Studies on Alkene Aziridination using  
N-Acetoxyaminoquinazolin-4(3H)-ones

A Thesis submitted for the Degree of
Doctor of Philosophy
by
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in the
Faculty of Science
of the
Department of Chemistry
at the
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MARCH 1989
To my Mother
STATEMENT

The accompanying thesis submitted for the degree of Doctor of Philosophy entitled "Studies on Alkene Aziridination using N-acetoxyaminoquinazolin-4(3H)-ones" is based on work conducted by the author in the Department of Chemistry of the University of Leicester between the period October 1985 and September 1988.

All the work recorded in this thesis is original unless otherwise acknowledged in the text or by references.

None of the work has been submitted for another degree in this or any other university.

Signed: ...............................  Date: ............................
ACKNOWLEDGEMENTS

First and foremost I would like to express my gratitude to Dr. R. S. Atkinson for his friendship and excellent supervision throughout my postgraduate years at Leicester.

It would not have been possible for me to even contemplate these postgraduate studies without the support and encouragement of my mother and family, for that I shall always be grateful.

I would also like to thank:
Dr. P. R. Jenkins for many useful discussions on chemistry and life;
Vicky for typing this thesis; Ann for drawing the diagrams; and my fellow students and staff of this Department for making my stay in Leicester a pleasurable one.

Finally, I am indebted to all my friends, in particular I would like to thank Iain, Stewart, Cath, Juliet and Mary for their friendship during my years at Leicester.
ABBREVIATIONS

Ac - acetyl
b.p. - boiling point
Bu - butyl
Bu^ - tert-butyl
Bz - benzyl
DME - dimethoxyethane
DMF - N,N-dimethylformamide
DMSO - dimethylsulphoxide
Et - ethyl
Ether - diethyl ether
h - hour
het - heterocycle
LTA - lead tetra-acetate
LTB - lead tetra-benzoate
mCPBA - m-chloroperbenzoic acid
Me - methyl
m.p. - melting point
Ph - phenyl
Phthal - phthalimide
Q - see below
TFA - trifluoroacetic acid
THF - tetrahydrofuran

Throughout this thesis

\[ Q = \begin{array}{c}
\text{N} \\
\text{N} \\
\text{O}
\end{array} \begin{array}{c}
\text{N} \\
\text{N} \\
\text{O}
\end{array} \]
ABSTRACT

The work contained in this thesis re-examines the mechanism of formation of aziridines from lead tetra-acetate (LTA) oxidation of N-aminoquinazolones in the presence of alkenes. Hitherto, the intermediates involved in these aziridinations were thought to be the corresponding N-nitrenes. However, evidence presented in this thesis shows that these intermediates are the corresponding N-acetoxyaminoquinazolones. This conclusion was supported, inter alia, by the low temperature (-20°C) ¹H n.m.r. spectra of N-acetoxyaminoquinazolones, obtained by LTA oxidation of the corresponding N-aminoquinazolones at -20°C. Solutions of N-acetoxyamino-2-ethylquinazolone were found to be stable at this temperature but brought about the aziridination of alkenes when allowed to warm to room temperature in the presence of the latter.

An analogy is drawn between aziridination of alkenes using N-acetoxyaminoquinazolones and epoxidation of alkenes using peracids. Using N-acetoxyamino-2-ethylquinazolone, aziridination of geraniol is more regioselective and aziridination of cyclohex-2-en-1-ol is more facially selective than epoxidation of these alkenes using peracids. Aziridination of cyclohex-3-en-1-ol is also examined and in contrast to epoxidation using peracids, aziridination of this alkene is stereospecific and gives only the syn-aziridine.

As solutions of the N-acetoxyamino-2-ethylquinazolone are stable at -20°C, it is now possible to bring about aziridination of LTA-labile alkenes: the addition of silyl ketene acetals to these solutions followed by warming to room temperature afforded the corresponding N-protected α-amino acid esters in excellent yields. The same methodology has been used to bring about aziridination of vinylstannanes and vinylsilanes. Desilylation of the derived silyl-substituted aziridines provides a new route to 2H-azirines and the presumed intermediate aziridinyl carbanions have been intercepted with benzaldehyde or protons as electrophiles.

Aziridination of alkenes by oxidative (LTA or PhI(OAc)₂) addition of N-aminoquinazolones in the presence of trifluoroacetic acid is also examined; the dramatic increases in yields in some cases are rationalised by protonated N-acetoxyaminoquinazolone intermediates.
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CHAPTER 1
The Chemistry of N-Nitrenes
1.1 INTRODUCTION

Univalent nitrogen intermediates R-N, were first proposed in the nineteenth century to explain the course of the Lossen and Curtius rearrangements. The intermediates now commonly called nitrenes,¹ are reactive intermediates and the nitrogen analogues of carbenes.¹ Nitrenes contain an electron-deficient nitrogen atom having only six electrons in their valence shell. Two of these electrons form the bond with the single ligand (R) while the other four can be arranged in two ways, i.e. as two pairs of electrons with spins paired on a nitrogen atom with an empty orbital giving rise to an electrophilic singlet nitrene (1), or as two electrons spin paired plus two electrons with parallel spins giving a triplet nitrene (2) [Figure 1].

![Figure 1](image)

The properties and reactions of nitrenes R-N are governed principally by the nature of R and by their spin states. The various nitrene classes studied include: R-N (alkynitrenes); Ar-N (arylnitrenes); H₂C=CH-N (vinylnitrenes); RO₂C-N (alkoxycarbonylnitrenes) and NC-N (cyanonitrenes).

In all these cases the nitrene nitrogen is bound to carbon. However, nitrenes attached to elements other than carbon have been recognised or postulated including oxygen,⁵ sulphur,⁶ fluorine,⁷ chlorine,⁸ hydrogen,⁹

¹: The current view on the mechanism of the Lossen and Curtius rearrangements is that they do not involve nitrenes. In both cases the evidence supports a mechanism in which bond migration is concerted with the departure of the leaving group.²,³,⁴
This thesis is mainly concerned with those nitrenes attached to nitrogen, the aminonitrenes $R_1R_2N\cdot N$. In this case the electron deficient nitrogen (N-2) is bonded to another nitrogen (N-1) and the substituents ($R_1$ and $R_2$) on this adjacent nitrogen may be alkyl or aryl groups or alternatively (of particular relevance to the work contained in this thesis) form part of a heterocyclic ring.

1.2 HETEROCYCLIC N-NITRENES

The oxidation of N-aminoheterocyclic compounds of type (3) supposedly generates the corresponding heterocyclic N-nitrenes (4). This can be achieved by using lead tetra-acetate (LTA) or alternatively benzene iodosodiacetate [PhI(OAc)$_2$] as the oxidising agent. The routine use of either LTA or PhI(OAc)$_2$ in oxidations of these N-amino compounds will later be seen to be of great significance [Figure 2].

Figure 2

The N-aminoheterocycles first oxidised in this way exhibited a dichotomy in their behaviour. One group does not undergo intermolecular reactions but spontaneously rearranges or fragments. For example, the oxidation of N-aminobenzotriazole (5) with LTA at 0°C gives benzyne (7) in virtually quantitative yield. In the absence of trapping agents, benzyne generated in this way dimerized to give biphenylene (8) in yields up to 83% [Scheme 1].

$^{\dagger}$: Throughout the introduction to this thesis the intermediates derived from the LTA or PhI(OAc)$_2$ oxidation of these heterocyclic N-amino-compounds will be referred to as N-nitrenes. However, subsequent chapters will reveal that in certain cases this formulation is incorrect and may indeed be incorrect for all cases.
A further example is 2-aminobenzotriazole (9) which when oxidized under the same conditions gave cis,cis-mucononitrile (11) as the sole product [Scheme 2].

While both postulated N-nitrene intermediates (6) and (10) fragment in different ways to produce benzyne (7) and cis,cis-mucononitrile (11) respectively, the N-nitrene (13) derived from the oxidation of 1-amino-indazole (12) undergoes a facile rearrangement to form 1,2,3-benzotriazine (14) with no loss of nitrogen [Scheme 3].
The other group of N-aminoheterocycles, when oxidized, gave, supposedly, N-nitrene intermediates whose intramolecular decay was sufficiently retarded for them to be trapped intermolecularly.\textsuperscript{16-18} They include the N-nitrenes derived from oxidation of N-aminophthalimide (NAP) (15), N-aminobenzoxazolinone (16), N-aminquinazolone (NAQ) (17), N-aminquinolone (18), N-aminopyrrole (19), N-aminotriazole (20), N-aminotriazolinone (21) and N-aminobenzimidazole (22) and, characteristically, they all yield aziridines when oxidized in the presence of alkenes [Figure 3].\textsuperscript{16-18}

![Chemical structures of N-aminoheterocycles](image)

Figure 3

Examination of the heterocycles in Figure (3) reveals that they all contain features that will reduce the availability of the lone pair on the substituted trivalent nitrogen (N-1) for donation to and stabilization of the univalent nitrene nitrogen. Thus either one or both of the N-1 substituents is a carbonyl or imino function or else the N-1 lone pair of electrons is part of an aromatic ring. The effect of competition for the N-1 lone pair by its substituents has two important consequences which are:

1. the contribution from the 1,1-diazene resonance canonical (24)\textsuperscript{19} is reduced and as a consequence the nitrene character (23) of N-2 made manifest,
(ii) the tendency for elimination of nitrogen is reduced since the \( \text{N=N} \) bond order is reduced [Figure 4].

\[
\begin{align*}
\begin{array}{c}
\text{R}^1 \\
\text{R}^2
\end{array} & \begin{array}{c}
\text{N} \\
\text{N}
\end{array} & \begin{array}{c}
\text{R}'^1 \\
\text{R}'^2
\end{array} \\
& \leftrightarrow \\
& \begin{array}{c}
\text{N} = \text{N} \\
\rightarrow
\end{array}
\end{align*}
\]

(23) \hspace{1cm} (24)

Figure 4

When the substituents on N-1 [Figure 4] above are alkyl groups, the transient species are more properly described as 1,1-diazenes (24). Recent work by Dervan et al. has shown that oxidation of the hydrazine (25) at \(-78^\circ\text{C}\) gave stable solutions of the 1,1-diazene (26), this was confirmed by ir, n.m.r. and visible absorption spectroscopy.

\[
\begin{align*}
\begin{array}{c}
\text{N} - \text{NH}_2 + \text{Bu}^+ \text{OCl}
\end{array} & \begin{array}{c}
\text{Et}_3\text{N}
\end{array} \\
\text{-78}^\circ\text{C} & \rightarrow \\
& \begin{array}{c}
\text{N} = \text{N}
\end{array}
\end{align*}
\]

(25) \hspace{1cm} (26)

The prolonged stability of (26) at \(-78^\circ\text{C}\) can be attributed to the substantial delocalization of the electron pair on N-1 into the vacant p-orbital on N-2.

Within the second group of N-aminoheterocycles [Figure 3], the most used and best studied is N-aminophthalimide (NAP) (15). The oxidative addition of NAP to a wide variety of alkenes has been accomplished and good yields of the corresponding aziridines are obtained. When oxidation was carried out in the absence of alkenes a range of products was isolated. Most of these products were assumed to arise from attack of the presumed N-nitrene intermediate on unoxidized NAP, although a small yield of benzo- cyclobutanedione (27) is produced by extrusion of nitrogen [Scheme 4].
The use of benzene iodosodiacetate in the oxidation of NAP (15) allows the isolation of the tetrazane (28) which is the presumed intermediate en route to phthalimide (29) [Scheme 5].

\[ \text{Phthal-NH}_2 + \text{Ph} \rightarrow \text{Phthal-NH-NH-Phthal} \]

Scheme 5

The postulated N-nitrene (31) derived from the oxidation of N-amino-triazole (30) is of interest because it shows characteristics of both groups of N-heterocyclic compounds referred to above. When (30) is oxidised in the presence of alkenes, intramolecular fragmentation occurs in competition with addition to the alkene [Scheme 6].
1.3 THE PROPERTIES AND CHARACTERISTICS OF THE INTERMEDIATES DERIVED FROM OXIDATIVE ADDITION OF (15)-(22) TO ALKENES

The intermediates derived from the oxidation of N-aminoheterocycles (15)-(22) exhibit properties some of which are not characteristic of nitrenes in their usual rôle as highly reactive intermediates.²⁵ Thus,

(i) they insert stereospecifically into alkene π bonds even at low concentrations of alkene and, accordingly, have singlet ground states,

(ii) there are no products from insertion into σ (sigma) bonds in their reactions,

(iii) they have an ambiphilic nature and readily insert into alkenes substituted with either electron withdrawing or electron donating groups often in excellent yields,

(iv) their reactions with monosubstituted alkenes gives rise to stereospecific formation of a single pyramid at the aziridine ring nitrogen
(syn-selectivity) which is often not the thermodynamically more stable one (see below),

they show considerable selectivity in competitive reactions with two different alkenes.

1.4 EVIDENCE FOR N-NITRENES AS INTERMEDIATES IN THE OXIDATION OF N-AMINO-HETEROCYCLES

One of the recurrent problems in the study of reactive intermediates is the correct identification of the transient species involved: this often must be based solely on inferences made from the type of reactions they undergo and the nature of the products they form. In the oxidation of NAP (15) with LTA, evidence against an oxidizing agent-nitrene complex (nitrenoid) description for the reactive intermediate is the generation, by three other independent routes, of a species showing apparently the same reactivity [Scheme 7] and hence formulated as the N-nitrene (32).

\[
\text{Phthal} - \text{NH}_2 \xrightarrow{LTA, \text{CH}_2\text{Cl}_2} \begin{array}{c}
\begin{array}{c}
\text{Phthal} \\
\text{NH}_2
\end{array}
\end{array}
\xrightarrow{\Delta \text{or hv}, -\text{Me}_2\text{S}} \begin{array}{c}
\begin{array}{c}
\text{Phthal} \\
N-\text{SMe}_2
\end{array}
\end{array}
\xrightarrow{, \text{Ph}} \begin{array}{c}
\begin{array}{c}
\text{Phthal}
\end{array}
\end{array}
\]

\[
\text{Phthal} \xrightarrow{\Delta} \text{Phthal} - \text{COCH}_3
\]

\[
\text{Phthal} \xrightarrow{, \text{Ph}} \text{Phthal} - \text{COCH}_3
\]

\[
\text{Phthal} \xrightarrow{, \text{Ph}} \text{Phthal} - \text{COCH}_3
\]

Scheme 7
The first of these routes (a) was reported by D. W. Jones. When the aziridine (33) was heated in the presence of alkenes in boiling benzene it brought about the aziridination of a number of different alkenes. The other two routes (β) and (γ) were reported by Rees. Common to all of these routes was the fact that the postulated N-nitrene (32) was trapped stereospecifically by cis- and trans-alkenes and [routes (α) and (β)] reacted readily with both electron-rich and electron-deficient alkenes, behaving, in fact, exactly as the species resulting from LTA oxidation of NAP. Moreover, oxidation of the N-aminotriazole (30) [Scheme 6] in the presence of alkenes with either LTA or benzene iodosodiacetate gave the same ratio of fragmentation to aziridine formation, again implying a common intermediate in both oxidations, and presumed to be the N-nitrene.

