction of 2-Methyl-2-azabicyclo[2.2.0]hex-5-en-3-one (118a) with tetrachloro-o-benzoquinone**

Tetrachloro-o-benzoquinone (1.0 g, 4 mmol) and 2-methyl-2-azabicyclo[2.2.0]hex-5-en-3-one (118a) (0.45 g) were heated together under reflux in benzene (5 ml) for 13 h. The solvent was removed to give a brown gum which contained only 1-methyl-2-pyridone (114a) and polymeric material.

Endo,anti-1,8,9,10-Tetrachloro-11,11-dimethoxy-4-methyl-4-azatetracyclo-[6.2.1.02'7.03'6]-undec-9-en-5-one (159a)

1,2,3,4-Tetrachloro-5,5-dimethoxycyclopentadiene 221 (3.0 g, 11.4 mmol) and 2-methyl-2-azabicyclo[2.2.0]hex-5-en-3-one (0.90 g, 8.3 mmol) were stirred together without solvent at 55° for 11 h. The product was purified by column chromatography (hexane and chloroform as eluting solvents) to give the title compound (159a) as a pale yellow oil (2.3 g, 74%). P.m.r. (CDCl₃): δ 2.82 (s, 3H, N-methyl), 3.09 (doublet, J 6.2 Hz, 1H, C7 proton), 3.26 (doublet of triplets, partly obscured by C6 proton resonance, J ca 6 Hz and ca 1.3 Hz, 1H, C2 proton), 3.52 (singlet, 6H, methoxyl protons), 3.67 (multiplet, 1H, C3 proton).

1,8,9,10-Tetrachloro-11,11-dimethoxy-4-azatetracyclo[6.2.1.02'7.03'6]-undec-9-en-5-one (159b)

2-Azabicyclo[2.2.0]hex-5-en-3-one (118b) (3.6 g) and 1,2,3,4-tetrachloro-5,5-dimethoxycyclopentadiene (10.0 g) were heated under reflux in benzene (30 ml) overnight. The solvent was removed and column chromatography (M&B silica gel; chloroform as eluting solvent) of the residue gave (159b) (3.2 g, 25%) as a pale brown solid, m.p. 135-140°. Recrystallisation from a small amount of methanol gave an analytical sample as fine white needles, m.p. 152-158° (dec.). (Found: C, 40.25; H, 3.30; N, 3.42; Cl, 39.30. C₁₂H₁₁NO₃Cl₄ requires C, 40.14; H, 3.09;
N, 3.90; Cl, 39.50%). $\lambda_{\text{max}}$ end absorption, shoulder at 225 nm; $e$ 2200.

$\nu_{\text{max}}$ 3150m, 3079w, 1760s, 1735m, 1653w, 1268w, 1197m, 1147w, 1120m, 1024m, 981m, 910w, 822w, 805w cm$^{-1}$. P.m.r. (CDCl$_3$): $\delta$ 3.19 (doublet, J 6.7 Hz, 1H, C7 proton), 3.35 (doublet of triplets, partially obscured by C6 proton resonance, J $\alpha$ 6.7 Hz and 1.4 Hz, 1H, C2 proton), 3.43 (multiplet, 1H, C6 proton), 3.57 (singlet, 6H, methoxyl protons), 3.80 (multiplet, 1H, C3 proton), 6.35 (broad singlet, 1H, N-H). Mass spectrum: $^+$ m/e 357(M$^+$ for $^{35}$Cl, trace only), 326(3%), 324(7.4), 322(7.8), 259(7), 258(5), 257(36.7), 256(12), 255(98.5), 254(11), 253(100), 211(5.2), 209(13.5), 207(14.9), 159(5), 59(14); metastable ions at 199(322+253) and 169.5(253-207).

Attempted Deketalisation of 1,8,9,10-Tetracloro-11,11-dimethoxy-4-
36
anatetraacyclo[6.2.1.0$^2$]undec-9-one (159b)

A solution of the title ketal (159) (0.5 g) in dichloromethane (5 ml) was shaken with concentrated sulphuric acid (2 ml) for 4 min. The mixture was run into ice-water (8 ml) and neutralised by addition of sodium bicarbonate. The aqueous phase was extracted with dichloromethane (2 x 30 ml), the extracts combined, washed well with water, dried and evaporated to give a dark brown oil which was not purified or characterised. P.m.r. (CDCl$_3$): $\delta$ 2.48 (broad doublet, J $\alpha$ 15 Hz), 2.84 (broad doublet, J $\alpha$ 15 Hz), 3.22 (broad singlet), 3.55 (singlet, methoxyl protons), 3.63 (singlet, methoxyl protons), 6.36 (broad singlet).

$^+$ Confirmation that the molecular ions at 322, 253 and 207 all contain 3 chlorine atoms is provided by the M:M+2:M+4 ratios, which are in substantial agreement with the theoretical ratios.222
Photolysis of 1,4,8-trimethyl-9,10-diphenyl-4-azatetracyclo[6.2.1.0^2,7.0^3.6]undeca-9-ene-5,11-dione (139a)

(i) in methanol

A solution of the ketone (139a) (111 mg) in methanol (7 ml) was irradiated at -20° in a quartz tube with a low pressure mercury lamp for 1h. The solvent was removed in vacuo at 0° to give a semi-crystalline residue which was found by p.m.r. analysis to be a clean mixture of 1,4-dimethyl-2,3-diphenylbenzene (92)† [p.m.r. spectrum (CDCl₃): δ 2.08 (singlet, 6H, methyls), 6.95-7.30 (multiplet with distinctive singlet at 7.22, 12H, aromatic protons)] together with (z)-(183) and (E)-(184) 3-methylamino-2-propenoic acid methyl ester in the ratio 1.25:1.

(ii) in tetrahydrofuran

A solution of the ketone (139a) (47 mg) in tetrahydrofuran (4 ml) was photolysed at -60° for 2h. The solution was quenched with excess cold methanol (10 ml) and allowed to warm to room temperature. The solvent was evaporated in vacuo to give a crystalline residue containing 1,4-dimethyl-2,3-diphenylbenzene (92) as the only product discernible by p.m.r. analysis.

(iii) in tetrahydrofuran-methanol

The ketone (139a) (119 mg, 0.32 mmol) was photolysed at -30° in tetrahydrofuran (7 ml) containing methanol (103 mg, 3.2 mmol) for 4h. The azetinone (166) formed was trapped quantitatively (as judged by p.m.r. analysis), giving the (Z)-isomer (183) and the (E)-isomer (184) in the ratio 1.25:1.

† This compound could readily be isolated by chromatography generally in quantitative yield, from all 1,2-photoaromatisation reactions. Recrystallisation from methanol gave white crystals, m.p. 111-113° (lit. m.p. 113°223).
(iv) in tetrahydrofuran-methylamine

A solution of the ketone (139a) (200 mg) in tetrahydrofuran (7 ml), which had been presaturated with anhydrous methylamine, was irradiated at -10° for 4h. The solvent was evaporated in vacuo to give a mixture of 1,4-dimethyl-2,3-diphenylbenzene (92) together with (2)-(185) and (E)-N-methyl-3-methylamino-2-propenoic amide (186) and several minor products. Preparative layer chromatography (20 x 20 cm silica plates, chloroform as eluting solvent) failed to yield either (185) or (186). The major band at Rf 0.45 gave a semi-pure unidentified compound, p.m.r. (CDCl3): δ 1.21 (singlet, 6H), 2.56 (singlet, 3H), 3.12 (multiplet, 1H), 3.40 (multiplet, 1H), 6.92-7.30 (aromatic protons), 7.88 (broadened doublet, J ca 7 Hz), which was not further investigated. The ratio of (185) to (186), as judged from the crude p.m.r. spectrum, was 1.2:1 and the total yield of these compounds less than 50%.

(v) in furan

A solution of the ketone (139a) 200 mg) in furan (7 ml) was photolysed at -30° for 3.5h. The solvent was removed in vacuo to give a residue of 1,4-dimethyl-2,3-diphenylbenzene (92) together with products exhibiting the following p.m.r. signals: δ 2.65 (doublet, J 5.5 Hz), 2.98 (doublet, J 4.5 Hz), 4.66 (multiplet), 6.21 (broad singlet), 6.60- (obscured by aromatics) (multiplet). Attempts to isolate these compounds by preparative layer chromatography on silica gel were not successful.

(vi) attempted trapping with benzaldehyde

A solution of the ketone (139a) (90 mg, 0.244 mmol) and benzaldehyde (33 mg, 0.31 mmol) in tetrahydrofuran (1 ml) was photolysed at -65° for 4h. The bright yellow solution which resulted was allowed to warm to room temperature and the volatiles removed in vacuo. P.m.r. analysis of
the residue indicated complete consumption of both (139a) and benzaldehyde. T.l.c. analysis (silica, chloroform as eluting solvent) indicated at least 9 compounds were present, the highest Rf component being 1,4-dimethyl-2,3-diphenylbenzene (92). The mixture was not further investigated.