1.5 THE STEREOSELECTIVE AZIRIDINATION OF ALKENES BY OXIDATIVE ADDITION OF N-AMINOHETEROCYCLIC COMPOUNDS

As has been previously mentioned, the stereospecificity of alkene aziridination using oxidative addition of N-aminoheterocycles (15)-(22), particularly at low concentration of alkene, has been interpreted as evidence for singlet ground states for the postulated N-nitrene intermediates. No experimental evidence is available to suggest that they react via anything other than the singlet state. This conclusion is an adaptation of Skell's hypothesis for the addition of singlet and triplet carbenes to alkenes, to nitrenes. Thus, the addition of the singlet nitrene is concerted and stereospecific with the alkene configuration retained in the aziridine. The addition of a triplet nitrene is stepwise and non-concerted which occurs via a diradical intermediate in which the parallel spins of the electrons in the triplet nitrene are conserved. Before ring closure can take place to give the aziridine, spin inversion
must occur. If spin inversion is slow when compared to carbon-carbon bond rotation then the alkene configuration is not wholly retained in the aziridine.

Most nitrenes studied do not possess substituents that can stabilize the singlet state: ethoxycarbonyl nitrene; EtO₂C-N is one such example which has been widely studied\textsuperscript{2} and was shown to have a triplet ground state, adding non-stereospecifically to alkenes at low alkene concentration. In the postulated N-nitrenes derived from oxidation of (15)-(22), it was assumed that the singlet ground state could be resonance stabilized by donation of the lone pair of electrons on the adjacent nitrogen into the empty p-orbital on the singlet nitrene nitrogen [Figure 5]. The fact that the N-2 substituents in (15)-(22) were invariably those which would disfavor such electron donation was never satisfactorily explained.

![Figure 5](image)

The triplet state has no available empty orbital and cannot be similarly stabilized although some of the most stable free radicals known are those in which the unpaired electron is adjacent to a heteroatom bearing an electron pair. Calculations by Goddard\textsuperscript{30} and others\textsuperscript{31,32} have shown that in most cases the singlet state when at optimum singlet geometry is of lower energy than the triplet state. Conceivably, the conversion from the singlet to the triplet state may be very slow compared to its rate of reaction. However, since these aziridinations have been shown to be stereospecific even at low alkene concentrations this explanation is not a
1.6 SYN-SELECTIVITY EFFECTS IN OXIDATIVE ADDITIONS OF N-AMINOHETEROCYCLES TO ALKENES

The oxidative addition of N-aminoheterocycles (15), (16), (17) and (22) to olefins bearing a single \( \pi \)-electron containing substituent in conjugation with the double bond leads firstly and rather surprisingly to the aziridine (34), where the heterocycle and the substituent on the alkene (R) are on the same side of the aziridine ring (34) (syn-selectivity). Depending on the heterocycle involved, this cis-aziridine (34) then undergoes inversion at nitrogen at a measurable rate to the sterically and thermodynamically more favoured trans-aziridine (35) at temperatures between \(-20^\circ\text{C}\) and \(0^\circ\text{C}\) [Scheme 8].

![Scheme 8](image)

Where: \( R = \text{Ph, CO}_2\text{Me, CH}=\text{CH}_2 \text{ etc.} \)

The observation of syn-selectivity in aziridinations of alkenes was first reported using oxidative addition of N-aminophthalimide (15) to methyl acrylate.\(^3\) At room temperature two invertomers (36a) and (36b) are observed in the \(^1\text{H}\) n.m.r. of this aziridine in a 5:1 ratio respectively [Scheme 9].\(^4\)

\( ^{\dagger} \) The other heterocycles have not been examined for this syn-selectivity in their oxidative additions to alkenes but presumably would behave similarly.
However, if the oxidation of (15) is carried out (in CDCl₃) at less than -10°C (a temperature at which the rate of inversion at the aziridine ring nitrogen is negligible) and the CDCl₃ solution examined by ¹H n.m.r. at less than -30°C, without any intermediate warming, only signals from the thermodynamically less stable aziridine (36b), are observed. As the temperature is gradually raised to ambient, the growth of a set of new signals is observed in the ¹H n.m.r. at the expense of those belonging to the syn-invertomer (36b). This new set of signals are those from the trans-aziridine (36a). When the temperature finally reaches ambient the 5:1 ratio is re-established. This ratio remained unchanged even on re-lowering the temperature to -30°C.³³ The cis-aziridine (36b), therefore, is the product of kinetic control in the reaction.

The stereospecific formation of the kinetically favoured cis-aziridine (36b) instead of the thermodynamically preferred trans-aziridine (36a) was attributed to an attractive interaction between the alkene substituent and the phthalimide ring in the transition state for N-nitrene addition to the alkene (a syn-interaction). This high syn-selectivity is likewise present in similar aziridinations of butadiene and styrene which give stereospecifically, as the kinetically formed products, those N-invertomers having a syn-relationship between the substituent and the heterocyclic ring.³⁵

Similar experiments have also been carried out in an attempt to determine whether alkyl groups show a similar syn-selectivity but the lack of
reactivity of simple alkyl-substituted alkenes in attempted aziridinations at low temperature did not allow any conclusion to be drawn on this point. However, although hydrogen has little, if any, attractive syn-interaction, when compared to π-electron containing substituents on the alkene, this is not the case with alkyl substituents. Thus, addition of phthalimido-nitrene (32) to styrene at -20°C results in exclusive formation of the syn-invertomer (37a) which, on warming to ambient temperature, inverts at nitrogen to give only the thermodynamically more stable anti-invertomer (37b) [Scheme 10].

By contrast, the use of β-methylstyrene under identical conditions gives a kinetically formed ratio of 94:6 for aziridines (38a) and (38b) respectively, illustrating that the methyl group has a small attractive syn-interaction which is less than that of a phenyl group though larger than that of a hydrogen. The precise nature of this attractive syn-interaction still remains unclear.
One of the most puzzling features of the behaviour of the intermediates in these aziridinations, formulated as N-nitrenes, has been their large preference for reaction with the s-cis conformations of e.g. α,β-unsaturated esters and 1-3 dienes.\textsuperscript{35} Thus, whereas α-methylene-γ-butyrolactone (39)\textsuperscript{36} and isoprene (40) are efficiently aziridinated by oxidative addition of N-aminophthalimide (15), their s-trans-configurated counterparts the butenolide (41) and 4-methylpenta-1,3-diene (42) gave no aziridine containing products at all.\textsuperscript{35,36}

This demand for the s-cis-configuration has been reconciled in terms of an attractive secondary interaction between the heterocycle and the alkene substituent: for example, in the transition state (43) [Scheme 11] for the addition of phthalimidonitrene (32) to butadiene or styrene. Nevertheless it was not obvious why a reactive intermediate should fail to react with an alkene without this (presumably small) supplementary assistance from the secondary interaction.

\begin{center}
\begin{tikzpicture}
\node (a) at (0,0) {\begin{tabular}{c}
\includegraphics[width=0.2\textwidth]{image1.png}
\end{tabular}};
\node (b) at (4,0) {\begin{tabular}{c}
\includegraphics[width=0.2\textwidth]{image2.png}
\end{tabular}};
\node (c) at (2,0) {\begin{tabular}{c}
\includegraphics[width=0.2\textwidth]{image3.png}
\end{tabular}};
\draw[->] (a) -- (b);
\draw[->] (a) -- (c);
\end{tikzpicture}
\end{center}

\textbf{Scheme 11}
1.7 TRANSITION STATE GEOMETRY FOR ADDITION OF N-NITRENES TO ALKENES

Knowledge of the geometry of the N-nitrene in relation to the alkene in the transition state for concerted aziridination is important for a better understanding of this aziridination and in particular its stereochemical features.

The approach illustrated in Figure (6) is used in which the heterocycle and the alkene (which is drawn in its preferred s-cis-conformation) are contained within parallel planes with the N-N bond of the heterocycle at right angles to the plane containing the alkene π-electrons. Using Figure (6) as a working model it is evident from the proximity of the substituent on the alkene and the carbon marked by an asterisk in Figure (6) that there exists the possibility of an attractive secondary interaction between them and hence aziridination using styrene, a diene or an α,β-unsaturated ester would lead initially to the kinetically-formed aziridines observed.

An attempt to provide experimental support for this transition state geometry was made using intramolecular aziridinations in which the alkene is bound to the heterocycle by means of a hydrocarbon chain. Here the results obtained were in best agreement with an orthogonal approach of the N-nitrene to the carbon-carbon double bond of the alkene as in Figure (6).

The transition state for aziridination shown in Figure (6) has also been explained in terms of frontier molecular orbital theory, where the assumption is made that aziridination of alkenes results from overlap of
complementary HOMO's and LUMO's on the nitrene and alkene as shown below in Figure (7).

**Figure 7**

1.8 TRAPPING OF THE INTERMEDIATES IN OXIDATION OF N-AMINOHETEROCYCLES WITH OTHER C=C DOUBLE BONDS AND NUCLEOPHILES

A variety of functional groups have also been used to intercept the intermediates in the oxidation of these N-aminoheterocycles and some of the results are summarized below.

i) intramolecular addition to alkenes

The intramolecular aziridination of a number of 2-substituted-3-amino-quinazolones have also been studied.\(^{30}\)

\[
\begin{align*}
\text{Scheme 12} \\
\text{(44) } R = H & \quad (45) \ R = H \ 50\% \\
\text{(46) } R = \text{Ph} & \quad (47) \ R = \text{Ph} \ 76\%
\end{align*}
\]

Thus, treatment of (44) and (46) with LTA gave the aziridines (45) and (47) respectively [Scheme 12].

ii) with allenes

Aziridination of methyl 2-methylbuta-2,3-dienoate (48) using NAP (15) has been reported to give a crystalline product isolated in 14\% yield.\(^{39}\)
On the basis of the spectroscopic evidence available, this was shown to be the 1,4-diazaspiro[2.2]pentane (49) [Scheme 13].

\[
\begin{array}{c}
\text{Me} \\
\text{CO}_2\text{Me}
\end{array}
\xrightarrow{\text{NAP, LTA}}
\begin{array}{c}
\begin{array}{c}
\text{N} \\
\text{Phthal}
\end{array}
\end{array}
\begin{array}{c}
\text{Me} \\
\text{CO}_2\text{Me}
\end{array}
\]

\[ (48) \rightarrow (49) \]

**Scheme 13**

iii) with alkynes

Aziridination of acetylenes using NAP (15) has been reported to occur in poor yield (1-15%).\(^4^0\) The products from attempted aziridination are 2H-azirines (51) which result from a spontaneous rearrangement of the first formed antiaromatic 1H-azirine (50) [Scheme 14].

\[
\begin{array}{c}
R' \equiv CR^2
\end{array}
\xrightarrow{\text{NAP, LTA}}
\begin{array}{c}
\text{Phthal} - \text{N} \\
\text{N}
\end{array}
\begin{array}{c}
R^1 \\
R^2
\end{array}
\]

\[ (50) \rightarrow (51) \]

\[ R^1 = \text{H}, R^2 = \text{Me, Pr or Bu} \]

\[ R^1 = \text{Et}, R^2 = \text{Et} \]

**Scheme 14**

An intramolecular version of this reaction proceeds in excellent yield.

iv) with aromatic rings

The oxidative addition of NAP (15) to both aromatic and heteroaromatic rings has also been studied.\(^4^2\) Only electron-rich rings were found to react and the products are transformation products of the initially formed aziridine. This is illustrated for the case of 2,5-dimethylfuran below [Scheme 15].\(^4^3\)

\[
\begin{array}{c}
\text{Me} \\
\text{O} \\
\text{Me}
\end{array}
\xrightarrow{\text{NAP, LTA, CH}_2\text{Cl}_2}
\begin{array}{c}
\text{Me} \\
\text{O} \\
\text{N}
\end{array}
\begin{array}{c}
\text{Phthal}
\end{array}
\]

\[ 41\% \]

**Scheme 15**
v) with allyl aryl sulphides

Sulphides, and in particular allyl aryl sulphides have been shown to be effective trapping agents for the intermediates in the oxidation of N-aminoheterocycles. Thus, oxidative addition of (15) to substituted allyl aryl sulphides (52) gave the corresponding N-allyl-N-heteroaryl sulphenamides (54) and (55) by a [2,3] sigmatropic rearrangement of the intermediate N-heteroarylsulphimides (53) [Scheme 16].

\[
\begin{align*}
\text{ArS} & \quad \text{NAP LTA} \\
\text{R} & \quad \text{Phthal} \\
\text{N} & \quad \text{Phthal} \\
(52) & \quad (53) & \quad (54) \quad R=H (61\%) \\
(55) & \quad R=Me (60\%)
\end{align*}
\]

Scheme 16

vi) with sulphoxides

Dimethyl sulphoxide and similar sulphoxides have also been used as efficient trapping agents for nitrenes. Heterocyclic N-nitrenes derived from (16), (15), (18) and (17) where \( R = CH_3 \), also react with sulphoxides and the products from the reaction are the corresponding sulphoximines (56) which are isolated in good yield [Scheme 17]. The efficiency of sulphoxides as trapping agents may derive from the fact that they can often be used as solvents in the oxidation thus maximising their concentration.

\[
R_2N - NH_2 + Pb(OAc)_4 \rightarrow R_2N - N=SMe_2
\]

N-Amino compound | Dimethylsulphoximine (%) |
---|---|
(16) | 60 |
(15) | 75 |
(18) | 52 |
(17) where \( R=CH_3 \) | 100 |

Scheme 17
The dimethylsulphoximines produced have also been claimed as precursors for N-nitrenes: when they are irradiated in the presence of alkenes the corresponding aziridines are produced. Thus, irradiation of the sulphoximine (57) in the presence of cyclohexene gave the aziridine (58) in 20% yield [Scheme 18] which was found to be identical to that isolated from the LTA oxidation of NAP (15) in the presence of cyclohexene.27

![Scheme 18](image)

1.9 TRICOORDINATE SP³-HYBRIDISED NITROGEN INVERSION

This topic has been extensively reviewed by J. M. Lehn50 and in view of this only a brief review of the factors affecting the rate of nitrogen inversion and its relevance to small rings will be discussed here.

The pyramidal nitrogen inversion process of (59) to (61) takes place via a planar transition state (60) when NR₁R₂R₃ undergoes a change in hybridization from sp³ to sp² [Figure 8].

![Figure 8](image)
While this is occurring, the lone pair of electrons on nitrogen in (59) undergo a change from occupying an sp$^3$-orbital to a p-orbital in the transition state (60).

1.10 FACTORS THAT AFFECT THE NITROGEN INVERSION BARRIER

i) Steric effects

These are exemplified in aziridines (62)$^{51}$ and (63)$^{52}$ where replacing an N-CH$_3$ by an N-C(CH$_3$)$_3$ leads to an approximate 2.5 kcal/mol decrease in the inversion barrier as a result of an increase in the ground state energy in (63).

\[ \begin{array}{c}
\text{N-CH}_3 \\
(62)
\end{array} \quad \begin{array}{c}
\text{N-C(CH}_3)_3 \\
(63)
\end{array} \]

ii) Ring strain

The inclusion of a nitrogen atom into a small (3 or 4) ring heterocycle increases the inversion barrier. This is a result of an increase in ring strain in going from the ground state (ideally sp$^3$) to the transition state (ideally sp$^2$). This is reflected in the inversion barriers of the cyclic amines (62), (67), (69) and (71) which show the highest inversion barrier for the three-membered ring (62) [Table 1].

iii) Conjugating substituents

Conjugation of the nitrogen lone pair with an adjacent $\pi$ system, as in (64), (65) and (66), lowers the barrier to inversion because delocalization is more effective in the transition state, when the lone pair occupies a p-orbital, than in the ground state where it possesses a higher degree of s-character.

iv) Heteroatoms bonded to nitrogen

The attachment of non-conjugating electronegative groups or atoms to nitrogen raises the inversion barrier. This has been explained in terms of
<table>
<thead>
<tr>
<th>Structure</th>
<th>R</th>
<th>$\Delta G^\ddagger$ (Kcal mol$^{-1}$)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N-R</td>
<td>(62) $R = Me$</td>
<td>$\sim 22$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(63) $R = Bu$</td>
<td>17.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(64) $R = Ph$</td>
<td>11.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(65) $R = CO Me$</td>
<td>&lt;6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(66) $R = NO_2$</td>
<td>&lt;8</td>
</tr>
<tr>
<td></td>
<td>N-R</td>
<td>(67) $R = Me$</td>
<td>10.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(68) $R = Cl$</td>
<td>13.4</td>
</tr>
<tr>
<td></td>
<td>N-R</td>
<td>(69) $R = Me$</td>
<td>8.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(70) $R = Cl$</td>
<td>10.3</td>
</tr>
<tr>
<td></td>
<td>N-R</td>
<td>(71) $R = Me$</td>
<td>6.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(72) $R = Cl$</td>
<td>9.2</td>
</tr>
</tbody>
</table>
either an increase in the lone pair – lone pair repulsion in the transition state, or the electron withdrawing inductive effect of the heteroatom (or a combination of both of these factors). The electron-withdrawing effect of the heteroatom (e.g. N, O, Cl) bonded to nitrogen increases the s-character of the lone pair orbital (by requiring more p-character in the exocyclic N-X bond) and results in destabilization of the transition state relative to the ground state as re-hybridization in the latter is made more difficult. This is exemplified in (68), (70) and (72).