Photochemical Conversion of 3-methylamino-2-propenoic acid methyl esters (183) and (184)

A solution in perdeuteriomethanol (0.3 ml) of the (Z)-isomer (183) and the (E)-isomer (184) (30 mg total) in the ratio 11:1 was irradiated at -20° using a vycor filtered low pressure mercury lamp. The isomerisation was monitored by p.m.r. spectroscopy, the isomer ratios being based on the relative N-methyl peak heights. After 120 min the (Z):(E) ratio was 3:1; after 240 min, 2.4:1; after 300 min, 2.4:1.

(Z)-3-Methylamino-2-propenoic acid methyl ester (183)

Anhydrous methylamine was slowly bubbled through a solution of methyl propiolate (2.1 g) in benzene (10 ml) at room temperature for 2h. The solvent was evaporated in vacuo at 25° to give a liquid containing the (Z)-isomer (183) and the (E)-isomer (184) in the ratio 2:3. Distillation caused considerable decomposition but gave the pure (Z)-isomer (183) (2.0 g, 69%), b.p. 80°/18 mm, lit. b.p. 90-93°/8 mm\(^{224}\). P.m.r. (CDCl\(_3\)): \(\delta\) 2.97 (doublet, 3H, N-methyl, J 5 Hz), 3.66 (singlet, 3H, O-methyl), 4.51 (doublet, J 8 Hz, 1H, C2 proton), 6.64 (doublet of doublets, J(H2,H3) 8 Hz, J(H3,NH) 13 Hz, 1H, C3 proton), 7.70 (broad singlet, 1H, amino proton).

(E)-3-Methylamino-2-propenoic acid methyl ester (184)

The (Z)-isomer (183) was allowed to stand at room temperature for 3 months. This gave (E)-isomer (184) of ca 90% purity. P.m.r. (CDCl\(_3\)): \(\delta\) 2.77 (doublet, 3H, N-methyl, J 5 Hz), 3.68 (singlet, 3H, O-methyl),
4.70 (doublet, J 13 Hz, C2 proton), 5.8 (broad singlet, 1H, amino proton),
7.66 (doublet of doublets, J(H2,H3) 13 Hz, J(H3,NH) 7 Hz, 1H, C3 proton).

(Z)- and (E)-N-methyl-3-methylamino-2-propenoic amides, (185) and (186)

Methyl propiolate (8.4 g, 0.1 mol) was added dropwise over 5 min
to a stirred solution of 33% alcoholic methylamine (30 ml, equivalent to
0.3 mol of methylamine) which was maintained at -70°. After 15 min
further stirring, the solution was allowed to warm to room temperature.
A check indicated that it contained almost pure N-methylpropiolamide
(189) [p.m.r. (CDCl3): δ 2.80 (doublet, J εa 4 Hz, 3H, N-methyl),
2.98 (singlet, 1H, alkyne proton), 7.71 (broad singlet, 1H, amino
proton)]. Stirring was continued for 16h to give a mixture containing
(189) in addition to the (Z)-(185) and (E)-(186) isomers in the ratio
εa 1:1:1. Longer reaction times led to extensive decomposition of
(185) and (186). P.m.r. (CDCl3): [(Z)-isomer (185)] δ 2.66-2.90 (N-methyls),
4.37 (doublet, J 7.5 Hz, C2 proton), 6.55 (doublet of doublets, J(H2,H3)
7.5 Hz, J(H3,NH) 13.6 Hz, C3 proton); [(E)-isomer (186)] 2.66-2.90
(N-methyls), 4.68 (doublet, J 13.0 Hz, C2 proton), 7.45 (doublet of
doublets, J(H2,H3) 13.0 Hz, J(H3,NH) 12.4 Hz, C3 proton).

Photolysis of 1,8-dimethyl-9,10-diphenyl-4-azatetracyclo[6.2.1.02,7.02,6]-
undeca-9-ene-5,11-dione (139b)

A solution of the ketone (139b) (100 mg) in tetrahydrofuran (7 ml)
containing methanol (3 ml) was irradiated at 0° for 2h. The solvent was
removed in vacuo to give a residue which p.m.r. analysis showed to be a
clean mixture of 1,4-dimethyl-2,3-diphenylbenzene together with (Z)-(193)
and (E)-(194) 3-amino-2-propenoic acid methyl esters in the ratio 3:1.
(Z)- and (E)-3-amino-2-propenoic acid methyl esters (193) and (194)

Methyl propiolate (10 g, 0.12 mol) was stirred for 1 week at room temperature in a solution of benzene (30 ml) which was maintained saturated with ammonia. Removal of the solvent gave a mixture of (Z)-193 and (E)-194 isomers in the ratio 2.4:1. Distillation of the mixture up a column of glass helices led to extensive decomposition but gave 3.0 g (25%) of pure (Z)-isomer (193) as a colourless liquid, b.p. αα 20°/0.04 mm. λ max 270 nm; ε 16400. ν max 3460s, 3350s, 2980w, 2938m, 1660s, 1630s, 1550s, 1454s, 1423m, 1311s, 1221s, 1158s, 1091m, 1012w, 912w, 796m, 747m, 670w cm⁻¹. P.m.r. (CDCl₃): δ 3.67 (singlet, 3H, O-methyl), 4.52 (doublet with upfield line broadened; addition of D₂O gives a sharp doublet, J (olefinic) 8.7 Hz; 1H, C2 proton), 5.48 (very broad singlet, 1H, NH), 6.77 (triplet of doublets, J (olefinic) 8.2 Hz, J(H3-NH) 10.9 Hz; addition of D₂O gives a broadened doublet showing extra coupling†; 1H, C3 H), 7.28 (broad singlet, 1H, NH). Mass spectrum: m/e 101(M⁺, 45%), 71(6), 70(100), 68(5), 43(22), 42(25), 41(19), 40(10).

(E)-isomer (194). P.m.r. (CDCl₃): δ 3.67 (singlet, 3H, O-methyl), 4.91 (doublet, J 13.1 Hz, 1H, C2 proton), 7.50 (triplet of doublets, J (olefinic) 13.1 Hz, J(H3,NH) 11 Hz; still considerable coupling after addition of D₂O; 1H, C3 proton), NH chemical shifts uncertain.

Photolysis of 1,8-dimethyl-4,9,10-triphenyl-4-azatetracyclo[6.2.1.0²,⁷.0²,⁶]-undeca-9-ene-5,11-dione (139c)

(i) A deuteriochloroform solution of the ketone (139c) (αα 30 mg in 0.2 ml) in a quartz n.m.r. tube was photolyzed at -30°. Monitoring by p.m.r. spectroscopy at 30 min intervals failed to show evidence for the formation of any product but 1,4-dimethyl-2,3-diphenylbenzene. Particularly, the absence of signals at δ 6.19 and 8.24 confirmed that 4-quinolone (197) had not formed.

† probably coupling to deuterium.
(ii) A solution of the ketone (139c) (100 mg) in tetrahydrofuran was photolysed at -30° for 3 h. The solvent was removed in vacuo to give a residue containing (92) as the only product discernible by p.m.r. spectroscopy.

4-Quinolone (197)

4-Quinolone (197) was prepared from (E)-3-anilino-2-propenoic acid methyl ester in 38% yield by the method of Heindel et al. Recrystallisation from ethanol gave white crystals, m.p. 203° (lit. m.p. 209-211°). P.m.r. (DMSO-\textsubscript{d}\textsubscript{6}): δ 6.26 (doublet, J \textsubscript{\alpha} 7.5 Hz, 1H), 7.30 (multiplet, 1H), 7.58 (multiplet, 2H), 7.92 doublet, J \textsubscript{\alpha} 8 Hz, 1H), 8.13 (doublet, J \textsubscript{\alpha} 8 Hz, 1H), 11.8 (broad singlet, 1H, NH). Upfield doublet appears at δ 6.19 in deuteriochloroform solution.

Pyrolysis of 1,4,8-trimethyl-9,10-diphenyl-4-azatetracyclo[6.2.1.0\textsuperscript{2,7}.0\textsuperscript{3,6}]undec-9-ene-5,11-dione (139a)

The ketone (139a) (mixture of exo,anti- and endo,anti-isomers, (0.5 g) was heated without solvent under a nitrogen atmosphere at 190° for 75 min. Preparative layer chromatography of the residue (30% ethyl acetate-chloroform as the eluting solvent mixture) gave a band at R\textsubscript{f} 0.6 which yielded a mixture of 3,7,10-trimethyl-8,9-diphenyl-3-azatricyclo[4.4.0.0\textsuperscript{2,5}]dec-7,9-dien-4-one (165) and 3,6,9-trimethyl-4,5-diphenyl-9-azabicyclo[6.2.0]dec-2,4,6-trien-10-one (207) (0.20 g, 43%) in the ratio 1:4 (p.m.r. spectrum (CDCl\textsubscript{3}) of the diene (165): δ 1.52 (singlet, C-methyls), 2.94 (singlet, N-methyl), 2.82-3.23 (C1 and C6 protons, region obscured by small peaks due to impurities), 3.73 (multiplet, C5 proton) 3.95 (multiplet, C2 proton), 6.70-7.26 (multiplet, aromatic protons)].
A solution of 4-phenyl-1,2,4-triazoline-3,5-dione in chloroform was added dropwise to a solution of the diene (165) and the triene (207) in chloroform until a red colour persisted. The solution was concentrated in vacuo and the components separated by preparative layer chromatography (40% ethylacetate-petroleum spirit as eluting solvent).

The band at $R_f$ 0.5 gave the pure triene (165) (0.11g, 24%) as a yellow gum which could not be induced to crystallise. $\nu_{\text{max}}$ (CHCl$_3$) 1746 (C=O stretch) cm$^{-1}$. P.m.r. (CDCl$_3$): $\delta$ 1.77 (doublet of doublets, 3H, C6 methyl), 1.87 (doublet of doublets, 3H, C3 methyl), 2.84 (singlet, 3H, N-methyl), 4.27 (multiplet, 1H, C1 proton), 4.48 (multiplet, 1H, C8 proton), 5.47 (broadened quartet, $J$ 1.5 Hz, 1H, C7 proton), 5.62 (broadened quartet, $J$ 1.9 Hz, C2 proton), 7.19 (multiplet, 10H, aromatic protons).

The band at $R_f$ 0.1 gave 1,4,8-trimethyl-11,14,15-triphenyl-4,9,11,13-tetra-azapentacyclo[6.5.2.0$^{6,7}.0^{10},0^{13}]$pentadec-14-ene-5,10,12-trione (209) (55 mg, 8%). One recrystallization from ethyl acetate gave an analytical sample as tiny white needles, m.p. 272° (dec.). (Found: C, 74.03; H, 5.68; N, 10.59. C$_{32}$H$_{28}$N$_4$O$_3$ requires C, 74.40; H, 5.46; N, 10.85%). $\lambda_{\text{max}}$ 263 (shoulder), 259 (shoulder), 236 nm; $\epsilon$ 7600, 8100, 10100. $\nu_{\text{max}}$ 1752s, 1714s, 1505m, 1408m, 1211w, 1113w, 1081m, 1024m, 776w, 750m, 702m cm$^{-1}$. P.m.r. (CDCl$_3$): $\delta$ 1.75 (singlet, 3H, C-methyl), 1.78 (singlet, 3H, C-methyl), 2.90 (partially obscured doublet, 1H, C7 proton), 2.88 (singlet, 3H, N-methyl), 3.05 (doublet, $J$ ca 7 Hz, 1H, C2 proton), 3.52 (multiplet, 1H, C6 proton), 3.79 (multiplet, 1H, C3 proton), 6.83-7.28 (multiplet, 10H, C14 and C15 phenyls), 7.43 (broad singlet, 5H, N-phenyl). Mass spectrum: $m/e$: 518(8%), 517(36), 516(M$^+$, 100), 393(15), 340(24), 313(10), 312(23),

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† prepared by oxidation of 4-phenyl-1,2,4-triazolidine-3,5-dione with nitrogen dioxide.

‡‡ Identical results were obtained when a mixture of (165) and (207) was allowed to stand with excess trizolidinedione (208) at room temperature for 15h.
304(38), 298(27), 283(19), 282(24), 260(22), 259(16), 258(64), 257(17),
243(34), 242(16), 241(15), 228(20), 215(10), 178(10), 165(12), 119(12),
91(12), 42(12); all other peaks less than 10%. Metastable ions at
154.5, 229.0(258-243).

Reaction of 2-azabicyclo[2.2.0]hex-5-en-3-one (118b) with 2-pyrone (232)

A solution of 2-azabicyclo[2.2.0]hex-5-en-3-one (118b) (5.5 g, ca
80% pure, ca 0.046 mol) and 2-pyrone (232)† (6 g, 0.062 mol) in chloroform
(10 ml) was heated with stirring at 60° (oil bath temperature) for 3 days.
The chloroform was evaporated in vacuo and the excess 2-pyrone distilled
from the mixture at 75°/0.08 mm. Preparative layer chromatography (10
plates, 10% ethanol-chloroform) of the residue gave 2 diffuse bands at
ca Rf 0.8 (3.5 g) and Rf 0.5 (3.2 g).

The Rf 0.8 mixture was separated by column chromatography (Koch-
Light 200-300 mesh silica gel; 100 ml fractions; elution with chloroform
for fractions 1-15, then 3% ethanol-chloroform). Fractions 17-20 gave a
mixture of isomers 1 and 2* (total of 1.2 g). Early fractions were
enriched in isomer 1 but complete separation was not achieved. Fractions
21-23 contained predominantly isomer 2, with increasing amounts of isomer
3 (0.32 g). Fractions 24-27 contained mainly isomer 3 (0.81 g). Attempts
to crystallise the crude isomer 3 failed and the resultant gum decomposed
slowly. The combined residues from fractions 18-20 were crystallised
from a small volume of methanol to give an isomeric mixture as fine white
needles, m.p. 160-163° (dec.). (Found: C, 62.73; H, 4.54; N, 7.29.
C₁₀H₉N₂O₃ requires C, 62.82; H, 4.74; N, 7.33%). λ max 210 nm (end
absorption); ε 1450. ν max 3205s, 3085w, 1755s, 1357m, 1180m, 1152m,

† Prepared by the vapour phase pyrolysis of coumalic acid. 159

* Isomers 1 to 5 are unidentified isomers of 4-aza-9(10)-oxatetracyclo-
[6.2.2.0²⁷.0³⁶]dodec-11-en-5,10(9)-dione [(235) and (236)].
1120m, 1030m, 995m, 970m, 909m, 718s cm⁻¹. Mass spectrum: m/e 191(M⁺, < 1%), 147 (loss of carbon dioxide, 11), 146(7), 134(5), 122(5), 120(5), 119(19), 118(17), 105(8), 104(60), 103(19), 98(10), 95(26), 92(5), 91(25), 89(5), 80(7), 79(14), 78(100), 77(17), 70(10), 69(54), 68(11), 67(33), 66(8), 65(15), 63(12), 53(7), 52(23), 51(22), 50(11), 44(82), 42(18), 41(17); metastable ion at 58.5(104→78).

The Rf 0.5 mixture was also separated by column chromatography (Merck 70-325 mesh silica gel; elution with 5% ethanol-chloroform; 100 ml fractions). Fractions 6 and 7 gave a ca 1:1 mixture of 3-azatricyclo-[4.4.0.0²⁷]deca-7,9-dien-4-one (237) and 9-azabicyclo[6.2.0]deca-2,4,6-trien-10-one (238). [P.m.r. spectrum of (237) (CDCl₃): δ 3.25 (multiplet, 2H, Cl and C6 protons), 3.68 (multiplet, 1H, C5 proton), ca 3.96 (multiplet coincident with Cl proton of (238), 1H, C2 proton) 5.50-5.88 (multiplet, ca 4H, olefinic protons)]. Fraction 12 gave a mixture of isomers 4 and 5 in the ratio ca 3:2 (0.09 g). Fraction 13 (250 ml) yielded almost pure isomer 5 contaminated with 2-pyridone (0.20 g). Subsequent fractions consisted largely of 2-pyridone.

The p.m.r. spectra of all isomers are depicted in Figure 2.12.

9-Azabicyclo[6.2.0]deca-2,4,6-trien-10-one (238)

A mixture of isomers 1 and 2 [(235) or (236)] (1.67 g) was heated in vacuo (0.25 mm) at 175°. The sublimate from the pyrolysis was collected on an ice-cooled cold-finger. Preparative layer chromatography of the sublimate gave, in addition to unreacted starting material, 0.50 g (39%) of 9-azabicyclo[6.2.0]deca-2,4,6-trien-10-one (238) and 3-azatricyclo[4.4.0.0²⁷]deca-7,9-dien-4-one (237) in the ratio 3:1. Two recrystallisations from benzene/hexane gave the title compound (238) as white needles, m.p. 94-96°, which yellowed on prolonged atmospheric contact. (Found: C, 73.50; H, 5.95; N, 9.31. C₉H₇NO
requires C, 73.45; H, 6.16; N, 9.52%). \( \lambda_{\text{max}} \) 243 nm; \( \epsilon \) 1700. \( \nu_{\text{max}} \) 3215 s, 3092 w, 1742 s, 1317 m, 1290 w, 1221 w, 1180 m, 832 m, 809 m, 777 m, 695 m cm\(^{-1}\).