1.11 THE INVERSION BARRIER IN N-HETEROCYCLIC SUBSTITUTED AZIRIDINES

Characteristically, all the N-substituted aziridines derived from the oxidation of heterocycles (15)-(22) in the presence of alkenes exhibit slow inversion on the ^1H n.m.r. timescale at the aziridine ring nitrogen.\(^\text{33}\)

The barrier to inversion in these aziridines (i.e. the free energy of activation), \(\Delta G^*\), lies in the range of 18-22 kcal mol\(^{-1}\) and thus inversion barriers can be calculated by n.m.r. spectroscopy.

The slow rates of inversion in these N-substituted aziridines often results in the signals from two nitrogen invertomers being present in their n.m.r. spectra.\(^\text{35}\) Substituents on this aziridine ring may be either cis- or trans- to the heterocyclic ring on the aziridine nitrogen. Observation of signals from both invertomers is dependent on the position of the invertomer equilibrium, which in turn depends on the relative interaction of the substituents on the aziridine ring with the heterocycle.\(^\text{34}\)

The magnitude of the inversion barriers in aziridines bearing phthalimide [from (15)], benzoazolinone [from (16)], or benzimidazole [from (22)] groups is such that the inversion rate is effectively zero at -20°C, a fact which allows detection (and even isolation\(^\text{33}\)) of the kinetically formed syn-invertomers referred to above. In the case of the quinazolinone
N-substituted aziridines, however, the marginally smaller inversion barrier means that even at -20°C inversion proceeds slowly but at a measurable rate. This fact is of particular relevance to this thesis in which the aziridines to be discussed invariably are N-substituted with this particular heterocyclic ring.
CHAPTER 2

Aziridination by Oxidative Addition of N-Aminoquinazolones to Alkenes: Evidence for the Non-involvement of N-Nitrenes
2.1 INTRODUCTION

The intermolecular aziridination of alkenes using the heterocyclic precursors (15)-(22) has been shown in the previous chapter to afford aziridines, often in excellent yields. A further development within this area has been a study\textsuperscript{41} of intramolecular aziridination to assess the importance of the secondary interaction referred to earlier and to gain some experimental evidence for the preferred transition state geometry in the aziridination. In an attempt to provide experimental evidence for an attractive methyl-quinazolone interaction in the aziridination transition state, a low temperature oxidation of the N-amino-2-substituted-quinazolone (73) was carried out by M. Grimshire (this work was later repeated and confirmed by the author).\textsuperscript{41}

\begin{center}
\includegraphics[width=0.2\textwidth]{image.png}
\end{center}

Examination of the crude product by 300 MHz $^1$H n.m.r. at -30°C showed only one product to be present apart from acetic acid which is an unavoidable by-product in oxidations involving LTA. It was evident from this $^1$H n.m.r. spectrum that the product was not an aziridine as the two olefinic protons were still intact. Neither was this product the de-aminated quinazolone ($N$-NH$_2$ → N-H), a commonly observed by-product in these oxidations, because the methylene protons (at $\delta$ 3.16 and $\delta$ 2.97) adjacent to the quinazolone ring were non-equivalent. This latter evidence also excluded the N-nitrene structure for this intermediate. The presence of the characteristic pattern from the quinazolone ring proton signals suggested this ring system had been unaffected.
One possible structure considered at the time was the tetrazane (74) [Figure 9].

![Structure of tetrazane](image)

Evidence for tetrazanes as intermediates in the oxidation of a number of N-aminoheterocycles (but not quinazolones) has been obtained by Rees.\textsuperscript{23} Thus, oxidation of N-aminophthalimide (15) with [bis(acetoxy)iodo]benzene gave the tetrazane (28) [Scheme 19].

![Scheme 19](image)

Further work by Dreiding\textsuperscript{56} has suggested that phthalimide (29) is formed by fragmentation of the tetrazane (28). Such a mechanism could also operate for other tetrazanes which have an α-carbonyl, e.g. (74) [Figure
9], which would lead to the de-aminated quinazolone (75) as the major product on warming, as is found to be the case.

\[
\text{\begin{figure}[h]
\centering
\includegraphics[width=0.2\textwidth]{image.png}
\caption{Structure (75) with \( R = (\text{CH}_2\text{CH} = \text{CHMe}) \)}
\end{figure}}
\]

Conclusive evidence against the tetrazane structure (74), however, came from a study of the stoichiometry of the reaction of the N-aminoquinazolone (73) with LTA: formation of (74) requires only 0.5 mole equivalent of LTA whereas a full mole equivalent was found to be required for complete consumption of (73).

On allowing the \(^1\text{H}\) n.m.r. solution from low temperature oxidation of (73) above to warm up from \(-30^\circ\text{C}\) to ambient, the signals due to the diastereotopic methylene protons at \( \delta 3.16 \) and \( \delta 2.97 \) diminished with the corresponding growth of new signals. The rest of the spectrum became more complicated but most interestingly there appeared to be a small amount of the aziridine (76) produced during this warming process.

\[
\text{\begin{figure}[h]
\centering
\includegraphics[width=0.2\textwidth]{image.png}
\caption{Structure (76)}
\end{figure}}
\]

Following on from these observations made on the product from low temperature oxidation of (73), the LTA oxidation of 3-amino-2-ethylquinazolone (77) also at low temperature was examined by the author. The reason for choosing this particular compound was that firstly, it was considerably easier to make than (73) and secondly, the methylene protons
adjacent to the heterocycle should again be non-equivalent if an analogous product to that obtained from oxidation of (73) is formed at -30°C.

2.2 LOW TEMPERATURE (-25°C) OXIDATION OF 3-AMINO-2-ETHYLQUINAZOLONE (77) USING LTA

Oxidation of 3-amino-2-ethylquinazolone (77) with LTA at -25°C (see Experimental) afforded a product whose ¹H n.m.r. spectrum at -20°C showed a distinctive ABX₃ pattern for the two apparently diastereotopic protons adjacent to the quinazolone (§ 3.11), a low field singlet integrating for one proton (§ 10.98) and the expected triplet from the ethyl side chain. The characteristic pattern for the quinazolone ring protons at 300 MHz confirmed that this heterocycle was still intact. Other than residual acetic acid, the only other species present in the above solution was a small amount (ca. 5%) of the de-aminated quinazolone (79) which was shown to be identical to the species that results from de-amination of (77) using nitrous acid. Removal of acetic acid from the n.m.r. solution by careful washing with saturated sodium hydrogen carbonate solution at low temperature revealed that the major product from the oxidation of (77) also contained a methyl group which was obscured by the acetic acid signal [see Figure 10].

Assignment of the N-acetoxyaminoquinazolone structure (78) [Scheme 20]

![Scheme 20](image)

to this product, which is stable only below 0°C and has not been isolated, is supported by a low temperature (-20°C) i.r. spectrum of the oxidation
FIGURE 10
H n.m.r. spectrum of N-acetoxyminoquinazolone (78): s (CDCl₃, 300 MHz, T = -20°C).

\[ \text{IR: } 1768 \text{ cm}^{-1}, \quad \delta_{\text{H}}: 5.169, 5.18 \text{ ppm} \]

\[ \delta_{\text{C}}: 169.46, 168.98 \]
product (in deuterochloroform) which contained a prominent band at 1768 cm⁻¹ that disappeared as the temperature was raised to ambient, and also by a low temperature ¹³C n.m.r. spectrum of the crude oxidation product that contained two additional carbon resonances (at δ 169.46 and δ 18.98) besides those expected for the 2-ethylquinazolone. The non-equivalence of the protons in the methylene group of (78) which appear as a doublet of quartets (at δ 3.19 and δ 3.03) may be the result of retarded inversion at the exocyclic nitrogen or, less likely, a result of hindered rotation around the N-N bond (a chiral axis). The major product that results from allowing a solution of (78) to warm to ambient is the de-aminated quinazolone (79) which can be isolated from the crude reaction mixture by flash chromatography over silica as colourless crystals in approximately 70% yield.

2.3 A POSSIBLE MECHANISM LEADING TO THE FORMATION OF (78)

In spite of the fact that a large number of (substituted) amine oxidations with LTA have been reported, there have been few reports of N-acetoxylation using this reagent.⁵⁷

The first step in the formation of (78) is likely to be nucleophilic attack at lead by the N-aminoquinazolone (77) with the loss of acetate. Conceivably, the second step could be nucleophilic attack by the liberated acetic acid at the nitrogen in (80) and cleavage of the N-Pb bond which would lead directly to (78).

However, in view of the difficulty of nucleophilic substitution at nitrogen combined with the relatively poor nucleophilic character of acetic acid, this pathway seems unlikely. A more plausible and entropically favoured route to (78) may be the concerted (?) intramolecular attack by one of the acetate ligands on lead as shown below. This mechanism leads
directly to (78) with the formation of a stable lead(II) salt [Scheme 21].

\[
\begin{align*}
Q - \text{NH}_2 + \text{Pb} - \text{OAc} & \rightarrow Q - \text{N} - \text{Pb(OAc)}_2 + \text{HOAc} \\
(77) & \rightarrow (80)
\end{align*}
\]

Scheme 21

2.4 MECHANISM OF FORMATION OF THE DE-AMINATED QUINAZOLONE (79)

LTA oxidation of (77) at -20°C results in the formation of (78) and 5% of the de-aminated quinazolone (79). Because of the prolonged stability of (78) at this temperature, the formation of this small amount of (79) is unlikely to result from the decomposition of (78). It is only when the temperature is raised to ambient that (78) decomposes to give (79). This indicates that there must be two routes to the de-aminated quinazolone (79).

Evidence for the formation of (79) at -20°C by a route involving the nucleophilic attack on the N-acetoxyaminoquinazolone (78) by N-aminoquinazolone (77) at this temperature, was obtained from a study of the products from decomposition of the preformed N-acetoxy-2-methylquinazolone (82) in the presence of 2 mole equivalents of the N-amino-2-ethylquinazolone (77) [Scheme 22].

Examination of the crude products from the above reaction by high field n.m.r. showed that substantial de-amination of (77) had taken place with formation of both (84) and (79). This could have occurred by attack of
(77) on the N-acetoxyaminoquinazolone intermediate (82) resulting in the tetrazane (83). This tetrazane could then undergo decomposition to (79) and (84) by the mechanism referred to earlier.

An additional mechanism for conversion of N-acetoxyaminoquinazolone (78) into NH-quinazolone (79) must also be occurring at a temperature >0°C by unimolecular decomposition of (78) but the mechanism by which this occurs is at present unknown.

2.5 DECOMPOSITION OF THE N-ACETOXYAMINOQUINAZOLONE (78) IN THE PRESENCE OF ALKENES

\[
\begin{align*}
\text{Q} & \quad \xrightarrow{\text{HNOAc}} \quad \text{Q} \\
\text{HNOAc} & \quad \text{ + } \quad \text{ + } \\
\text{78} & \quad \text{78} \\
\end{align*}
\]

Addition of alkenes to solutions of (78) prepared at -20°C followed by warming to room temperature results in the isolation of the corresponding...
aziridines. A summary of the results using a variety of alkenes is given in Table 2 and Table 3.

Methanol has also been found to react with the intermediate from LTA oxidation of (77). The oxidative addition of (77) to a solution of methanol afforded the N-methoxyaminoquinazolone (96) in 23% yield [Scheme 23].

\[ (77) + \text{LTA} \xrightarrow{\text{MeOH, RT}} (96) \quad 23\% \]

Scheme 23

The reactivity of N-acetoxyaminoquinazolone (78) both towards electron-rich and electron-deficient alkenes is very similar to that previously ascribed to N-aminoheterocyclic-derived nitrenes.

The rate of decomposition of (78) in the presence of the individual alkenes in Table 2 was followed by variable temperature \(^1\text{H}\) n.m.r. (300 MHz). The general procedure that was carried out for this study was as follows: the N-acetoxyaminoquinazolone (78) was prepared as a deuterochloroform solution at -25°C as described earlier; this solution was then transferred to an n.m.r. tube and inserted into the n.m.r. probe at -40°C without allowing the temperature to rise above -25°C throughout and an n.m.r. spectrum recorded to confirm the formation of (78); the n.m.r. tube was then temporarily removed from the probe, placed in a dewar at -40°C, and a measured amount of the alkene added to the solution of (78); the tube was then re-inserted back into the n.m.r. probe at -40°C. The following results were obtained:

(i) using styrene (1.5 mol equiv.)

the low temperature \(^1\text{H}\) n.m.r. spectrum at -40°C showed the major product to be the N-acetoxyaminoquinazolone (78). A minor product (ca.
TABLE 2
Decomposition of (78) in the presence of various alkenes

<table>
<thead>
<tr>
<th>ALKENE</th>
<th>PRODUCT ISOLATED C</th>
<th>YIELD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><img src="https://example.com/image1.png" alt="Image" /></td>
<td>11 b</td>
</tr>
<tr>
<td></td>
<td><img src="https://example.com/image2.png" alt="Image" /></td>
<td>76 a</td>
</tr>
<tr>
<td></td>
<td><img src="https://example.com/image3.png" alt="Image" /></td>
<td>58 b</td>
</tr>
<tr>
<td></td>
<td><img src="https://example.com/image4.png" alt="Image" /></td>
<td>62 a</td>
</tr>
<tr>
<td></td>
<td><img src="https://example.com/image5.png" alt="Image" /></td>
<td>81 a</td>
</tr>
<tr>
<td></td>
<td><img src="https://example.com/image6.png" alt="Image" /></td>
<td>70 a</td>
</tr>
</tbody>
</table>

a using 1.5 mol equiv. of the alkene;
b using 3.0 mol equiv. of the alkene;

C 0 = ![Chemical Structure](https://example.com/structure.png)
### TABLE 3
Aziridination of various alkenes using solutions of N-acetoxyaminoquinazolone (78)

<table>
<thead>
<tr>
<th>ALKENE</th>
<th>PRODUCT ISOLATED</th>
<th>YIELD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>H₂C=CHPh</td>
<td>O,N-CH₃N-Ph (91)</td>
<td>61 b,e</td>
</tr>
<tr>
<td>O</td>
<td>O,N-OC-OC (92)</td>
<td>62 a</td>
</tr>
<tr>
<td>CO₂MeCH₃</td>
<td>O,N-CO₂Me (93)</td>
<td>67 b</td>
</tr>
<tr>
<td>H₃C=CO₂Me</td>
<td>O,N-CO₂Me (94)</td>
<td>58 a</td>
</tr>
<tr>
<td></td>
<td>QN (95)</td>
<td>44 a</td>
</tr>
</tbody>
</table>

a this aziridine exists as a 1.5:1 ratio of invertomers, the major invertomer has the CH₃ cis to Q as shown;
b using 3 mol equiv. of the alkene;
c using 1.5 mol equiv. of the alkene;
d this aziridine exists as a 2:1 ratio of invertomers, the major invertomer has CO₂Me cis to Q;
e using 3.5 mol equiv. of the alkene;
f this aziridine was obtained by the oxidative (LTA) addition of (77) to a solution of the alkene in dichloromethane at room temperature;
g this aziridine exists as a 4:1 ratio of invertomers, the major invertomer has CO₂Me cis to Q.
10% was the syn-aziridine (86a), there was no evidence from the \(^1\text{H}\) n.m.r. to suggest that any of the anti-aziridine (86b) was present at \(-40^\circ\text{C}\) [Figure 11].