P.m.r. (CDCl\(_3\)): \( \delta \) 3.96 (multiplet, 1H, C1 proton), 4.36 (multiplet, 1H, C8 proton), 5.93 (multiplet, 6H, olefinic protons), 6.64 (broad singlet, 1H, amido proton). Mass spectrum: \( m/e \) 147(M\(^{+}\), 5%), 146(5), 118(12), 117(6), 105(10), 104(100), 103(30), 91(16), 80(5), 79(5), 78(55), 77(11), 69(11), 67(7), 65(9), 63(8), 52(10), 51(13), 50(7); metastable ion at 58.5 (104→78).

Thermolysis of the lactone adducts [(235) or (236)] in trigol

A mixture of isomers 1 and 2 [(235) or (236)] (400 mg) was heated under reflux in trigol (b.p. 275-295\(^{\circ}\)) (20 ml) for 8 min. The solution was cooled, poured into chloroform (100 ml) and extracted twice with water. The chloroform solution was dried and evaporated to give a mixture of at least 10 products (as judged by t.l.c.). Preparative layer chromatography (5% ethanol-chloroform as eluting solvent) enabled the isolation of 1-isoquinolone (248) (25 mg, 8%). Recrystallisation from acetone gave (248) white needles, m.p. 208\(^{\circ}\) (lit. m.p. 208\(^{\circ}\) 228\(^{\circ}\)). \( \lambda_{\text{max}} \) 336 (shoulder), 322, 313 (shoulder), 281, 274, 245, 236, 229 nm. 229 P.m.r. (CDCl\(_3\)): \( \delta \) 6.66 (doublet, 1H), 7.36 (multiplet, 2H), 7.68 (multiplet, 2H), 8.54 (slightly broadened doublet, 1H). Mass spectrum: \( m/e \) 147(5), 146(18), 145(M\(^{+}\), 100), 118(26), 117(14), 116(9), 90(27), 89(25), 63(12), 62(5).

1-Carbomethoxy-1,2-dihydropyridine (259a)

1-Carbomethoxy-1,2-dihydropyridine was prepared by the method of Fowler,\(^{86}\) giving \( \approx \) 90% pure product which was used for all further preparations. P.m.r. (CDCl\(_3\)): \( \delta \) 3.79 (singlet, 3H, O-methyl), 4.40 (multiplet, 2H, C2 protons), 5.16 (broad triplet, 1H), 5.58 (multiplet, 1H), 5.82 (multiplet, 1H), 6.75 (Multiplet, 1H).
2-Carbomethoxy-2-azabicyclo[2.2.0]hex-5-ene (260a)

A solution of 1-carbomethoxy-1,2-dihydropyridine (259a) (10 g) in dichloromethane (1 l) was irradiated for 16h using a 450W American Hanovia lamp and Corex filter. The solvent was removed in vacuo below 40° to give a brown oil which was extracted with cold ether (2 x 150 ml). The ether extracts were combined and evaporated to give a clear yellow oil containing ca 40% of (260a), which was used for all further preparations. P.m.r. (CDCl₃): δ 3.68 (singlet, 0-methyl), 4.86 (multiplet, C1 proton), 6.57 (multiplet, C5 and C6 protons), other assignments ambiguous.

exo,anti-4-Carbomethoxy-1,8-dimethyl-9,10-diphenyl-4-azatetracyclo-[6.2.1.0²7.0³6]undec-9-en-11-one (267)

2-Carbomethoxy-2-azabicyclo[2.2.0]hex-5-ene (260a) (total crude from a 10 g scale preparation; ca 4 g, 0.029 mol) and the dimer of 2,5-dimethyl-3,4-diphenylcyclopenta-2,4-dienone (6.0 g, 0.023 mol of monomer) were heated together under reflux in chloroform (20 ml) for 3h. The solvent was removed and the residue purified by column chromatography (M&B silica gel; chloroform as eluting solvent) to give a mixture of the exo,anti-(267) and endo-anti-(268) adducts (9.0 g, 31% from (259a)). Recrystallisation from methanol gave the exo,anti-isomer (267) pure. A further recrystallisation gave an analytical sample as fluffy white needles, m.p. 155-165° (dec.). (Found: C, 78.42; H, 6.36; N, 3.37. C₂₆H₂₅NO₃ requires C, 78.17; H, 6.31; N, 3.51%). λₘₐₓ 259, 227 nm; ε 10000, 13400. νₘₐₓ 1761s, 1693s, 1210m, 1161m, 1114m, 785m, 712ms cm⁻¹. P.m.r. (CDCl₃): δ 1.20 (singlet, 3H, C8 methyl), 1.27 (very slightly broadened singlet, 3H, C1 methyl), 2.59 (multiplet, 1H, C6 proton), 2.81 (broadened doublet, J 6.8 Hz, 1H, C7 proton), 2.94 (broad singlet; sharpens to doublet, J ca 6.8 Hz, at 40°; 1H, C2 proton), 3.72 (singlet, 3H, 0-methyl), 4.04 (doublet of doublets, J (gem) 9.0 Hz, J (vic) 2.2 Hz, 1H, C5 proton syn to cyclobutyl ring), 4.28 (partially obscured
multiplet, 1H, C3 proton), 4.39 (doublet of doublets, J (gem) 9.0 Hz, J (vic) 7.1 Hz, C5 proton anti to cyclobutyl ring), 6.96-7.12 (multiplet, 10H, aromatic protons). Mass spectrum: m/e 399(M+, <1%), 371 (loss of carbon monoxide, <1), 284(14), 269(5), 259(23), 258(100), 257(5), 243(11), 178(5), 165(9), 140(18), 139(11), 138(11), 124(6), 116(5), 115(11), 91(8), 59(12), 42(7); metastable ion at 229 (258-243).

syn,exo,anti-4-Carboxethoxy-1,8-dimethyl-9,10-diphenyl-4-azatetracyclo-[6.2.1.0^2,7.0^3,6]undec-9-en-11-ol (269)

exo,anti-4-Carboxethoxy-1,8-dimethyl-9,10-diphenyl-4-azatetracyclo-
[6.2.1.0^2,7.0^3,6]undec-9-en-11-one (267) (300 mg) and sodium borohydride (100 mg) were stirred together in ethanol (15 ml) at room temperature for 12h. The mixture was poured into water and extracted with chloroform (300 mg, 100%) as a colourless oil which crystallised when triturated with petroleum spirit. Recrystallisation from benzene-hexane gave an analytical sample as white prisms, m.p. 214-216°. (Found: C, 78.00; H, 6.49; N, 3.52. C_{26}H_{27}NO_{3} requires C, 77.78; H, 6.78; N, 3.49%).

λ_max 258, 229 nm; ε 5900, 7000. v_max 3470 (sharp OH), 1678s, 1197m, 1151m, 1127m, 1082m, 979m, 764ms cm^{-1}. P.m.r. (CDCl_3): δ 1.27 (singlet, 3H, C8 methyl), 1.32 (slightly broadened singlet, 3H, C1 methyl), 2.32 (broad singlet; disappears upon addition of D_2O; 1H, hydroxyl proton), 2.59 (doublet, J 6.4 Hz, 1H, C7 proton), 2.72 (broad singlet; sharpens slightly on warming to 40°; 1H, C2 proton), 3.00 (broad multiplet, 1H, C6 proton), 3.39 (singlet; sharpens upon addition of D_2O; 1H, C11 proton), 3.68 (singlet, 3H, O-methyl), 3.83 (doublet of doublets, J (gem) 9 Hz, J (vic) 2.7 Hz, 1H, C5 proton syn to cyclobutyl ring), 4.31 (doublet of doublets J (gem) 9 Hz, J (vic) 7.1 Hz, 1H, C5 proton anti to cyclobutyl ring), 4.68 (broad multiplet, 1H, C3 proton), 6.88-7.24 (multiplet, 10H, aromatic protons).
exo, anti-1,8-Dimethyl-9,10-diphenyl-4-azatetracyclo[6.2.1.0^2,7.0^3,6]undec-9-en-11-one (270)

exo, anti-4-Carbomethoxy-1,8-dimethyl-9,10-diphenyl-4-azatetracyclo[6.2.1.0^2,7.0^3,6]undec-9-en-11-one (267) (3.9 g, 9.8 mmol) was heated under reflux in 400 ml of a 10% w/v solution of potassium hydroxide in 85% aqueous methanol for 14h. The solution was poured into water (500 ml) and extracted with chloroform (3 x 100 ml). The chloroform extracts were combined, washed well with water, dried and evaporated to give (270) as a crude brown oil (ca 3.5 g). Attempted chromatography on both silica gel and neutral alumina caused extensive decomposition and effected little purification. P.m.r. (CDCl₃): δ 1.20 (two overlapping singlets, 6H, C methyls), 2.2-3.0 (broad multiplet, 3H?), 3.4-4.4 (very broad multiplet, 4H?), 6.98-7.32 (multiplet, 10H, aromatic protons).

exo,anti-1,8-Dimethyl-9,10-diphenyl-4(p-toluenesulphonyl)-4-azatetracyclo[6.2.1.0^2,7.0^3,6]undec-9-en-11-one (271)

exo,anti-1,8-Dimethyl-9,10-diphenyl-4-azatetracyclo[6.2.1.0^2,7.0^3,6]-undec-9-en-11-one (270) (crude from the previous preparation) was stirred with p-toluenesulphonyl chloride (1.86 g, 9.8 mmol) in pyridine (30 ml) for 2h at room temperature. The solution was poured into water (100 ml) and extracted with chloroform. The chloroform extract was washed with water, dried and evaporated. The residue was allowed to stand under high vacuum to remove residual pyridine and then purified by preparative layer chromatography (chloroform as eluting solvent) to give the title compound (271) (2.6 g, 54% for the 2 steps). Two crystallisations from benzene gave an analytical sample, m.p. 225-226° (dec.) (Found: C, 75.6; H, 5.61; N, 2.67. C₃₁H₂₉NO₃S requires C, 75.12; H, 5.90; N, 2.83%).

λ_max 253, 233 nm; ε 10700, 17200. ν_max 1752 (s, CO stretch), 1165 (s, SO stretch), 1027s cm⁻¹. P.m.r. (CDCl₃): δ 1.13 (singlet, 3H, C8 proton), 1.23 (singlet, 3H, C1 proton), 2.44 (singlet coincident with broad multiplet, 4H, C6 and aromatic methyl protons), 2.87 (slightly broadened...
doublet, J 6.7 Hz, 1H, C7 proton), 3.16 (sharp doublet, J 6.7 Hz, 1H, C2 proton), 4.04-4.17 (multiplet, 3H, C3 and C5 protons), 6.88-7.26 (multiplet, 10H, C9 and C10 phenyl protons), 7.32 (doublet, J 8 Hz, sulphonyl aromatic protons), 7.70 (doublet, J 8 Hz, sulphonyl aromatic protons).

Mass spectrum: m/e 495(M^+; 1%), 285(15), 284(56), 269(9), 259(23), 258(100), 243(10), 236(6), 235(12), 234(7), 155(11), 91(15), 80(6).

\( \text{syn, exo, anti-1,4,8-Trimethyl-9,10-diphenyl-4-azatetracyclo[6.2.1.0^2,7.0^3,6]-undec-9-en-11-ol (273)} \)

Lithium aluminium hydride (0.5 g) was added to a slurry of exo, anti-4-carbomethoxy-1,8-dimethyl-9,10-diphenyl-4-azatetracyclo[6.2.1.0^2,7.0^3,6]-undec-9-en-11-one (267) (1.6 g, 2.5 mmol) in anhydrous ether (100 ml) and the mixture stirred overnight at room temperature. The aluminium salts were decomposed by the addition of 2 ml of 20% aqueous sodium hydroxide. The ether solution, was filtered, dried and evaporated to give 0.2 g of product. Two further extractions of the solid residue with chloroform gave a further 1.02 g of (273) (1.22 g, 82% in total).

Recrystallisation from methanol gave fine white crystals, m.p. 169.5-170.5°. (Found: C, 84.16; H, 7.83; N, 3.78. C_{25}H_{27}NO requires C, 83.99; H, 7.61; N, 3.92 %). \( \lambda_{\text{max}} \) 257, 227 nm; \( \epsilon \) 6900, 9600. \( \nu_{\text{max}} \) 3440 m, 1112 m, 758 m, 702 s cm\(^{-1}\). P.m.r. (CDCl\(_3\) - DMSO-d\(_6\)): 6 1.17 (singlet C1 and C8 methyls), 1.38 (singlet N-methyl), 2.74-3.02 (multiplet), 3.68 (multiplet), 3.96 (multiplet), 4.88 (broad singlet), 6.88-7.24 (multiplet, aromatic protons). Mass spectrum: m/e 358(19%), 357(M^+; 66), 342(10), 329(20), 328(24), 315(12), 314(44), 300(20), 285(13), 271(17), 262(12), 261(19), 258(13), 257(10), 255(10), 246(10), 243(12), 241(10), 232(23), 230(10), 229(12), 228(10), 129(10), 125(10), 115(15), 109(10), 105(10), 96(45), 95(50), 94(80), 91(25), 82(12), 77(12), 76(11), 75(16), 70(27), 44(100), 42(35); all other peaks less than 10%. 

\( \text{P.m.r.} \)
Oxidation of syn,exo,anti-1,4,8-trimethyl-9,10-diphenyl-4-azatetracyclo-
[6.2.1.0^2,7.0^3,6]undec-9-en-11-ol (273)

The alcohol (273) (400 mg) was stirred with excess Jones reagent
(4 ml of a solution of 1.4 g of chromium trioxide and 1.22 ml of
concentrated sulphuric acid in 10 ml of water) in acetone (40 ml) at
room temperature for 17h. Water (100 ml) and isopropanol (40 ml) at
were added and stirring continued for 30 min. The solution was extracted
with chloroform (3 x 50 ml) and the extracts combined, washed, dried
and evaporated to give an intractable residue. Preparative layer chroma-
tography (10% ethanol-chloroform) of this solid gave 1,4,8-trimethyl-9,10-
diphenyl-4-azatetracyclo[6.2.1.0^2,7.0^3,6]undec-9-en-11-one (261d) (20 mg,
5%). The p.m.r. spectrum of this compound was indistinguishable from
that of the major isomer obtained from the addition of 2-methyl-2-
azabicyclo[2.2.0]hex-5-ene (260d) to the dienone (138).

2-Methyl-2-azabicyclo[2.2.0]hex-5-ene (260d)

2-Carbomethoxy-2-azabicyclo[2.2.0]hex-5-ene (260a) (total crude
from a 10 g scale preparation) in anhydrous ether (100 ml) was added
dropwise to a stirred slurry of lithium aluminium hydride (3.0 g) in
ether (50 ml) at 0°. After a further 90 min stirring, 20% aqueous
sodium hydroxide was added to decompose the aluminium salts. The ether
solution was dried with anhydrous sodium sulphate, filtered and
evaporated in vacuo at room temperature to give a yellow oil (5.2 g)
containing (260d) which was used directly in the next step. P.m.r.
(CDC13): δ 2.28 (singlet, N-methyl), 4.44 (multiplet, C1 proton), 6.36
(multiplet, C5 proton), 6.68 (multiplet C6 proton), other signals
obsured.
1,4,8-Trimethyl-9,10-diphenyl-4-azatetracyclo[6.2.1.0^2.7.0^3.6]undeca-9-en-11-one (261d)

2-Methyl-2-azabicyclo[2.2.0]hex-5-ene (260d) (crude product from above, 5.2 g) and the dimer of 2,5-dimethyl-3,4-diphenylcyclopenta-2,4-dienone (5.2 g) were heated together under reflux in chloroform (20 ml) for 3 h. The solvent was removed and the residue purified by column chromatography (silica gel; chloroform followed by 5% methanol-chloroform as eluting solvents) to give slightly impure (261d) (2.35 g). Further purification by preparative layer chromatography (10% methanol-chloroform as eluting solvent) gave pure (261d) (1.55 g, 6% from (259a)) as a gum which could not be induced to crystallise. \( \lambda_{\text{max}} \) 259, 232 nm, \( \epsilon \) 11000, 13700. \( \nu_{\text{max}} \) (neat) 2940s, 2840m, 1760s, 1721m, 1440s, 1380ms, 1264m, 1182m, 1076m, 759m, 740ms, 705s cm\(^{-1}\). P.m.r. [exo,anti-isomer (274)] (CDC\(_3\)) \( \delta \) 1.20 (singlet, 6H, Cl and C8 methyls), 2.43 (singlet, 3H, N-methyl), 2.53 (multiplet, 1H, C6 proton), 2.73 (slightly broadened doublet, J 6.7 Hz, 1H, C7 proton), 3.09 (doublet, J 6.7 Hz, 1H, C2 proton), 3.39 (doublet of doublets, J (gem) 8.3 Hz, J (vic) 3.2 Hz, 1H, C5 proton \( \text{syn} \) to cyclobutyl ring), 3.55 (doublet, J 4.7 Hz, 1H, C3 proton), 3.84 (doublet of doublets, J (gem) 8.3 Hz, J (vic) \( \alpha \) 7 Hz, 1H, C5 proton \( \text{anti} \) to cyclobutyl ring), 7.00-7.36 (multiplet, 10H, aromatic protons); [endo,anti-isomer (275)] \( \delta \) 1.35 (singlet, Cl and C8 methyls). Mass spectrum: \( m/\epsilon \) 355(M\(^+\), 6%), 312(4), 286(5), 284(10), 258(6), 243(5), 232(11), 215(5), 165(5), 124(6), 115(7), 97(8), 96(100), 95(15), 94(23), 82(6), 69(19), 68(20).