![Figure 11](image)

As the temperature was raised gradually from \(-40^\circ\text{C}\) to ambient, signals from the anti-aziridine (86b) were also observed by n.m.r. and these grew in intensity whilst those from the syn-invertomer (86a) diminished and then disappeared. The disappearance of signals due to the N-acetoxyaminoquinazolone (78) was also observed as faster reaction with styrene occurred as the temperature was raised to ambient. This resulted in a 76% isolated yield of the aziridine (86).

(ii) using indene (1.5 mol equiv.)

apart from signals due to the intermediate (78), formed as the major product (ca. 90%), the low temperature n.m.r. \((-30^\circ\text{C}\) was complicated by two sets of aziridine ring protons which were assigned to the two rotameric forms (88a) and (88b) of the syn-aziridine, present in a 1:1.3 ratio (not necessarily respectively) [Figure 12].

![Figure 12](image)

As the temperature is raised from \(-40^\circ\text{C}\) to ambient, broadening of the
aziridine ring protons at 0°C was observed and growth of signals from the thermodynamically more stable anti-aziridine (88) occurred at the expense of the broadened signals from the minor invertomers.

(iii) the remaining alkenes in Table 2

for the remaining alkenes in Table 2, no syn-aziridine was ever observed. At -40°C the n.m.r. showed only the N-acetoxyaminoquinazolone (78) to be present together with unreacted alkene. It was only when the temperature was raised to -0°C that decomposition of (78) occurred, accompanied by formation of the corresponding thermodynamically more stable anti-aziridine invertomer.

For the cases of styrene and indene above, it was quickly established that the corresponding syn-aziridines were the kinetically-formed invertomers formed by oxidation of NAQ (77) with LTA in the presence of either alkene at -30°C. Aziridination of most of the alkenes in Tables 2 and 3 had been carried out many years ago by oxidation of 3-amino-2-methylquinazolone with LTA in their presence. However, this difference in the two modes of aziridination is of significance when the alkene is not stable to LTA as is discussed in Chapter 4.

2.6 SECONDARY INTERACTIONS

The observation of a kinetically-formed syn-product in the low temperature aziridination of both styrene and indene, demonstrates that an attractive secondary interaction is operating between some part of the quinazolone ring in (78) and the aromatic ring of these two alkenes in the transition state for aziridination. A similar interaction had previously been postulated to account for the formation of syn-aziridines as kinetically-formed products from the LTA oxidation of N-aminoheterocycles (15), (16), (17) and (22) in the presence of styrenes, α,β-unsaturated
esters and dienes but was interpreted as involving N-nitrene intermediates. A modified transition state representation which accommodates an N-acetoxy intermediate is illustrated for the aziridination of styrene (97) and would initially lead to the syn-aziridine (86a) [Figure 13].

As implied in Figure 13, the attractive secondary interaction results from overlap of orbitals in the phenyl ring and the quinazolone carbonyl. The importance of such an overlap is suggested by the requirement for an s-cis conformation for a diene or α,β-unsaturated ester (styrene may be regarded in this context as a diene locked in an s-cis conformation) and from the examination of models of (97). The preferred geometry of approach depicted in Figure 13 is that which is supported experimentally by the intramolecular aziridination study referred to earlier.

Although Figure 13 indicates that this secondary interaction is specifically between the carbonyl group and the phenyl ring, there is little evidence to exclude an alternative or competing transition state geometry in which overlap is between the imino group of the quinazolone and the phenyl ring [Figure 14].
The involvement of both the C=O and C=N sites in secondary interactions may explain why two rotamers were formed in a near 1:1 ratio in the reaction of (78) with indene at low temperature. Thus, the aziridination of indene at low temperature may be the result of two competing transition state geometries, one the result of C=O-phenyl interaction (98), the other the result of C=N-phenyl interaction (99) [Figure 15].

![Figure 15](image)

An examination of models of the syn-aziridines (88a) and (88b) [Figure 12] suggests that the barrier to their interconversion by rotation around the N-N bond may be significant although the possibility that slow interconversion between the rotamers is occurring (and that the 1:1 ratio of rotamers observed is an equilibrium value) cannot be excluded.

2.7 THE RATE OF DECOMPOSITION OF (78) IN THE PRESENCE OF STYRENE AND METHYL ACRYLATE

The decomposition of the N-acetoxyaminoquinazolone (78) (prepared at low temperature by the method outlined earlier) was followed at 10°C by ¹H n.m.r. spectroscopy (300 MHz) by monitoring the decrease in height of the NH singlet at δ 10.98 with respect to time. The results indicated that (78) exhibits first order kinetics in its decomposition over four half lives with a rate constant of $k_{10^{-1}} = 3.68 \times 10^{-4} \text{ sec}^{-1}$ [see Appendix 1]. The addition of styrene to solutions of (78) at -40°C has previously been
shown to produce the syn-aziridine (86a) at a measurable rate, therefore, the rate of disappearance of (78) must be increased by the presence of styrene. At \(-10^\circ C\) the initial rate of disappearance of (78) in the presence of 4 mole equivalents of styrene \((K_{10} = 2.9 \times 10^{-3} \text{ sec}^{-1}, \text{treated as first order})\) is ca. twice as fast as in the presence of 1.5 mole equivalents where \(K_{10} = 1.4 \times 10^{-3} \text{ sec}^{-1}\) [see Appendix 2]. Furthermore, methyl acrylate effects a small but detectable increase in the rate of disappearance of (78) which appeared to be a function of its concentration although good first order kinetics were not obtained.

2.8 ATTEMPTED EXCHANGE OF THE N-H AND N-ACETOXY GROUPS IN (78) USING D\(_4\)-ACETIC ACID

From the results above and those listed in Tables 2 and 3 it would appear that the N-acetoxyaminooquinazolone (78) is playing the rôle previously assigned to the corresponding N-nitrene (100). The possibility that the nitrenium ion (101) or even the N-nitrene (100) could still be the reactive intermediate in these aziridinations through the existence of a reversible equilibrium between these species and (78) [Scheme 24] could be eliminated since no exchange of either the N-H or the N-acetoxy group took place in the \(^1\text{H} \text{n.m.r.}\) spectrum of (78) when an acetic acid-free solution was treated with 4 mole equivalents of CD\(_3\)CO\(_2\)D at \(-20^\circ C\).

![Scheme 24](image)
2.9 INTRA- AND INTERMOLECULAR AZIRIDINATIONS OF OTHER 2-SUBSTITUTED N-AMINOQUINAZOLONES

(i) Intramolecular aziridinations

The discovery of the N-acetoxyaminoquinazolone (78) as an intermediate in the LTA oxidation of (77), prompted a re-examination at lower temperatures of a number of intramolecular aziridinations of 2-substituted quinazolones which had previously been assumed to occur via N-nitrene intermediates.\textsuperscript{58-60}

In intramolecular aziridinations, the presence of the secondary interaction which is thought to assist the intermolecular reaction with alkenes, did not appear to be mandatory.\textsuperscript{38} Thus efficient aziridination of the trans-mono-substituted alkene in (46) occurred in 76\% yield in a reaction in which a favourable secondary interaction resembling that in Figure 13 between the phenyl substituent and the quinazolone cannot exist. Likewise, aziridination of (44) gave (45) in 50\% yield [Figure 16].

\begin{figure}[h]
\centering
\includegraphics[width=0.7\textwidth]{figure16}
\caption{}
\end{figure}

When the products from oxidation of (44) at -40°C were re-examined at low temperature by n.m.r. it was clear that as in the oxidation of NAQ (77), aziridination proceeded via an intermediate, in this case N-acetoxyaminoquinazolone (102) [Figure 17].

Thus, for the case of the N-amino-2-butenylquinazolone (44) in which only three bonds separate the quinazolone ring from the alkene double bond,
oxidation at -40°C in CDCl₃ gave both the corresponding N-acetoxy intermediate (102) and the aziridine (45) in a 65:35 ratio respectively. On raising the temperature from -40°C to ambient over a period of 30 min., the conversion of (102) to the aziridine (45) was observed by n.m.r. Likewise, oxidation at -40°C of the N-aminoquinazolone (103), in which the quinazolone and the alkene are separated by four bonds, also gave a corresponding N-acetoxy intermediate (104) in quantitative yield. The absence of any aziridine (105) at this temperature may be attributed to the increased separation of the alkene from the N-acetoxyamino group in the transition state for aziridination in (104) when compared to that of (102). However, as the temperature was raised from -40°C, the appearance of signals from the aziridine (105) were observed at the expense of those from the unstable intermediate (104).

A similar pattern also emerged in the low temperature oxidations of N-aminoquinazolones bearing bifurcated chains: thus, oxidation of (106) at -40°C gave the N-acetoxyaminoquinazolone (107) as a 1:1 mixture of stereoisomers due to the additional chiral centre in the side chain [Figure 18].

If a solution of (107) is allowed to warm to room temperature then the ratio of attack on the two alkene double bonds and the ratios of attack on each face of these individual double bonds are practically identical to
those values for these ratios obtained when oxidation of (106) is carried out at room temperature.\textsuperscript{41} This demonstrates that (107) must also be the intermediate in this room temperature oxidation and eliminates the possibility that aziridination may occur, even in part, by interception of the nitrogen-lead species which is presumed to be the intermediate in the formation of (107) [see Scheme 21].

Oxidation of (108), however, could not be accomplished at a temperature low enough to allow observation of any product other than the derived aziridine (109) [Figure 19].

(ii) Intermolecular aziridinations

It was also established that analogous N-acetoxyaminoquinazolone intermediates to (78), stable at -20°C, were obtained in oxidation of other N-aminoquinazolones, e.g. (111) [Figure 20]. Aziridination using (111) had previously been assumed to proceed via a transient N-nitrene.\textsuperscript{61}
The low temperature LTA oxidation of (111) was shown by n.m.r. to give N-acetoxyaminoquinazolone (110) which apparently exists as a 4:1 ratio of stereoisomers [see Figure 21]. Aziridination of α,β-unsaturated esters using (111) in the presence of TFA brought about asymmetric aziridination of the alkene in good yield. Preliminary experiments with (110) suggested that it was no more stable than the 2-ethyl analogue (78) as both were found to decay at similar rates when their decomposition was monitored at 10°C by n.m.r. spectroscopy.

In an attempt to find a more stable N-acetoxyaminoquinazolone intermediate with a view to its eventual isolation at room temperature, the low temperature oxidation of the N-amino-2-hydroxymethylquinazolone (112) was attempted in the expectation that hydrogen bonding between the hydroxyl in the side chain and the N-H or N-acetoxy would enhance the stability of the intermediate (113a) or (113b) [Figure 22].

However, support for the formation of (113a) or (113b) in the n.m.r. spectrum of the products from low temperature oxidation of (112) at -25°C,
FIGURE 21

H n.m.r. spectrum of N-acetoxyaminoguanazolone (110): δH (CDCl3, 300 MHz, T = -20°C).
was not forthcoming. This was possibly a consequence of low solubility of (112) in CDCl$_3$ at this temperature and the difficulty in obtaining a well-resolved n.m.r. spectrum. As the temperature of the n.m.r. solution above was raised to ambient, no visible change was observed until +10°C and from this it was concluded that, assuming (113a) or (113b) is present (see above), it may have a greater stability than the N-acetoxyaminoquinazolones prepared hitherto.

Addition of styrene (3 mol equiv.) to this solution at -25°C and warming to room temperature resulted in a crude product which, by n.m.r., was seen to contain the two aziridines (114) and (115) in a 3:1 ratio respectively.

\[
\text{ratio of (114):(115) } = 3:1
\]

Chromatography over silica permitted the separation of these aziridines which were obtained in yields of 32% and 13%. However, conversion of (114) to (115) occurs when the mixture is allowed to stand in the presence of acetic acid. The structure of (115) was confirmed by acetylation of (114) using pyridine and acetic anhydride which afforded an 80% yield of (115).

Interestingly, oxidation of (112) at room temperature in the presence of styrene (3 mol equiv.) gave a relatively poor yield (47%) of (114) [without conversion to the acetylated product (115)]: quantitative formation of the presumed N-acetoxyaminoquinazolone (113), therefore, may not be occurring in the oxidation of (112) but no other homogeneous products from the reaction were identified.
In an attempt to retain the benefits of intramolecular hydrogen bonding (if present) but to overcome the problem of insolubility, oxidation at low temperature of the N-amino-2-benzylxoymethylquinazolone (116) was undertaken.

\[
\begin{align*}
\text{BzO} & \quad \text{NH}_2 & \quad \text{BzO} & \quad \text{NOAc} \\
\text{H} & \quad \text{H} & \quad \text{H} & \quad \text{Ph} \\
\text{BzO} & \quad \text{NH} & \quad \text{BzO} & \quad \text{N} \\
\text{N} & \quad \text{N} & \quad \text{N} & \quad \text{N}
\end{align*}
\]

Inspection of the low temperature ^1H n.m.r. at -40°C revealed that the major product was the expected N-acetoxyaminoquinazolone (117) with a characteristic NH resonance at δ 10.75 in its n.m.r. spectrum. However, from comparison of the integral of this NH signal with that from H-5 it was apparent that (117) was only formed in ~50% yield along with an unidentified product. Hence it was not surprising to find that addition of styrene to this solution resulted in only a 53% yield of the corresponding aziridine (118). By contrast, oxidation of (116) at room temperature in the presence of styrene gave a 73% yield of the same aziridine.

To summarise, it is now clear that the formation of N-acetoxyaminoquinazolones by LTA oxidation of N-aminoquinazolones at low temperature is a general phenomenon: such an intermediate was undoubtedly formed in the original observation from low temperature oxidation of (73).

These N-acetoxyaminoquinazolone intermediates are responsible for bringing about both inter- and intramolecular aziridination of alkenes and although their existence has only been demonstrated spectroscopically (so far) in oxidation of N-aminoquinazolones, it does seem likely that aziridination of alkenes by LTA oxidation of other N-aminoheterocycles will proceed via analogous intermediates.
2.10 Evidence for an Unstable N-Acetoxyaminophthalimide Intermediate in the LTA Oxidation of NAP (15) at -50°C

It was of particular interest to examine whether an analogous N-acetoxyamino intermediate (119) was involved in the oxidation of NAP (15) with LTA since it was the generation of apparently the same intermediate by four different routes, as outlined in Scheme 7 in the previous chapter, that had constituted the best evidence for an N-nitrene intermediate in these aziridinations. The low temperature (-50°C) LTA oxidation of NAP (15) followed by separation of the insoluble lead di-acetate at -45°C with the subsequent addition of styrene (3 mol equiv.) gave the aziridine (37) in 40% yield after work-up.