1-Carbobenzoxy-1,2-dihydropyridine (258e)

1-Carbobenzoxy-1,2-dihydropyridine was prepared by a method similar to that used for 1-carbomethoxy-1,2-dihydropyridine,\(^{86}\) to give an 88% yield of almost pure product. P.m.r. (CDC\(_3\)): \( \delta \) 4.40 (multiplet, 2H, C2 protons), 5.20 (singlet coincident with broad multiplet, 2+1H, benzyl...
methylene protons), 5.55 (multiplet, 1H), 5.84 (multiplet, 1H), 6.78 (multiplet, 1H), 7.36 (almost singlet, aromatic protons).

2-Carbobenzoxy-2-azabicyclo[2.2.0]hex-5-ene (260e)

1-Carbobenzoxy-1,2-dihydropyridine (259e) (2 g) in dichloromethane (400 ml) was irradiated with 450W medium pressure mercury lamp through a pyrex filter for 4h. Nitrogen ebulution was maintained during the photolysis. The solvent was removed in vacuo at room temperature. Column chromatography (silica gel; hexane and chloroform as eluting solvents) gave a fraction containing a small quantity (<5%) of the title compound (260e). P.m.r. (CDCl$_3$): $\delta$ 3.40 (multiplet, C4 proton), 3.96 (doublet of doublets, J and J' ca 8 Hz ?, C3 proton), 4.84 (broad singlet, C1 proton), 5.11 (benzyl methylene protons), 6.48 (multiplet, C5 and C6 protons), other protons ambiguous.

1-Methanesulphonyl-1,2-dihydropyridine (258f)

1-Methanesulphonyl-1,2-dihydropyridine was prepared by a method similar to that used for 1-carbomethoxy-1,2-dihydropyridine, except that a slightly longer reaction time was required to give a ca 50% yield of moderately pure product. P.m.r. (CDCl$_3$): $\delta$ 2.93 (singlet, methyl protons), 4.05 (multiplet, C2 protons), 4.88-6.56 (multiplets, olefinic protons).

Photolysis of 1-methanesulphonyl-1,2-dihydropyridine (258f)

A solution of 1-methanesulphonyl-1,2-dihydropyridine (2 g) in dichloromethane (400 ml) was irradiated until complete consumption of starting material with a 450W medium pressure lamp through a Corex filter. No 2-methanesulphonyl-2-azabicyclo[2.2.0]hex-5-ene (260f) was present in the photolysate.
A solution of 1-carbomethoxy-1,2-dihydropyridine (2.15 g) in dichloromethane (20 ml) was added dropwise to a stirred solution of freshly prepared 4-phenyl-1,2,4-triazoline-3,5-dione (2.60 g) in dichloromethane at 0°. After addition the solvent was evaporated and the residue recrystallised from ethyl acetate/hexane to give the title compound as fine white prisms, m.p. 150-154° (dec.); [lit. m.p. 152-156° (dec.)] (Found: C, 56.71; H, 4.55; N, 17.47. \( \text{C}_{15}\text{H}_{14}\text{N}_4\text{O}_4 \) requires C, 57.32; H, 4.49; N, 17.83%). P.m.r. (CDCl\(_3\)): \( \delta \) 3.27 (doublet, \( J \) (gem) 11 Hz, 1H, C9 proton), 3.80 (singlet, 3H, O-methyl), 3.88 (doublet, \( J \) (gem) 11 Hz, 1H, C9 proton), 5.10 (multiplet, 1H, C1 proton), 6.39-6.84 (multiplet, 3H, C7, C10 and C11 protons), 7.39 (multiplet, 5H, aromatic protons). Mass spectrum: \( m/ e \) 314(M\(^+\), 23%), 140(9), 139(100), 138(63), 124(45), 119(8), 94(19), 91(6), 80(19), 59(9), 53(9).

Attempts to prepare the Diels-Alder adduct of this compound and 2,5-dimethyl-3,4-diphenylcyclopenta-2,4-dienone (138) using both chlorobenzene and benzene as solvents, were unsuccessful.

**Attempted ketalisation of exo,anti-1,8-dimethyl-9,10-diphenyl-4-azatetracyclo[6.2.1.0\(^2\).0\(^7\).0\(^8\).6]undeca-9-ene-5,11-dione (140b)**

(1) The ketone (140b) 100 mg) was heated under reflux with excess ethyl orthoformate and ammonium nitrate (100 mg) in ethanol (10 ml) for 12h. No reaction occurred.

(2) The method of Andersen and Uh\(^{184}\) was followed but, again, unchanged (140b) was recovered.

**Reduction of exo,anti-1,8-dimethyl-9,10-diphenyl-4-azatetracyclo-[6.2.1.0\(^2\).0\(^7\).0\(^8\).6]undeca-9-ene-5,11-dione (140b)**

(i) A solution of 1,8-dimethyl-9,10-diphenyl-4-azatetracyclo-
[6.2.1.0^2.7.0^3.6]undec-9-ene-5,11-dione (140b) (1.0 g, 2.8 mmol) in anhydrous tetrahydrofuran (50 ml) was added dropwise to a stirred slurry of lithium aluminium hydride (1.0 g, 26 mmol) in tetrahydrofuran (10 ml) at 0°. When addition was complete the mixture was heated under reflux overnight. After the solution had been cooled to 0° and diluted to 150 ml with extra tetrahydrofuran, 5 ml of 20% aqueous sodium hydroxide solution was added to destroy the aluminium salts. The supernatant solution was filtered, dried with anhydrous magnesium sulphate and evaporated. The crude product was purified by preparative layer chromatography (5% ethanol-chloroform as the eluting solvent mixture) to give an unidentified product (0.65 g, 65%). P.m.r. (CDCl₃): δ 1.22 (singlet, 3H, C methyl), 1.29 (singlet, 3H, C methyl), 1.77-2.56 (multiplet, ca 5H), 2.85 (doublet with extra fine coupling, J ca 13 Hz, 1H), 3.12 (broadened doublet, J ca 13 Hz), 3.32 (broadened singlet, 1H), 4.76 (multiplet, 1H), 6.86-7.24 (multiplet, 10H, aromatic protons).

Mass spectrum: m/e 344(14%), 343(M⁺, 46), 316(6), 315(21), 273(6), 272(9), 262(10), 259(36), 258(12), 246(5), 244(6), 243(5), 241(5), 229(6), 228(5), 215(6), 165(6), 91(5), 81(13), 80(8), 57(22), 56(100); strong metastable ion at 289(343-315).

(ii) Preparation of the N-p-toluene sulphonyl derivative

The amine (ca 650 mg, 1.9 mmol) from the above preparation was stirred with p-toluene sulphonyl chloride (360 mg, 1.9 mmol) in pyridine (5 ml) at room temperature for 3h. The excess pyridine was removed in vacuo at ca 50° and the residue purified by preparative layer chromatography (chloroform as eluting solvent) to give the N-tosyl derivative (500 mg). Recrystallisation from methanol gave an analytical sample as fluffy white needles, m.p. 174-175°. (Found: C, 74.91; H, 6.34; N, 2.66; S, 6.31. C₃₁H₃₁NO₃S requires C, 74.82; H, 6.28; N, 2.81; S, 6.44%). λmax 253 (shoulder), 230 nm; ε 10000, 20100. λmax 1583w, 1329s, 1251w, 1150s, 1104m, 1061, 1023m, 951m, 854w, 802w, 759w, 710ms,
666 m cm$^{-1}$. P.m.r. (CDCl$_3$): $\delta$ 1.13 (singlet, 3H, C methyl), 1.22 (singlet, 3H, C methyl), $\alpha$ 1.43 (partially obscured doublet of doublets $\gamma$, 1H), 2.12-2.68 (multiplet, 3H), 2.42 (singlet, 3H, sulphonyl methyl), 3.06 (doublet with extra coupling, J $\alpha$ 12 Hz, 1H), 3.36 (broadened singlet, 1H), 3.56 (doublet with extra coupling, J $\alpha$ 12 Hz, 1H), 5.60 (multiplet, 1H), 6.88-7.28 (multiplet, 10H, phenyl protons), 7.33 and 7.77 (doublets, J 9 Hz, sulphonyl aromatic protons). Mass spectrum: m/e 498(23), 497($M^+$, 63), 469(16), 342(18), 314(30), 271(13), 262(35), 261(78), 259(100), 258(88), 257(10), 244(21), 243(17), 241(11), 239(10), 236(16), 235(25), 229(15), 228(13), 215(11), 211(15), 210(83), 198(19), 165(13), 155(65), 91(81), 84(60), 56(23); all other peaks less than 10%.

Metastable ions at 443(497-469), 114.4(210-155), 53.3(155-91), 46.4(91-65).

**1-Carbomethoxy-2-azetine (282)**

A solution of 4-carbomethoxy-1,8-dimethyl-9,10-diphenyl-4-azatetracyclo[6.2.1.0$^2$.7.0$^3$.6]undec-9-en-11-one (261a) (800 mg) in
dichloromethane (400 ml; carefully purified and dried) was cooled with an external ice-bath and purged with dry nitrogen. The solution was irradiated with a 450W medium pressure lamp through a Corex filter for 2h. The solvent was removed at 0° to give a clean mixture of 1,4-dimethyl-2,3-diphenylbenzene (92) and 1-carbomethoxy-2-azetine (282). Short-path distillation (0°, 0.1 mm) onto a liquid nitrogen cooled cold-finger gave (28) (60 mg, 26%) as a colourless liquid. P.m.r. (CDCl₃): δ 3.72 (singlet, 3H, O-methyl), 4.47 (slightly broadened singlet, 2H, C4 protons), 5.62 (slightly broadened singlet, 1H, C3 proton), 6.64 (slightly broadened singlet, 1H, C2 proton). Mass spectrum: m/e 131(7%), contamination from the hydrolysis product (287), 114(6), 113(M⁺, 35), 103(20), 88(46), 83(8), 82(25), 76(15), 75(15), 72(10), 70(11), 68(37), 59(65), 58(8), 56(12), 55(11), 54(20), 52(7), 46(8), 45(14), 44(14), 43(18), 42(100), 41(16), 39(9), 32(63), 31(95).

N-Methoxycarbonyl-3-amino-1-propanol (287)

A solution of 4-carbomethoxy-1,8-dimethyl-9,10-diphenyl-4-azatetracyclo[6.2.1.0²,7.0³,6]undec-9-en-11-one (261a) (400 mg) in dichloromethane (350 ml; purified), to which 0.35 ml (0.1%) of water had been added was irradiated at room temperature with a 450W medium pressure lamp through a Corex filter for 30 min. The solvent was removed at 0° to give a clean mixture of 1,4-dimethyl-2,3-diphenylbenzene (92) and the aldehyde (287). Short-path distillation (25°, 0.05 mm) onto a liquid nitrogen cooled cold-finger gave pure (287) as a colourless liquid. P.m.r. (CDCl₃): δ 2.77 (triplet, J 5.9 Hz, 2H, C2 protons), 3.51 (doublet of triplets, J 5.9 Hz, J (CH-NH) ca 6 Hz, 2H, C3 protons), 3.70 (singlet, 3H, O-methyl), 5.18 (broad singlet, 1H, amino proton), 9.88 (singlet, 1H, aldehyde proton).

† The low isolated yield is probably due to the high volatility of the azetine.
Photochemical Preparation of N-methoxycarbonyl-3-amino-1-propanal diethyl acetal (285)

A solution of 4-carbomethoxy-1,8-dimethyl-9,10-diphenyl-4-azatetracyclo[6.2.1.02,7.03,6]undec-9-en-11-one (267) (1.8 g) in dichloromethane (May and Baker, unpurified; 400 ml) was irradiated with a 450W medium pressure lamp through a Corex filter for 2h. The solvent was removed in vacuo at room temperature and the residue chromatographed twice on thick-layer silica plates using chloroform as eluting solvent to give (285) (0.2 g, 22%). Short-path distillation (25°, 0.05 mm) gave (285) as a colourless oil which had p.m.r. and mass spectra indistinguishable from a sample of (285) prepared by unambiguous synthesis.

3-Chloro-1-propanal diethyl acetal (283)

3-Chloro-1-propanal diethyl acetal (283) was prepared by the method of Witzemann et al.189 Distillation gave a colourless liquid, b.p. 67-60°/15 mm (lit. b.p. 58-62°/8 mm189). P.m.r. (CDCl₃): δ 1.20 (triplet, J ca 5.5 Hz, 6H, acetal methyls), 2.07 (doublet of triplets, both J ca 5.5 Hz, 2H, C₂ protons), 3.38-3.88 (complex multiplet, 6H, acetal methylene and C₃ protons), 4.72 (triplet, J ca 5.5 Hz, 1H, C₁ proton).

3-Amino-1-propanal diethyl acetal (284)

The method of Albers et al.190 was followed. Short path distillation (ambient, 0.1 mm) gave (284) as a colourless liquid. P.m.r. (CDCl₃): δ 1.23 (triplet, 6H, acetal methyls), 1.78 (doublet of triplets, J(H₁,H₂) 5.6 Hz, J(H₂,H₃) 6.8 Hz, 2H, C₂ protons), 2.47 (fairly sharp singlet, 2H, amino protons), 2.79 (triplet, J 6.8 Hz, 2H, C₃ protons), 3.34-3.85 (complex multiplet, 4H, acetal methylene protons), 4.60 (triplet, J 5.6 Hz, 1H, C₁ proton).
Methyl chloroformate (0.90 g) was added dropwise to a stirred solution of 3-amino-1-propanal diethyl acetal (284) (1.38 g) in pyridine (4 ml) at 0°. After addition was complete, stirring was continued for 1 hr at room temperature. The mixture was diluted with ether (20 ml) and the precipitated pyridinium hydrochloride filtered off. The filtrate was evaporated *in vacuo* at 60° to give (285) (1.1 g, 56%) contaminated with a small amount of pyridine. Short-path distillation (50°, 0.15 mm) gave pure (285) as a colourless oil. (Found (M-0Et), 160.0974. C\textsubscript{7}H\textsubscript{14}N\textsubscript{3} requires mol. wt, 160.0974). \(\lambda_{\text{max}}\) 262, 256, 250, 246 (shoulder) nm; \(\varepsilon\) 1800, 2300, 2100, 1500. \(\gamma_{\text{max}}\) 3340 brs, 2973 ms, 2927 m, 2879 m, 1710 s, 1536 ms, 1445 m, 1375 m, 1345 w, 1262 m, 1195 w, 1130 s, 1060 s, 780 w cm\(^{-1}\).

P.m.r. (CDCl\(_3\)): \(\delta\) 1.22 (triplet J 7.1 Hz, 6H, acetal methyls), 1.84 (doublet of triplets, J(H\(_1\),H\(_2\)) 5.7 Hz, J(H\(_2\),H\(_3\)) \approx 7 Hz, 2H, C\(_2\) protons), 3.30 (partially obscured doublet of triplets, both J \approx 7 Hz, 2H, C\(_3\) protons), 3.36-3.88 (complex multiplet, acetal methylene protons), 3.69 (singlet, O-methyl), 4.60 (triplet J 5.7 Hz, 1H, C\(_1\) proton), 5.24 (broad singlet, 1H, amino proton). Mass spectrum: \(m/e\) 205(M\(^+\)), 165(5), 160((M-0Et)+, 31), 159(15), 144(8), 130(20), 128(11), 115(5), 114(24), 104(7), 103(100), 102(6), 100(12), 89(12), 88(75), 87(4), 86(8), 85(47), 79(10), 76(7), 75(52), 73(13), 72(16), 61(9), 59(18), 58(9), 57(22), 56(5), 55(6), 52(6), 47(65), 45(16), 44(37), 43(13), 42(6); metastable ions at 54.7, 45.1, 29.3.