It appears, therefore, that in the oxidation of (15), an intermediate, presumably (119), is formed which is stable in solution at low temperature and brings about aziridination of styrene. Further support for this interpretation comes from a comparison of the selectivities of the intermediates in LTA oxidations of NAP (15) and NAQ (77) in reaction with two alkenes. Thus oxidation of NAP (15) in the presence of a 1:1 mixture of α-methylene-γ-butyrolactone and methyl methacrylate gave the aziridines (120) and (121) in a 2.1:1 ratio. This selectivity is very close to that from oxidation of NAQ (77) in the presence of the same two alkenes (2:1) [Scheme 25].

Similarly, competitive aziridination of styrene and methyl acrylate at room temperature by oxidative addition of NAP (15) gave similar ratios of attack on the two double bonds as the same competitive reaction using NAQ
(77) suggesting that the same intermediates are involved in these aziridinations [Scheme 26].†

If the active aziridinating agent in LTA oxidation of NAP is the N-acetoxyaminophthalimide (119), then how can this be reconciled with the apparent generation of the same intermediate by the thermolysis of (33) as in Scheme 7 (p. 8).

A re-examination of the supposedly common intermediate in oxidation of NAP (15) and route (α) Scheme 7, however, has shown that its selectivity in reaction with two alkenes is quite different. Thus, heating aziridine (33) in a benzene solution containing a 1:1 mixture of styrene and methyl acrylate (3 mol equiv. of each) for 5h gave a 1:3 ratio of the aziridines (37) and (36) respectively [Scheme 27]. By contrast, oxidation of NAP with LTA in the presence of the same ratio of alkenes in boiling benzene over 20

†: When NAQ (77) was oxidised at low temperature (-20°C) followed by the addition of the same two alkenes a 9:1 ratio of the aziridines (86) and (89) was obtained, again suggesting that aziridinations at both room temperature and low temperature proceed via the same intermediate (78).
min. gave the same aziridines but in a ratio of 1.5:1 [Scheme 27]. The 1:3 ratio of (37):(36) was not affected by heating for 4h in benzene under reflux, with or without the addition of 2 mole equivalents of acetic acid (which is also produced in oxidation of NAP (15) with LTA).

\[
\text{(33)} \quad \text{Ph}\quad \text{COCH}_3
\]

\[
\text{NAP(15)} \quad \text{Ph}\quad \text{CO}_{2}\text{Me}
\]

\[
\text{(37) 1:3 (36)} \quad \text{Ph}\quad \text{Ph}\quad \text{N}\quad \text{CO}\quad \text{CO}\quad \text{Me}
\]

\[
\text{(37) 15:1 (36)} \quad \text{Ph}\quad \text{Ph}\quad \text{N}\quad \text{CO}\quad \text{CO}\quad \text{Me}
\]

Scheme 27

It appears, therefore, that the intermediate in the thermal decomposition of aziridine (33) is not identical with that generated by oxidation of N-aminophthalimide (15).

It was this non-identity of the intermediates from thermolysis of aziridine (33) and oxidation of NAP which raised doubts as to whether the N-nitrene was in fact an intermediate in thermal decomposition of (33) and prompted an investigation of alternative routes by which aziridination of alkenes using this route could be brought about.

2.11 THE NATURE OF THE INTERMEDIATE IN THE THERMOLYSIS OF AZIRIDINE (33) WHICH BRINGS ABOUT AZIRIDINATION OF ALKENES

Two alternative mechanisms for aziridination of alkenes using thermolysis of (33) which avoid N-nitrene intermediates suggest themselves: the first, is that shown in Scheme 28 where the aziridine (33) functions itself directly as the aziridinating agent and the N-aminophthalimide unit is transferred directly to the alkene.

A good analogy for the above mechanism is the demonstration by F. Davis et al. that the epoxidation of alkenes by the transfer of oxygen from the
2-sulphonyl oxaziridine (122) is apparently a single step reaction [Scheme 29].

The mechanism proposed in Scheme 28, in contrast to that in which the generation of the N-nitrene is the rate determining step, predicts that the rate of disappearance of aziridine (33) should be accelerated by an increase in the concentration of the alkene. In practice this was found to be the case: in the absence of any alkene, the decomposition of aziridine (33) was monitored at 80°C (in boiling benzene) by $^1$H n.m.r. using the integral value of the aziridine ring proton singlet in the major invertomer.
to measure the rate of decay. This was found to be first order with a rate constant of $K_{g0^c} = 1.5 \times 10^{-4}$ sec$^{-1}$ [see Appendix 3].

Addition of either styrene or methyl acrylate accelerated the rate of decomposition of aziridine (33) at 80°C. However, methyl acrylate was found to have a greater effect than the equivalent amount of styrene. Thus, the addition of 1.5 mole equivalents of styrene gave an initial rate constant of $K_{g0^c} = 2.2 \times 10^{-4}$ sec$^{-1}$ (treated as first order) for the decomposition of (33) whereas the same concentration of methyl acrylate gave a corresponding rate constant of $K_{g0^c} = 3.05 \times 10^{-4}$ sec$^{-1}$ [see Appendix 3]. Increasing the concentration of methyl acrylate to four mole equivalents had a measurably greater effect on the rate of decomposition of (33) and gave a first order rate constant of $K_{g0^c} = 4.02 \times 10^{-4}$ sec$^{-1}$ over four half lives [see Appendix 3].

However, for these results above to unambiguously exclude the N-nitrene intermediate (32), it was necessary to show that aziridine (33) reacts preferentially with the alkene and to exclude an equilibrium between (33) [Scheme 30] and phthalimidonitrene (32): the effect of the alkene concentration on the rate of decomposition of (33) in this latter case could be explained by removal of phthalimidonitrene from this equilibrium.

\[ \begin{align*}
\text{COCH}_3 + \text{Phthal} & \rightarrow \text{COCH}_3 + \text{Phthal} - \text{N} \\
\text{COCH}_3 & \quad \text{(123)} \\
(33) & \quad \text{(32)}
\end{align*} \]

Scheme 30
To test for the existence of such an equilibrium, synthesis of the deuterium-labelled aziridine (124) was carried out by the oxidative addition of NAP (15) to 2-trideuteroacetylbenzofuran (125).

\[
\begin{align*}
&\text{COCO}_2, \text{Phthal-} \text{NH}_2 \xrightarrow{\text{LTA}, \text{CH}_2\text{Cl}_2} \text{N-Phthal} \\
&\text{COCD}_3
\end{align*}
\]

(125) \quad (124)

The aziridine (124) was then heated in d₆-benzene at 80°C in the presence of 2-acetylbenzofuran (123), monitoring the exchange of the 2-acetylbenzofuran unit by ¹H n.m.r. with and without methyl acrylate present. In the absence of methyl acrylate the ¹H n.m.r., recorded after 50% of the starting aziridine (124) had disappeared, showed only the aziridines (124) and (33) to be present in a 1:1 ratio.

\[
\begin{align*}
&(124) + \text{COCH}_3 \xrightarrow{} \text{N-Phthal} + \text{COCH}_3 \\
&(123) \quad (33) \quad (125)
\end{align*}
\]

When the above experiment was repeated with the additional presence of 4 mole equivalents of methyl acrylate then an n.m.r. spectrum recorded after 50% of the starting aziridine (124) had disappeared showed that the acrylate-derived aziridine (36) and (33) to be present in a 1:2.5 ratio respectively. From this it is clear that (124) brings about aziridination of 2-acetylbenzofuran at a rate at least 10 times faster than aziridination with methyl acrylate allowing for the different concentrations of alkenes used.

By itself, of course, this exchange observed does not prove the intermediacy of the N-nitrene since the unlabelled 2-acetylbenzofuran could be

\[\text{\textsuperscript{†}: Some decomposition of (33) back to 2-acetylbenzofuran and (124) will presumably be occurring.}\]

-52-
functioning as the alkene in the direct displacement mechanism in Scheme 28.

A distinction between a direct exchange and one possibly mediated by the free phthalimidonitrene can be made by measuring the kinetics for the disappearance of (124) in the presence of 2-acetylbenzofuran (123) as a function of their concentrations since a direct exchange should be dependent only on the concentration of (123) [see Appendix 4].

In the event, measurement of the rate constant for exchange of aziridine (124) with 2-acetylbenzofuran was unaffected by 2-fold or 4-fold dilution with benzene and this exchange with 2-acetylbenzofuran and presumably with other alkenes does not occur by the mechanism shown in Scheme 28.

Aziridination of alkenes using thermolysis of aziridine (33) is unavoidably accompanied by a competing thermal re-arrangement to give (127) [Scheme 31].

Although no direct evidence for (126) is available, it is a likely intermediate in the conversion of (33) to (127) and it is conceivable that it could possibly act as the aziridinating agent in the thermolysis of (33) [Scheme 32].
As a test for this possibility, the 2-acetyl-5-nitrobenzofuran (128) was prepared and converted to the aziridine (129) in the normal way [Scheme 33].

\[
\begin{align*}
\text{O}_2\text{N} & \quad \text{CH}_2\text{Cl} \\
\text{N} & \quad \text{OH} \\
\end{align*}
\]

\[\text{O}_2\text{N} \quad \text{CH}_2\text{PPh}_3\text{Cl} \]

\[\text{O}_2\text{N} \quad \text{COCH}_3
\]

\[\text{O}_2\text{N} \quad \text{N} \quad \text{Phthal}
\]

\[\text{O}_2\text{N} \quad \text{COCH}_3
\]

**Scheme 33**

**Reagents:**
(i) PPh₃; (ii) Et₃N, CH₃COOCl; (iii) NAP, LTA, CH₂Cl₂.

The aziridine (129) was then heated in boiling benzene in the presence of a 1:1 mixture of methyl acrylate and styrene and the ratio of aziridines (36) and (37) formed was found to be 3:1 respectively from examination of the crude reaction product [Scheme 34].

This ratio of aziridines (36) and (37) was identical, to within experimental error, with that previously obtained from thermolysis of the
aziridine (33) in the same mixture of alkenes [see Scheme 27].

These identical selectivities in aziridination using (33) and (129) make it unlikely that a mechanism such as that shown in Scheme 32 is operating, since the presence of the nitro group would be expected to effect a marked increase in the electrophilicity of the aziridinating agent.

The conclusion to be drawn from these results is that phthalimido-nitrene could still be the aziridinating species derived from thermolysis of both aziridines (33) and (129).

2.12 ATTEMPTS TO IDENTIFY N-ACETOXYAMINO-INTERMEDIATES FROM OXIDATION OF OTHER N-AMINO-HETEROCYCLES

Oxidations of other N-aminoheterocycles were re-examined at low temperature to determine whether analogous N-acetoxyamino-intermediates were also present in their oxidative additions to alkenes. However, when N-aminobenzimidazole (130) was oxidised at low temperature in a similar manner to the N-aminoquinazolone (77), no evidence for the corresponding N-acetoxyaminobenzimidazole was obtained. When styrene (3 mol equiv.) was added at -25°C to a solution of the product from the LTA oxidation of (130) at -25°C only the benzimidazoles (131) and (132) were isolated in a combined yield of 64%.

This suggests that little (if any) of the corresponding N-acetoxyaminobenzimidazole was present at -25°C and it must be concluded that the latter decomposes to (131) and (132) at -25°C at a significantly faster rate than
A similar picture was also observed for the case of \( \text{N-} \)-aminoquinolone (18). Oxidation of (18) at \(-25^\circ\text{C}\) followed by the addition of styrene afforded only quinolone (42%) with no aziridine being isolated.

Similarly, several attempts to show that \( \text{N-} \)-acetoxyaminophthalimide was an intermediate in the oxidation of NAP also resulted only in de-amination of the precursor (NAP). Thus when NAP was oxidised in the usual way at \(-25^\circ\text{C}\) and styrene added subsequently at \(-25^\circ\text{C}\), only phthalimide and residual styrene were present after work-up. Only when oxidation was carried out at a sufficiently low temperature (\(-50^\circ\text{C}\)) as described previously was it possible to infer that the analogous \( \text{N-} \)-acetoxyaminophthalimide (119) was present. Conceivably, oxidation of \( \text{N-} \)-aminoheterocycles (130) and (18) at lower temperatures might have given analogous results.

One of the major problems encountered using NAP in low temperature oxidations was its very low solubility in dichloromethane or chloroform: these solvents are invariably used in oxidations involving LTA. As a result of this insolubility, it was often necessary to carry out the oxidation over prolonged periods of time at low temperature in order to ensure that all the LTA and NAP had been consumed.

To overcome the problems associated with the insolubility of NAP, an attempt was made to solubilise it by making the trimethylsilyl (TMS) derivative (133).

\( \text{N-} \)-Trimethylsilylaminophthalimide (133) was prepared by adding tri-
methyldisilylchloride under nitrogen to a suspension of NAP (15) in dichloromethane containing triethylamine. After work-up (133) was obtained as a yellow oil.

![Chemical structure](image)

However, LTA oxidation of (133) at low temperature (-50°C) in the presence of methyl acrylate gave none of the expected aziridine (36); instead a moderate yield (46%) of N-methylaminophthalimide (134) was obtained. The production of this N-methyl compound (134) was found to occur with or without the presence of an alkene and may result from the mechanism shown below [Scheme 35].

\[
\text{Phthal-NHSiMe}_3 + \text{Pb(OAc)}_4 \rightarrow \text{Phthal-N}^{\text{SiMe}_3} + \text{HOAc}
\]

![Mechanism](image)

Scheme 35

2.13 OXIDATION OF NAP (15) AND NAQ (77) WITH OTHER TETRAVALENT LEAD SALTS

It has been demonstrated that oxidation of NAQ (77) and NAP (15) to their N-acetoxyamino-intermediates can be accomplished using LTA.
Similarly, lead tetra-benzoate (LTB) would be expected to give the corresponding N-benzoyloxyamino-intermediates.

LTB was readily prepared by the method of Wittmann from benzoic acid by warming it with lead tetra-acetate and distilling off the liberated acetic acid. When NAP (15) was oxidised at room temperature in the presence of styrene using LTB a 41% yield of the aziridine (37) was obtained: the presumed intermediate in this aziridination was the corresponding N-benzoyloxyaminophthalimide (135).

\[
\text{Phthal} - \text{NH}_2 \xrightarrow{\text{LTB, } \text{CH}_2\text{Cl}_2} \left[ \text{Phthal} - N \xrightarrow{\text{OCOPh}} \right] \xrightarrow{} \text{Phhal} - N - \text{H}
\]

(135)  (37)

More direct evidence for the formation of an N-benzoyloxyamino-intermediate came from the low temperature \(^1\)H n.m.r. The LTB oxidation of NAQ (77) at \(-30^\circ\text{C}\) in deuterochloroform gave a single product which was identified by n.m.r. (300 MHz) as (136).

\[
(77) \xrightarrow{\text{LTB, } -30^\circ\text{C, } \text{CDCl}_3} \text{OCOPh}
\]

(136)

The low temperature \(^1\)H n.m.r. spectrum of (136) showed a characteristic N-H resonance at \(\delta 11.32\) as well as an ABX\(_3\) system for the diastereotopic methylene protons in the ethyl side chain.

Monitoring the rate of decay of (136) by \(^1\)H n.m.r. suggested that it showed no greater stability than its N-acetoxyamino analogue (78) and from this point of view there is no advantage in the use of N-benzoyloxyamino-quinazolones in aziridination.
CHAPTER 3

Epoxidation and Aziridination of Allylic and Homoallylic Alcohols
3.1 INTRODUCTION

The epoxidation of alkenes by peracids is a widely used method in organic synthesis. Invariably the epoxide is prepared only to be ring-opened and the derived product further manipulated. Since epoxide ring-opening can be regio- and stereo-specific, the overall transformation is a versatile and controlled functionalization of the original double bond.

By contrast, the nitrogen analogue of epoxidation - aziridination is hardly used as a synthetic method although aziridines themselves have the same desirable features as epoxides as synthetic relay intermediates, viz. susceptibility to ring-opening in a controlled way.

It was considered that the mechanism for aziridination of alkenes when using the N-acetoxyaminoquinazolone (78) might be analogous to the traditional Bartlett mechanism by which epoxidation of alkenes using peracids is thought to proceed [Scheme 36].

![Scheme 36](image)

 Seeking support for this possible analogy between epoxidation and aziridination, the aziridination of a number of allylic alcohols was first examined.

3.2 AZIRIDINATION OF GERANIOL: COMPARISON WITH EPOXIDATION

Aziridination of geraniol was carried out either by using solutions of the N-acetoxyaminoquinazolone (78) or by the LTA oxidation of NAQ (77) in the presence of geraniol (3 mol equiv.).
Examination of the crude product by 300 MHz $^1$H n.m.r. showed the presence of two aziridines (137) and (138) formed in a 10:1 ratio and isolated by chromatography in 78% and 7% yield respectively [Figure 23].

![Figure 23](image)

**Figure 23**

Aziridination of geraniol using NAP (15) showed similar regioselectivity (ratio = 6:1) for the 2 double bonds. The major product (139) arose from attack on the 2,3-double bond and the minor product (140) from attack on the 6,7-double bond [Figure 23]. The similar regioselectivities in aziridination using (78) and from oxidative addition of NAP (15) are further support for the similarity of the intermediates involved.

By contrast, aziridination of geranyl chloride showed an inverse reactivity of the two double bonds by comparison with geraniol. Addition of geranyl chloride to a solution of the N-acetoxyaminoquinazolone (78) at low temperature afforded the aziridines (141) and (142) in a 6:1 ratio respectively [Figure 24], with the major product arising from a preferential attack on the 6,7-double bond.

![Figure 24](image)

**Figure 24**
Similarly, the simultaneous addition of NAP (15) and LTA to a solution of geranyl chloride gave aziridines (143) and (144) in a near identical ratio of 7:1 respectively.

Epoxidation of geraniol with peracids is not very regioselective: m-chloroperbenzoic acid gives a 2:1 ratio of epoxides from attack on the 6,7- and 2,3-double bonds respectively [Scheme 37].

It appears that the greater regioselectivity observed in aziridination of geraniol by comparison with epoxidation is a function of the stronger hydrogen bonding that exists between the N-acetoxyaminoquinazolone (78) and the hydroxy group in the transition state for aziridination.

When such hydrogen bonding is absent as, for example, in the aziridination of geranyl chloride, the presence of the electronegative chlorine atom deactivates the 2,3-double bond to electrophilic attack and results in the major product being derived from attack at the 6,7-double bond.

In the course of this work, aziridination of linalool (145), an isomer of geraniol, was also examined. The $^1$H n.m.r. spectrum of the crude oxidation product indicated that only the aziridine (146) was formed as a 1:1 ratio of diastereoisomers [Scheme 38] as shown by the doubling up of signals from the terminal olefinic protons.

Evidently the monosubstituted double bond in linalool, even with the benefit of hydrogen bonding is less reactive than the more nucleophilic trisubstituted double bond and hence only regioisomer (146) is obtained.
3.3 AZIRIDINATION OF CYCLOHEX-2-EN-1-OLS: COMPARISON WITH EPOXIDATION

Peracid epoxidation of cyclohex-2-en-1-ol (147) was first reported by Henbest and Wilson\(^66\) to proceed with high syn-stereoselectivity giving a 90:10 ratio of the two alcohols (148) and (149) respectively [Scheme 39].

\[
\begin{align*}
\text{(147)} \; R = H & \quad \text{(148)} \; 90 \quad \text{(149)} \; 10 \\
\text{(150)} \; R = \text{Ac} & \quad \text{(151)} \; 43 \quad \text{(152)} \; 57
\end{align*}
\]

This observation was explained in terms of a syn-directing effect of the allylic hydroxyl group and has been found to be general for a variety of allylic alcohols. It was thought to be the result of hydrogen bonding between the hydrogen of the allylic hydroxyl group and one of the oxygens of the peracid in the transition state for epoxidation.\(^67,68\)

In the absence of this allylic hydroxyl group, e.g. using the cyclohexenyl acetate (150), epoxidation was not very stereoselective and gave a 43:57 ratio of the epoxy acetates (151) and (152) [Scheme 39].\(^69\)

In view of the analogy drawn between aziridination and epoxidation above, it was of interest to examine whether aziridination of cyclohex-2-en-1-ol would respond stereoselectively to the presence of an allylic hydroxyl group in the same way as epoxidation using peracids. For this reason, the reaction of the N-acetoxyaminoquinazolone (78) with various
cyclohex-2-en-1-ols and their derivatives was examined.

Aziridination of cyclohex-2-en-1-ol was carried out by addition of the alcohol (3 mol equiv.) to a solution of the N-acetoxyaminoquinazolone (78) at low temperature. Chromatography of the crude oxidation product after work-up afforded the aziridine (153) as its syn-stereoisomer in 77% yield [Scheme 40]. The assignments of stereochemistry in this and other aziridines were supported by their high field ¹H n.m.r. spectra which will be discussed later in this chapter.

\[
\begin{align*}
\text{OR} & \quad \text{OR} \\
(147) & \quad (78) & \quad (153) \quad 95 : 5 & \quad (154) \\
(150) & \quad \text{Ac} & \quad (155) < 5 : >95 & \quad (156)
\end{align*}
\]

\text{Scheme 40}

In contrast to epoxidation, aziridination of 2-cyclohexenyl acetate (150) gave, stereospecifically, the anti-aziridine acetate (156), which was isolated by chromatography in 7% yield (m.p. 120-123°C) [Scheme 40]. The major product from this latter aziridination and others that proceeded in poor yield was the de-aminated quinazolone (79).

The assignment of the anti-configuration to this aziridine acetate (156) was supported by the acetylation of the syn-aziridine alcohol (153) which gave the syn-aziridine acetate (155) (m.p. 93-95°C) in 83% yield and which was clearly different from (156) [Scheme 41].

\[
\begin{align*}
\text{OAc} & \quad \text{OAc} \\
(153) & \quad \text{Pyr.} (\text{CH}_3\text{CO})_2\text{O} \quad \text{ca. 8h, 25°C} \\
(155) & \quad 83\%
\end{align*}
\]

\text{Scheme 41}

Using the same acetylation conditions, the stereoselectivity in
aziridination of cyclohex-2-en-1-ol was examined. A 300 MHz \( ^1H \) n.m.r. spectrum of the crude aziridination product after acetylation showed that approximately 5% of the epimeric acetate (156) was also produced. This would lead to the conclusion that the stereoselectivity in aziridination of cyclohexenol was 95:5 providing that acetylation of both alcohols (153) and (154) was equally efficient and proceeded in each case with retention of configuration at the hydroxyl-bearing carbon. However, since acetylation of the isomeric alcohol (157) (albeit under different acetylation conditions) resulted in a 3:1 mixture of the epimeric aziridine acetates (158) and (159) [Scheme 42], it was conceivable that the 5% of aziridine (156) could have been produced in the acetylation process.

\[
\begin{align*}
Q & \quad \text{Ac}_2O, \text{NaOAc} \\
(157) & \quad \rightarrow \quad (158) + (159)
\end{align*}
\]

\text{ratio of (158):(159) = 3:1}

\text{Scheme 42}

However, acetylation of the pure syn-aziridine alcohol (153) and subsequent examination of the crude reaction product by \( ^1H \) n.m.r. showed no trace of the epimeric acetate (156) and hence the 95:5 ratio of aziridines (153) and (154) as shown in Scheme 40 does represent the stereoselectivity in the aziridination of cyclohexenol.

The \text{anti}-\text{stereospecificity} observed in the aziridination of the acetate (150) is not paralleled by epoxidation using peracids:\(^6^9\) the poor 7% yield cf (156), however, was unexpected. As will be discussed later [see Chapter 6] it was found that aziridination of unreactive alkenes such as (150) could be improved by the simultaneous addition of LTA and the N-aminoquinazolone (77) to a solution of the alkene in the presence of TFA (3 mol
equiv.). Under these conditions, aziridination of (150) proceeded in much better yield (66%) but with almost complete loss of stereospecificity. Examination of the crude oxidation product by $^1$H n.m.r. showed that the aziridine acetates (155) and (156) were formed in a 1.2:1 ratio respectively.

Aziridination of cyclohex-2-enyl methyl ether (160) has also been examined since the effects of the methoxy on the double bond were expected to be similar to those of the hydroxyl group although the hydrogen bonding capability is absent [Scheme 43].

The yield of aziridine (161) after chromatography was still low (19%) with the major product being the NH-quinazolone (79), but, as in the aziridination of cyclohexenyl acetate (150), the reaction appeared to proceed highly stereoselectively anti. The directing effects of allylic oxygen-bonded substituents on the facial selectivity of the alkene have been noted in a number of other electrophilic reactions.  

It seems likely, therefore, that in the absence of its hydrogen bonding ability, the hydroxyl group would similarly possess an anti-directing (and deactivating) effect in the aziridination.

Aziridination of 3-methylcyclohex-2-en-1-ol (162) has also been achieved and the aziridine (163) was isolated in 71% yield [Scheme 44]. The presence of the methyl group on the aziridine ring in this compound facilitated interpretation of its n.m.r. spectrum [Table 4, see below].

Similarly, aziridination of 3-phenylcyclohex-2-en-1-ol (164) and the
acetate (166) [Scheme 44] has also been accomplished using (78). However, the stereochemistry and conformations of the six-membered rings in both derived aziridines (165) and (167) were not proven: assignment of the syn-aziridine to (165) and the anti-aziridine to (167) was based on the parallel behaviour observed in aziridination of cyclohex-2-enols (147) and (162) and the derived acetate (150).

The improved yield in aziridination of the acetate (166) over acetate (150) can be explained by the presence of the phenyl group on the double bond which enhances the reactivity of this alkene via a secondary interaction in the transition state for aziridination [see Chapter 1].

The $^1$H n.m.r. spectrum of this aziridine acetate (167) showed a broadening of the aziridine ring proton signal which was suggestive of hindered rotation around the N-N bond. This phenomenon has been observed in similar cases in which the quinazolone ring is located on the same side of the aziridine ring as a phenyl group [see Chapter 5].

For comparison purposes in $^1$H n.m.r. analyses of these 7-azabicyclo-[4.1.0]heptanes the aziridination of 3-methylcyclohex-1-ene was also examined.

3.4 AZIRIDINATION OF 3-METHYLCYCLOHEX-1-ENE (168)

Aziridination of 3-methylcyclohex-1-ene was accomplished at room temperature by continuous and portionwise addition of NAQ (77) and LTA to a
solution of the 3-methylcyclohex-1-ene (3 mol equiv.) in dichloromethane [Scheme 45].

\[
\begin{align*}
(168) \quad \xrightarrow{\text{LTA, RT}} \quad (169) \quad + \quad (170)
\end{align*}
\]

Scheme 45

5:1 ratio of isomers

Examination of the crude reaction product by 300 MHz \(^1\text{H}\) n.m.r. revealed the presence of 2 stereoisomers formed in a 5:1 ratio. The stereoselectivity observed in this experiment is a consequence of the preferred attack on the less hindered face of the cyclohexene which should lead to aziridine (169) as the major product. Chromatography of this crude oxidation product over silica separated both aziridines in 4% and 14% yields and their relative configurations were supported by n.O.e. difference spectra. As predicted, the major stereoisomer was (169) in which the methyl group is on the opposite side to the aziridine ring, and this was confirmed by n.O.es. The ethyl methylene protons adjacent to the quinazolone showed large n.O.es of 3.5% and 2.3% with \(H_{5\alpha}\) and \(H_{2\alpha}\), respectively, whereas no n.O.e. was observed with either the trans-\(Me_2\beta\) or \(H_5\beta\).

In the minor stereoisomer (170) in which the aziridine ring and the cyclohexyl methyl group are cis to each other, n.O.es are again observed for these methylene protons with \(H_{5\alpha}\) and \(Me_{2\alpha}\) of 1.2% and 1% respectively. Similarly, no n.O.es were observed between the foregoing methylene protons and either \(H_{2\beta}\) or \(H_{5\beta}\) which are trans to the aziridine ring.

Assignments of conformation in these and other compounds above follow from their \(^1\text{H}\) n.m.r. spectra (see below).
3.5 **ANALYSIS OF THE N.M.R. SPECTRA OF 2-SUBSTITUTED-7-AZABICYCLO[4.1.0]-HEPTANES**

From the n.m.r. spectra of a number of examples of this bicyclic ring system (171) that have been examined, all of which bear a single substituent on the four carbon bridge, a number of conclusions can be drawn:

(i) $J_{H_iH_{26}}$ and $J_{H_6H_{56}}$ are small, typically 0-1.5 Hz,
(ii) $J_{H_1H_{26}}$ is ca. 4 Hz and only marginally smaller than $J_{H_6H_{56}}$ at 6-7 Hz.

These conclusions are similar to those obtained from analysis of the $^1H$ n.m.r. spectra of 2-substituted-7-oxabicyclo[4.1.0]heptanes that have been reported elsewhere.\(^7\)

Together, (i) and (ii) make assignment of configuration at C-2 in the foregoing aziridines straightforward provided that $J_{H_1H_{26}}$ or $J_{H_1H_{26}}$ can be measured. Fortunately, the only other aziridine ring coupling $J_{H_1H_6}$ has, reliably, a value of 7.5-8.0 Hz: even if $J_{H_1H_{26}}$ or $J_{H_1H_{26}}$ cannot be directly measured from the multiplicity of the $H_1$ signal, it is often possible to do so from analysis of the signals from $H_{2\alpha}$ or $H_{2\beta}$.

Using the above values for $J_{H_1H_{26}}$ it was clear [Table 4] that (153), (155), (163) and (170) with $J_{H_1H_{26}}$ values of 4.0, 4.0, 4.4 and 3.9 Hz respectively have their 2-substituents cis to the aziridine ring whereas (156), (161) and (169) with $J_{H_6H_6}$ values of ca. 1, 0.8 and <1 Hz respectively, have their 2-substituents trans to the aziridine ring. However, in drawing these conclusions, the assumption has been made that the six-membered ring in the bicyclo[4.1.0] system adopts a half-chair conformation (an examination of Dreiding models suggested that if this ring adopted one particular half-boat conformation, the configurational assignments above
<table>
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<th></th>
<th>( J_{1,2\alpha} )</th>
<th>( J_{1,2\beta} )</th>
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<th>( J_{\mathrm{H}<em>{1},\mathrm{H}</em>{6}} )</th>
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</table>
TABLE 4 (Continued) ....

a In this Table only aziridines (163), (156), (161) and (169) have been re-numbered to allow comparison to be made with all half chains having the same conformational presentation to the reader.

b The spread of values of this coupling constant is in part the result of differing substituent electronegativity.

would have to be reversed).

The best evidence available for the expected half-chair conformation for the six-membered ring in these compounds came from the $^1$H n.m.r. spectra of aziridines (153) and (163) in which enough coupling constants between protons on this ring were measurable to allow comparison with the $^1$H n.m.r. spectrum of aziridine (169) to be made. The n.m.r. spectrum of (169) showed clearly from its axial-axial (pseudoaxial) coupling constants of $J_{H_2,H_3} = 10$Hz, $J_{H_3,H_4}$ = 11.5Hz and $J_{H_4,H_5} = 10.5$Hz together with the values of its H-1 and H-6 coupling constants that it must adopt a half-chair conformation. The similarities between the respective coupling constants in (169) and those in (153) and (163) suggested that in these latter cases their six-membered rings also have half-chair conformations and this is most likely for all the aziridines listed in Table 4.