4-Carbomethoxy-1,8,11-trimethyl-14,15-diphenyl-4,11-diaza-1,2,6,7,9,10,12,13-octadecacyclo-
[6.6.2.0\(^2\),0\(^3\),6\(^9\),13\(^7\)]pentadec-14-ene-10,12-dione (299)

(i) Photochemical Preparation

A solution of 4-carbomethoxy-1,8-dimethyl-9,10-diphenyl-4-
azatetracyclo[6.2.1.0\(^2\),7.0\(^3\),6\(^9\)]undec-9-ene-11-one (261a) (500 mg, 1.25 mmol) and N-methylmaleimide (139 mg, 1.4 mmol) in dichloromethane (4 ml) was
irradiated with a low pressure mercury lamp for 3h at ca 30°. The solvent was evaporated and the residue purified by preparative layer chromatography (chloroform as eluting solvent) to give, as a single band, a mixture of compounds (ca 300 mg). Crystallisation of this mixture from methanol/water gave the major component (299) (150 mg, 25%). Recrystallisation from a small volume of methanol afforded an analytical sample as white crystals m.p. 227-229°. (Found: C, 74.29; H, 6.06; N, 5.63. C_{30}H_{30}N_2O_4 requires C, 74.67; H, 6.27; N, 5.80%). \( \lambda_{\text{max}} \) 241, 230 nm; \( \epsilon \) 4500, 4500. \( \nu_{\text{max}} \) 1765s, 1693s, 1299m, 1200w, 1159w, 1130w, 764m, 730m, 709m cm\(^{-1}\). P.m.r. (CDCl\(_3\)): \( \delta \) 1.32 (singlet, 3H, C8 methyl), 1.38 (broadened singlet, 3H, C1 methyl), 2.59 (doublet, J(H7,H2) 8 Hz, 1H, C7 proton), 2.69 (broad multiplet, 2H, C2 and C6 protons), 2.75 (singlet, 2H, C9 and C13 protons), 3.10 (singlet, 3H, N-methyl), 3.69 (singlet, 3H, O-methyl); 4.04-4.56 (multiplet; 3H, C3 and C5 protons), 6.76 (broad multiplet, 4H, aromatic protons), 7.06 (multiplet, 6H, aromatic protons). Mass spectrum: \( m/e \) 482(M\(^+\), 3%), 480(6), 344(24), 343(82), 340(13), 259(10), 258(44), 257(6), 256(7), 243(15), 242(7), 241(9), 239(5), 229(5), 228(7), 215(5), 165(6), 140(10), 139(100), 138(20), 124(17), 94(5), 91(5), 59(10); metastable ions at 194.2 (343-124), and 110.5(139-124).

(ii) Thermal Preparation

(a) A solution of exo,anti-4-carbomethoxy-1,8-dimethyl-9,10-diphenyl-4-azatetracyclo[6.2.1.0\(^2\),7.0\(^3\),6]undec-9-en-11-one (267) (300 mg, 0.75 mmol) and N-methylmaleimide (75mg, 0.75 mmol) in dimethyl sulphoxide (3 ml) was heated at 160-170° for 105 min. No reaction occurred.

(b) The ketone (267) and N-methylmaleimide, in the same quantities as in (a), were heated together without solvent at 160-180° for 15 min. Again, no reaction occurred.

(c) The same mixture was heated under a nitrogen atmosphere at 200° (Woods metal bath) for 50 min. The pyrolysate was purified by
preparative layer chromatography (2% methanol-chloroform as the eluting solvent mixture) to give the title adduct (299) (110 mg, 30%), indistinguishable from that prepared via photochemical decarbonylation.

Reactions of 1-carbomethoxy-2-azetine (282)

(i) with tetracyanoethylene

Tetracyanoethylene (28 mg, 0.22 mmol) was added to a solution of the azetine (282) (ca 25 mg, 0.22 mmol) in deuteriochloroform (0.4 ml). No reaction occurred at room temperature and heating the solution to 60° caused polymerisation of the azetine (282).

(ii) with 1,3-diphenylisobenzofuran

1,3-Diphenylisobenzofuran (59 mg, 0.22 mmol) was added to a solution of the azetine (282) (ca 25 mg, 0.22 mmol) in deuteriochloroform (0.4 ml). Again no reaction occurred at room temperature and heating caused polymerisation of (282).

(iii) with 3,6-di(2'-pyridyl)-s-tetrazine (302)

A solution of 3,6-di(2'-pyridyl)-s-tetrazine (302) (470 mg, 2 mmol) and the azetine (282) (ca 2 mmol) in dichloromethane (20 ml) was allowed to stand overnight. The solvent was removed in vacuo and the residue purified by preparative layer chromatography (10% ethanol-chloroform as eluting solvent) to give two close-running bands at Rf 0.7-0.8. The lower Rf band yielded an unidentified 1:1 adduct as a semi-pure gum (150 mg). This deposited a small amount of white crystals, m.p. 143-147°, upon prolonged standing. \( \lambda_{\text{max}} \) 295, 268 nm; \( \epsilon \) 7950, 4800. P.m.r. (CDCl₃): \( \delta \) 3.25 (broadened singlet, 3H, O-methyl), 3.78 (multiplet, 1H), 4.41 (multiplet, 3H), 6.39 (multiplet, 1H, disappears upon addition of D₂O), 7.16-8.80 (multiplets, 8H, pyridyl protons). Mass spectrum: \( m/e \)

322(6%), 321(M⁺, 24), 320(11), 262(15), 247(15), 235(25), 234(95), 207(6),
The higher R_f band yielded an inseparable mixture of the pyridazine adduct (303) and the tetrazine (302). The mixture was dissolved in a small volume of chloroform and the tetrazine (302) was converted to 3,6-di(2'-pyridyl)pyridazine by the addition of excess bicyclo[2.2.1]heptadiene. The volatiles were removed in vacuo and the residue purified by preparative layer chromatography (conditions the same as before) to give \(N\)-carbomethoxy-[3,6-di(2'-pyridyl)pyridazinyl]methylamine (303) (175 mg, 27%). Recrystallisation from ethanol gave an analytical sample as fawn needles, m.p. 124°. (Found: C, 63.54; H, 4.37; N, 21.75.

C\(_{17}\)H\(_{15}\)N\(_5\)O\(_2\) requires C, 63.54; H, 4.71; N, 21.79%.) \(\lambda_{\text{max}}\) 286, 248 nm; \(\epsilon_{\text{max}}\) 3400w, 1726s, 1586m, 1501w, 1401w, 1301w, 1255m, 1146w, 1092w, 1030w, 989w, 885w, 790m, 772m, 739, 730m cm\(^{-1}\). P.m.r. (CDCl\(_3\)): \(\delta\) 3.71 (singlet, 3H, 0-methyl), 4.75 (doublet, J \(\text{ca}\) 6.5 Hz, 2H, methylene protons), 6.77 (broad triplet, J \(\text{ca}\) 6.5 Hz, 1H, amino proton), 7.44 (multiplet, 2H), 7.95 (multiplet, 2H), 8.47 (doublet, J \(\text{ca}\) 7.5 Hz, 1H), 8.79 (multiplet, 3H). Mass spectrum: \(m/e\) 322(21%), 321(M\(^{+}\), 100), 290(5), 263(5), 262(22), 248(18), 247(89), 246(10), 235(8), 218(5), 217(6), 211(5), 205(12), 158(5), 78(9); metastable ion at 190.0(321-247).

\(N\)-(p-Toluenesulphonyl)-2-azetine (326)

A solution of 1,8-dimethyl-9,10-diphenyl-4-(p-toluenesulphonyl)-4-azatetracyclo[6.2.1.0\(^2\).7.0\(^3\).6]undec-9-en-11-one (271) (700 mg) in dichloromethane (180 ml; purified) was irradiated with a 450W medium pressure lamp through a Corex filter for 2h. The solvent was removed in vacuo below room temperature and the residue washed several times with hexane to remove 1,4-dimethyl-2,3-diphenylbenzene (92). The crude azetine (326) thus obtained was purified by preparative layer chromatography (20 x 20 cm alumina plates, dichloromethane as eluting solvent) to give
(326) (97 mg, 33%) as a slightly oily solid. Attempted recrystallisation from methanol was not successful. P.m.r. (CDCl₃): δ 2.47 (singlet, 3H, aromatic methyl), 4.16 (singlet, 2H, C₄ protons), 5.70 (singlet with fine coupling, 1H, C₃ proton), 6.52 (broadened singlet, 1H, C₂ proton), 7.38 (doublet, J 8 Hz, 2H, aromatic protons), 7.80 (doublet, J 8 Hz, 2H, aromatic protons). The chemical shifts in DMSO-d₆ solution are δ 2.44, 4.08, 5.86, 6.74, 7.50, 7.80. Mass spectrum: m/e 209(M⁺, 23%), 156(5), 155(57), 139(6), 92(10), 91(100), 89(5), 65(18); metastable ions at 115.0(209+155), 53.3(155+91), 46.4(91-65).

Attempted synthesis and trapping of azete (309a)

(i) Potassium tert-butoxide (40 mg; freshly sublimed) was added to a solution of N-tosyl-2-azetine (23 mg) in DMSO-d₆ (0.4 ml). Monitoring by p.m.r. spectroscopy indicated immediate reaction and polymerisation of the ring fragment (all signals save those of the p-toluenesulphonyl group disappeared).

(ii) N-Tosyl-2-azetine (35.4 mg, 0.169 mmol), 1,3-diphenyliso-benzofuran (45.7 mg, 0.169 mmol) and potassium tert-butoxide (45 mg, 0.4 mmol) were stirred together at room temperature in dimethyl sulphoxide (2 ml) for 15 min. The mixture was added to water (75 ml) and extracted with dichloromethane (2 x 25 ml). The dichloromethane extracts were combined, washed twice with water, dried and evaporated to give ca 50 mg of residue (contaminated with DMSO) which was almost pure 1,3-diphenyliso-benzofuran. It was not investigated further.
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