The data in Table 4 also suggested that the hydroxyl groups in (153) and (163), and the methyl group in (169) occupy pseudoequatorial positions since the CHMe(OH) signal contained a pseudoaxial-axial coupling constant of 7-8-10.5Hz.

3.6 AZIRIDINATION AND EPOXIDATION OF CYCLOHEX-3-EN-1-OL (172)

Epoxidation of cyclohex-3-en-1-ol with perbenzoic acid is not very stereoselective $^72$ [ratio of epoxides obtained = 40:60 anti:syn, Scheme 46]$^73$ although high syn-stereoselectivity in epoxidation of (172) has been
accomplished by using t-butylperoxide and metal catalysts.\textsuperscript{72}

\[
\text{\begin{array}{c}
\text{[Image of reaction scheme]}
\end{array}}
\]

\[
\text{ratio of (174):(173) = 40:60}
\]

Scheme 46

It was of interest to examine the aziridination of homoallylic alcohol (172) with N-acetoxyaminoquinazolone (78) and to determine the stereoselectivity in this reaction.

Reaction of the cyclohex-3-en-1-ol (172) (3 mol equiv.) with (78) prepared in situ by oxidation of N-aminoquinazolone (77) with LTA at -20°C in dichloromethane, afforded the aziridine (157) in 77% yield after chromatography [Scheme 47].

\[
\text{\begin{array}{c}
\text{[Image of reaction scheme]}
\end{array}}
\]

Scheme 47

A number of factors conspired to make assignment of configuration of the hydroxyl group in (157) uncertain: the fact that the latter is predominantly axially disposed (none of the coupling constants for H\textsubscript{5} was >7Hz) and also that JH\textsubscript{1}H\textsubscript{2x} and JH\textsubscript{1}H\textsubscript{2β} do not differ sufficiently from JH\textsubscript{5}H\textsubscript{5α} and JH\textsubscript{5}H\textsubscript{5β} to allow unambiguous distinction between (157) and (175) [Figure 25].

\[
\text{\begin{array}{c}
\text{[Image of Figure 25]}
\end{array}}
\]
Acetylation of alcohol (157) by brief heating under reflux with acetic anhydride and sodium acetate gave a crystalline acetate (158) in 65% yield whose configuration could be unambiguously assigned from detailed analysis of its 400 MHz $^1$H n.m.r. spectrum.

In contrast to the alcohol (157), the acetoxy group in (158) was equatorially disposed with H-3β showing axial-(pseudo)axial coupling constants of 12.5Hz (with H-4α) and 10Hz (with H-2α) and a further axial-pseudoaxial coupling constant of 12.5Hz between H-5β and H-4α. A clear distinction between (158) and (176) can be made since H-2α is distinguishable from H-2β by the small value of its coupling constant with H-1 (1.2Hz) and its large pseudoaxial-axial coupling with H-3β defines the configuration of the acetoxy group as cis in (158). Whilst the $J_{H_1H_2\alpha}$ coupling constant in (176) would also be small (ca. 1Hz), $J_{H_2\alpha H_3\alpha}$ in this case would not be expected to exceed 5Hz.

Acetylation of alcohol (157) might be expected to proceed with retention of configuration at the hydroxy bearing carbon. However, examination of the crude acetylation product by 300 MHz $^1$H n.m.r. before crystallization of (158) showed the presence of an additional product which was subsequently identified as the epimeric acetate (159) [ratio of (158):(159) = 3:1]. A 1:1 mixture of the same two acetates (158) and (159) was also obtained in low yield (18%) from aziridination of cyclohex-3-enyl acetate (177) using (78) [Scheme 48].

Acetylation of alcohol (157), therefore, was not stereospecific and it cannot be assumed that it proceeded with predominant retention of config-
uration at the hydroxyl bearing carbon. To prove that this was the case, the alcohol (157) was subjected to a Mitsunobu reaction using acetic acid which is known to proceed with inversion of configuration [Scheme 49].

The product (159) was found to be identical by $^1$H n.m.r. with the minor product from acetylation of alcohol (157) which had not previously been obtained free from its epimer (158). Like alcohol (157), the acetate product from the Mitsunobu reaction (159) existed with its acetoxy group predominantly in an axial position on the half-chair and not equatorial as in (158). This conclusion followed most directly from the width of the signal from the CHOAc proton in the $^1$H n.m.r. spectrum of 23Hz (in which axial-axial coupling constants are absent) by comparison with a width of 36Hz for the same proton in the epimer (158).

Final proof for the correctness of these configurational assignments came from the hydrolysis of the ester linkage in acetate (159) which gave only the alcohol (178) which was different from that obtained from aziridination of the cyclohexenol (172). These interconversions are summarised in Scheme 50.
3.7 $^1$H N.M.R. ANALYSIS OF 3-SUBSTITUTED-7-AZABICYCLO[4.1.0]HEPTANES

Table 5 (see below) shows selected coupling constants which have been assigned in the $^1$H n.m.r. spectra of aziridines (157), (158), (159) and (178). These indicated that, with the exception of acetate (158), all these aziridines had hydroxyl or acetoxy groups in axial positions. The data also suggested that the same half-chair conformation was present in every case with values for the measurable coupling constants comparable to those found in a number of 2-substituted-7-azabicyclo[4.1.0]heptanes previously given in Table 4. These assignments were also supported by n.O.es in (158) between H-4α, H-2α (2.8%) and H-5β, H-3β (4.6%).

It is not surprising that the energy difference between axial and equatorial substituents in this bicyclic system should be reduced for 3- (or 4-) substituted compounds by comparison with that obtaining in a normal cyclohexane (which is in any case small for OH or OAc) since the two
### Table 5: Selected coupling constants of 3-substituted-7-azabicyclo[4.1.0]heptanes

<table>
<thead>
<tr>
<th>Structure</th>
<th>$J_{1,2\alpha}$</th>
<th>$J_{1,2\beta}$</th>
<th>$J_{2\alpha,3\alpha}$</th>
<th>$J_{2\alpha,3\beta}$</th>
<th>$J_{2\beta,3\alpha}$</th>
<th>$J_{2\beta,3\beta}$</th>
<th>$J_{3\alpha,4\beta}$</th>
<th>$J_{3\beta,4\alpha}$</th>
<th>$J_{4\alpha,5\alpha}$</th>
<th>$J_{4\alpha,5\beta}$</th>
<th>$J_{4\beta,5\alpha}$</th>
<th>$J_{4\beta,5\beta}$</th>
<th>$J_{5\alpha,6}$</th>
<th>$J_{5\beta,6}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>(157)</td>
<td>$&lt;1$</td>
<td>$4.5$</td>
<td>$5.0$</td>
<td>$7.5$</td>
<td>$2.4$</td>
<td>$7$</td>
<td>$4.5$</td>
<td>$9$</td>
<td>$7.2$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(158)</td>
<td>$1.2$</td>
<td>$3.6$</td>
<td>$4.6$</td>
<td>$12.5$</td>
<td>$5.2$</td>
<td>$7.4$</td>
<td>$11.8$</td>
<td>$3.6$</td>
<td>$10.2$</td>
<td>$6.6$</td>
<td>$b$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(159)</td>
<td>$1.6$</td>
<td>$4.5$</td>
<td>$5.8$</td>
<td>$5.8$</td>
<td>$7.9$</td>
<td>$4.8$</td>
<td>$1.2$</td>
<td>$6.0$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(178)</td>
<td>$-2.0$</td>
<td>$4.5$</td>
<td>$4.5$</td>
<td>$4.5$</td>
<td>$8$</td>
<td>$4.5$</td>
<td>$1.4$</td>
<td>$6.6$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
TABLE 5 (Continued) ....

a Aziridines (158), (159) and (178) have been re-numbered to allow comparison to be made with all half chains having the same conformational presentation to the reader.

b These two signals were assigned as shown (rather than the reverse) by reference to the corresponding signals in alcohol (157).

c These coupling constants may be interchanged.

1,3-diaxial interactions in the latter are reduced to a single 1,3-axial-pseudoaxial interaction in, e.g. (157), (159) and (178). It is not clear, however, why the aziridine (158) should have a clear preference for the equatorial position of its acetoxy by comparison with the axial preference of this substituent in its epimer (159). This same phenomenon was also found to occur in the corresponding 7-oxabicyclo[4.1.0]heptanes.

3.8 EPOXIDATION OF CYCLOHEX-3-ENYL ACETATE (177)

Epoxidation of cyclohex-3-enyl acetate (177) with m-chloroperbenzoic acid gave a mixture of the two epoxides (179) and (180) in a ratio of 1.2:1 respectively [Scheme 51].

\[
\begin{align*}
\text{cyclohex-3-enyl acetate} & \xrightarrow{m\text{CPBA}} \text{epoxide mixture} \\
(177) & \quad (179) \quad (180) \\
\text{i) } & \text{Bu}_3\text{OOH, VO(acac)}_2 \\
\text{ii) } & \text{Ac}_2\text{O, pyridine}
\end{align*}
\]

Scheme 51

The signals from the protons on the carbons bearing acetoxy groups in
this mixture of (179) and (180) were remarkably similar in chemical shift difference, signal width and coupling constants to the corresponding signals in the \( ^1H \) n.m.r. of the 1:1 mixture of aziridine acetates (158) and (159). On this basis, therefore, a similar axial or equatorial conformational preference for the acetoxy group is present in (179) and (180).

This unexpected difference in conformational preference between the two aziridine acetates (158) and (159) and the corresponding two epoxide acetates (179) and (180) has been used to provide additional support for the configurational assignments made above to aziridines (158) and (159). Thus, when the cyclohex-3-enol (172) was epoxidized using \( t \)-butylhydroperoxide and \( VO(acac)_2 \) [a reaction which is known to give the cis-epoxyalcohol (173), Scheme 51]\(^{73} \) and the product acetylated with pyridine and acetic anhydride, the CHOAc signal in the \( ^1H \) n.m.r. spectrum of the epoxyacetate product (179) closely resembled that at higher field having the broader signal width in the mixture of (158) and (159). This CHOAc signal has been previously assigned to the cis-aziridine acetate (158) and the assignment of cis-configuration is in agreement with the correlation with the cis-epoxyacetate established above.

It appears, therefore, that the subtle conformational effects which are present are probably the result of the 3-membered ring fusion. [Only single invertomers of aziridines (157), (158), (159) and (178), having the quinazolone ring exo, were present as shown in Table 5].

Comparison of the \(^1H \) n.m.r. spectra of epimeric alcohols (157) and (178) revealed that the multiplet at \( \delta 3.96 \) in (178) did not overlap with any resonance from alcohol (157). Examination of the \(^1H \) n.m.r. spectrum of the reaction product from aziridination of cyclohex-3-enol (172) after removal of excess of the latter by chromatography over silica revealed no evidence for the presence of aziridine (178). A mixture of aziridines
(157) and (178) in an 8:1 ratio respectively was shown to be unchanged by $^1$H n.m.r. after chromatography over silica.

It appeared therefore that, in contrast to epoxidation of (172) with peracids, aziridination of cyclohex-3-en-1-ol (172) by N-acetoxyaminoquinazolone (78) was stereospecific.

3.9 POSSIBLE TRANSITION STATE GEOMETRIES IN AZIRIDINATION OF CYCLOHEXENOLS

The stereospecificities observed in the aziridination of cyclohexenols (172) and (147) can be rationalised by the transition states depicted in (181) and (182) respectively, where the quinazolone ring is exo and directs the HNOAc group towards the hydroxyl group in both cases.

Thus, the increased stereoselectivity in aziridination of (172) when compared to epoxidation may be the result of acetic acid elimination via a 7-membered ring as shown in (181). Elimination of acetic acid from peracids in epoxidation would be expected to be easier than from the N-acetoxyaminoquinazolone (78) in aziridination since:

(i) the O-O bond is weaker than the N-O bond and
(ii) the O-H proton in a peracid is more acidic than the NH proton in (78).

The involvement of both atoms of the hydroxyl group as shown in (181) may offer an easier pathway for loss of acetic acid in aziridination. A preferred 'parallel plane' or perpendicular approach for epoxidation [Figure 26] would be less favourable for aziridination because of the location of the quinazolone ring which would direct the other two substituents of the nitrogen towards the hydroxy group as shown in (182).
In the aziridination of allylic alcohols it is proposed that the transition state resembles (182). The hydrogen bonding present in (182) appears to be easier from models with the hydroxyl group equatorially disposed. Whitham et al.\(^{69}\) have previously shown that an equatorially fixed hydroxyl group brings about a greater acceleration rate than an axial hydroxyl group in epoxidation of substituted cyclohex-2-enols.

The similarity between the stereoisomeric ratios produced in epoxidation (using perbenzoic acid) and aziridination [using (78)] of cyclohex-2-enol suggests that similar transition state geometries may be involved in both cases [see (182) and (183)].

On the other hand, the possibility that different transition state geometries are involved in the above reactions comes from the results from epoxidation and aziridination of cyclohex-3-enol using the same reagents where the stereoselectivities obtained are very different.

3.10 AZIRIDINATION OF DIOL (184)

The diol (184) has two double bonds both of which have allylic and homoallylic hydroxyl substituents. However, the presence of an electron
withdrawing trifluoromethyl group deactivates one double bond towards electrophilic aziridination.

Addition of (184) (2 mol equiv.) to a solution of the N-acetoxyaminoquinazolone (78) at low temperature afforded, on warming to ambient, the bicyclohept-2-ene (185). Chromatography of the crude oxidation product over silica afforded (185) in 74% yield as one regio- and stereoisomer [Scheme 52].

![Scheme 52](image)

The regiochemistry of (185) was evident from the appearance of only one olefinic proton in its n.m.r. The stereochemistry of (185) was assigned by analysis of its $^1$H n.m.r. spectrum which showed that H-4, from the magnitude of its $J_{H_4,H_5}$ coupling constant of 4.7 Hz and from its 4 bond 'W' coupling to H-6 of 2.0 Hz, adopts a pseudo-equatorial position in a conformation for (185) as shown.

When aziridination of diol (184) was repeated at room temperature in the presence of Ti(OPr$^i$)$_4$, no aziridine was isolated and only the N-H quinazolone (79) was recovered in near quantitative yield.

Hence, using a solution of the N-acetoxyaminoquinazolone (78) it is possible to bring about aziridination of diol (184) which would otherwise be cleaved in the presence of LTA.
CHAPTER 4
Aziridination of Enol Ethers and Silyl Ketene Acetals
4.1 INTRODUCTION

The development of aziridination as a synthetic method will be assisted if it is widely applicable to a range of alkenes. Prior to the discovery that solutions of the N-acetoxyaminoquinazolone (78) are stable at -20°C, it was possible to aziridinate only those alkenes which were stable to the highly oxidative conditions that the presence of LTA imposes.

By using solutions of (78), in the formation of which all the LTA has been consumed, it is now possible to bring about aziridination of alkenes that would otherwise be readily attacked by LTA.

This chapter examines the aziridination of enol ethers and silyl ketene acetals using solutions of (78): both of these classes of nucleophilic alkenes are rapidly attacked by LTA in preference to oxidation of the N-amino group. These types of alkenes are widely used in organic synthesis as nucleophilic synthons for ketones, aldehydes and esters: functionalization of these carbonyl compounds with an electrophile at their α positions is the overall reaction which results [Scheme 53].

\[
\begin{align*}
RCH_2CO_2Me & \xrightarrow{1 \text{ LDA}} RCH = \underset{\text{OSiMe}_3}{\text{RCHCO}_2Me} \\
& \xrightarrow{\text{E}^+} \text{E}\ 
\end{align*}
\]

Scheme 53

4.2 ATTEMPTED AZIRIDINATION OF ENOL ETHERS

The N-acetoxyaminoquinazolone (78) was prepared at low temperature in the usual way. Addition of ethyl vinyl ether (1.5 mol equiv.) to a solution of (78) at -20°C and then warming to room temperature afforded the acetal (187) after chromatography in 69% yield as colourless crystals [Scheme 54].
Formation of this acetal (187) may occur by ring opening of the unstable intermediate aziridine (186) by acetic acid. The acetic acid which brings about this ring opening of (186) is a by-product from the formation of both (78) and (186).

The silyl enol ether (189), $^{79}$ prepared by palladium catalysed Brook rearrangement of the chloroketone (188), $^{60}$ also reacts with solutions of (78).

The crude reaction product from addition of (189) to a solution of N-acetoxyaminoquinazolone (78), was triturated with hot light petroleum and the insoluble chloroketone (191) was separated off. Recrystallization from ethanol afforded (191) as colourless crystals in 58% yield. Evaporation of the filtrate after removal of the chloroketone (191) revealed that it contained the acetal (192) which was isolated in 10% yield but was not fully characterised [Scheme 55].

In Scheme 55 the aziridine (190) is postulated as an intermediate although no evidence for (190) was ever obtained. Formation of both (191) and (192) could then be brought about by nucleophilic attack of residual acetic acid at two different sites in (190): whereas the chloroketone (191) results from the desilylation and ring opening of (190), the acetal (192)
Scheme 55

is produced by acetic acid ring opening of (190) without desilylation.

Initial attempts to isolate the chloroketone (191) by flash silica chromatography were unsuccessful as there was a near-quantitative conversion of (191) to the iminoketone (193) possibly by the mechanism shown below [Scheme 56].

Scheme 56

After chromatography, the acetal (192) and the iminoketone (193) were obtained in 8% and 60% yield respectively. After recrystallization of (193) from ethanol its 300 MHz n.m.r. showed that it exists as only one double bond isomer.

In the light of these successes with LTA-labile alkenes, it was decided to examine the reaction of (78) with silyl ketene acetals as this should directly provide a novel route to the synthesis of N-protected α-amino acid esters. The following brief review of the recent literature demonstrates the synthetic utility of silyl ketene acetals in the synthesis of α-amino acids.
4.3 ELECTROPHILIC AMINATION OF SILYL KETENE ACETALS: FORMATION OF AMINO ACID DERIVATIVES

As only a few of the known α-amino acids are abundant in nature, the interest in both their achiral and enantioselective synthesis is growing. α,β-Unsaturated esters are difficult to attack with electrophilic aminating agents although addition of alkoxy carbonyl nitrenes to α,β-unsaturated esters has been reported to give mainly aziridine carboxylic esters; ring opening of similar compounds by alcohols, thiols, and Wittig reagents has been shown more recently to produce α-amino acids with good selectivity.

Silyl ketene acetal may be considered as substrates of choice for electrophilic amination aimed at α-amino acid synthesis and several recent examples have been reported. Thus the reaction of bistrimethylsilyl ketene acetal (194) with nitrosobenzene (195) has been reported by Ohno to give silylated α-hydroxyamino acid silyl esters (196).

\[
\text{Me}_3\text{SiO} + \text{C}_6\text{H}_5 - \text{N} = \text{O} \rightarrow \text{Me}_3\text{SiO} \quad \text{CHCl}_3, 20^\circ\text{C} \quad \text{Me}_3\text{SiO} \quad \text{C}_6\text{H}_5 \quad \text{N} \quad \text{O} \quad \text{SiMe}_3
\]

After replacement of chloroform by methanol, the crude compounds (196) are directly transformed to the α-N-phenylamino acids (197) in moderate yield by catalytic hydrogenation [Scheme 57].

Similar strategy has been used by Tanaka in the reaction of the silyl ketene acetal (198) with benzene diazonium tetrafluoroborate which
gave a mixture of (E) and (Z) isomers of the hydrazono esters (199). The α-hydrazono esters (199) formed were readily converted to the α-amino acid esters (200) in nearly quantitative yields when treated with hydrogen in the presence of palladium on carbon [Scheme 58].

![Scheme 58](Image)

**Reagents:**  
(i) PhN₂BF₄, 0°C, 2h, Pyridine;  
(ii) H₂ (5 atm.), Pd-C, room temp., 2.5h, MeOH.

Amination of silyl ketene acetals has also been accomplished with nitrenes: thermolysis of N-(ethoxycarbonyl)-N,O-bis(trimethylsilyl)-hydroxylamine (201) generates ethoxycarbonylnitrene (202).

![Reactions](Image)

If (201) is heated in the presence of silyl ketene acetalts (203) as solvent, moderate yields of the N-protected-α-amino esters (204)-(207) are obtained by the proposed reaction pathway depicted in Scheme 59.

Mitani has accomplished the same conversion by photolysis of ethyl azidoformate (208) in the presence of silyl ketene acetalts (209) (2.5 mol
equiv.) to give the α-amino ester derivatives (210)-(212) in yields of 45-75%.

These methods result in racemic products. However, the reaction of chiral enolates and chiral silyl ketene acetals with azodiesters has also been used to synthesise amino acids with high levels of enantiomeric excess.85-89 Oppolzer98 has used the silyl ketene acetal (213) to synthesize enantiomerically pure α-amino acids. Treatment of (213) with di-(tert-butyldiazodicarboxylate, TiCl4 and Ti(OPr)i, gave the N,N'-di[(tert-butoxy)carbonyl]hydrazino esters (214) which on deacylation, hydrogenolysis,
transesterification and acid hydrolysis furnished α-amino acids (215) in high enantiomeric purity [Scheme 60].

\[
\begin{align*}
\text{X}^* &= \begin{array}{c}
\text{SO}_2\text{N}(\text{O})\
\end{array} \\
\text{R} &= \begin{array}{c}
\text{SO}_2\text{N}(\text{O})\
\end{array}
\end{align*}
\]

\[ (213) \quad (214) \]

Scheme 60

Reagents: (i) LiN(i-Pr)_2, Me_3SiCl; (ii) Bu^tO_2C-N=N-CO_2Bu^t, TiCl_4 and Ti(OiPr)_4.

4.4 REACTION OF (78) WITH Silyl Ketene Acetals: A NEW ROUTE TO N-PROTECTED α-AMINO ACID ESTERS

The products from the reaction of the N-acetoxyaminoquinazolone (78) with various acetals (216)-(218) (3.5 mol equiv.),^99,100 are shown in Scheme 61.

\[
\begin{align*}
(78) + & \quad \begin{array}{c}
\text{R}^1\text{=Me} \\
\text{R}^2\text{=Me} \\
\text{R}^1\text{=Ph} \\
\text{R}^2\text{=Me} \\
\text{R}^1\text{=R}^2\text{=Me} \\
\text{R}^1\text{=R}^2\text{=Me} \\
\text{R}^1\text{=R}^2\text{=Me} \\
\text{R}^1\text{=R}^2\text{=Me} \\
\text{R}^1\text{=R}^2\text{=Me} \\
\text{R}^1\text{=R}^2\text{=Me} \\
\text{R}^1\text{=R}^2\text{=Me} \\
\text{R}^1\text{=R}^2\text{=Me} \\
\text{R}^1\text{=R}^2\text{=Me} \\
\text{R}^1\text{=R}^2\text{=Me} \\
\text{R}^1\text{=R}^2\text{=Me} \\
\text{R}^1\text{=R}^2\text{=Me} \\
\end{array}
\end{align*}
\]

\[ (216) \quad (217) \quad (218) \quad (219) \quad (220) \quad (221) \]

Scheme 61
As expected, the products in excellent yields were the N-protected α-amino acid esters (219)-(221), presumably formed by acetic acid desilylative ring-opening of intermediate aziridines.

The use of 3.5 mole equivalents of the ketene acetals in these amination reactions was necessary as they are themselves desilylated by acetic acid to their corresponding esters: thus, addition of 1.5 mole equivalents of the acetal (216) to a solution of the pre-formed (78) at -25°C followed by warming to room temperature afforded the amino ester (219) in only 22% yield. An additional product in this latter amination was the benzoxazinone (222) (11%) which was not formed when 3.5 mole equivalents of the acetal (216) was used.

\[
\begin{align*}
\text{(222)} & \\
\text{(223)}
\end{align*}
\]

If the hindered base (223) is first added to a solution of (78) at low temperature, then the subsequent addition of 1.5 mole equivalents of (216) resulted in an improved 63% yield of the corresponding amino ester (219). Presumably addition of 2,6-di-tert-butyl-4-methylpyridine (2 mol equiv.) (223) sequesters the acetic acid which causes desilylation of the acetal (216), resulting in an increased yield of (219).

The structures of these amino esters were confirmed by their spectral data: in the 400 MHz n.m.r. spectrum of (220) at -90°C in CD₂Cl₂, sharp signals from N-N bond rotamers are present in a 3:1 ratio.

Addition of 1-methoxy-1-trimethylsilyloxy-3-methylbutadiene (224),¹⁰¹ to a solution of (78) at low temperature affords a mixture of products after warming to ambient. Analysis of the 300 MHz ¹H n.m.r. spectrum of the crude reaction product shows that (225) and (226) are produced in an
approximate 1:1 ratio.

\[
\begin{align*}
(78) + & \quad \begin{array}{c}
\text{OSiMe}_3 \quad \text{O} \quad \text{Me} \\
\text{H} \quad \text{Q} \quad \text{NH} \\
\text{C}_2\text{H}_5 \quad \text{Q} \quad \text{NH} \\
\text{Me}_2\text{SiO} \quad \text{O} \quad \text{Me}
\end{array} \\
\text{(224)} & \quad \rightarrow \quad \begin{array}{c}
\text{H} \quad \text{Q} \quad \text{NH} \\
\text{C}_2\text{H}_5 \quad \text{Q} \quad \text{NH} \\
\text{Me}_2\text{SiO} \quad \text{O} \quad \text{Me}
\end{array} \\
\text{(225)} & \quad \text{(226)}
\end{align*}
\]

ratio of \((225):(226) = \text{ca. } 1:1\)

Chromatography over silica separated \((225)\) and \((226)\) which were obtained in 43% and 42% yields respectively. Further examination of the n.m.r. spectrum of both the crude oxidation product and that of the pure compound reveals that in both cases \((226)\) contains a 1:1 ratio of geometrical isomers. In order to account for this ratio it is proposed that the steric interaction that exists between the trimethylsilyloxy group and the methyl group in the postulated aziridine intermediate \((228)\) is of the same magnitude as that between the methylene of the aziridine ring and the trimethylsiloxy group in \((227)\).

\[
\begin{align*}
(227) & \quad \begin{array}{c}
\text{QN} \\
\text{Me}_2\text{SiO} \quad \text{OMe}
\end{array} \\
(228) & \quad \begin{array}{c}
\text{QN} \\
\text{Me}_2\text{SiO} \quad \text{OMe}
\end{array}
\end{align*}
\]

It is the desilylative ring opening of these proposed intermediate aziridines \((227)\) and \((228)\) that results in the formation of \((226)\) as a 1:1 ratio of double bond isomers. The same argument would still apply even if the starting acetal \((224)\) has the opposite geometry around the double bond.

The reaction of \(N\)-acetoxyaminoquinazolones with silyl ketene acetals resulting in the formation of amino acid esters was found to be common to all 2-substituted quinazolones that were studied [Scheme 62].

Thus, oxidation of the \(N\)-aminoquinazolone \((116)\) afforded 56% of the amino ester \((229)\) after chromatography. The comparatively low yield of
observed in this case is consistent with an earlier finding that the conversion of (116) into its corresponding N-acetoxyamino derivative (117) occurs in only ~50% yield.

\[
\begin{align*}
\text{(116)} & \quad R = -\text{CH}_2\text{OCH}_2\text{Ph} \\
\text{(230)} & \quad R = -\text{Bu}^+ \\
\text{(232)} & \quad 35\%
\end{align*}
\]

\[
\text{Scheme 62}
\]

It was also interesting to note that 35% of the amino ester (232) resulted from addition of the N-acetoxyamino derivative (231) to the acetal (217). Although the yield of amino ester (232) is low, it is nevertheless higher than any that have been obtained in aziridinations using this N-aminoquinazolone (230). For example, only 8% of the aziridine derived from styrene was obtained using oxidative addition of (230) and no aziridines were obtained in the attempted oxidative addition of (230) to various electron-deficient alkenes (see Chapter 6).

The simplicity of the reaction of N-acetoxyaminquinazolones with LTA-labile alkenes under the mildest of conditions makes this a valuable addition to the limited number of electrophilic aminating agents reported earlier in this chapter. The potential for extending the method to the synthesis of optically active amino acid esters using the chiral N-aminoquinazolone (111) is also present.
CHAPTER 5

Aziridination of Vinylsilanes and Vinylstannanes
5.1 **INTRODUCTION**

This chapter describes the continuing developments in using N-acetoxy-aminooquinazolones to bring about aziridination as applied in this section to both vinylsilanes and vinylstannanes.

Despite the availability and synthetic utility of these two classes of alkenes in organic synthesis,\(^{76,102}\) relatively few of the derived 2- (or 3-) silyl-substituted aziridines are known\(^{103-107}\) and a literature search revealed no examples of 2- (or 3-) stannyl-substituted aziridines. It should be possible to bring about aziridination of vinylsilanes and vinylstannanes in a single step by adding them to solutions of (78) at low temperature, and in practice this was found to be the case.

5.2 **AZIRIDINATION OF VINYL SILANES (235) AND (236)**

In view of the relative ease of epoxidation of vinylsilanes [Scheme 63],\(^{108}\) it was of interest to examine whether aziridination of similar alkenes proceeded with equal facility.

\[
\begin{align*}
&\text{SiMe}_3 \\
&\text{CH}_2\text{Cl}_2, 0\degree\text{C, 3h.} \\
&\text{mCPBA} \\
&\text{SiMe}_3, 0
\end{align*}
\]

**Scheme 63**

Initially, the aziridination of trimethylvinylsilane, the simplest vinylsilane was examined but without success (de-amination product (79) was the only identifiable product) and it was decided to incorporate into the vinylsilane a substituent that was known to enhance the reactivity of the alkene. This was the reasoning behind the attempted aziridination of (233) [Scheme 64].\(^{109}\)

However, no silyl-substituted aziridine was isolated and after chromatography aziridine (234) was recovered in 11% yield. The major product from this latter aziridination and others which proceed in poor
yield was the de-aminated quinazolone (79). This aziridine (234) was identical to the product resulting from the oxidative addition of (77) to methyl vinylketone and may arise via a desilylation of (233) or, more likely, of the unstable 2-silylaziridine.

Phenyl groups substituted on the alkene increase the reactivity of the latter towards aziridination (via an attractive secondary interaction) and for this reason the vinylsilanes (235) and (236) were synthesised with a view to increasing the efficiency of the aziridination. The required vinylsilanes were prepared by the method of Chan\textsuperscript{10} using the Shapiro reaction.\textsuperscript{111} Thus, treatment of the benzene sulphonylhydrazone of aceto-phenone (237) with n-butyllithium followed by the addition of trimethyl-silylchloride afforded α-trimethylsilylstyrene (235) in 70% yield [Scheme 65].

\[
\text{PhSO}_2\text{NHNN} \quad \xrightarrow{1. \text{n-BuLi}} \quad \xrightarrow{2. \text{Me}_3\text{SiCl}} \quad \text{Ph} \quad \text{SiMe}_3
\]

(237) (235) 70%

Scheme 65

Surprisingly, aziridination of (235) using the N-acetoxyamino intermediate (78) gave, after chromatography, a poor yield (25%) of the corresponding aziridine (238) [Scheme 66].

Examination of the n.m.r. spectrum of this aziridine (238), showed it to exist as a 13:1 ratio of invertomers at nitrogen in which the major invertomer has the trimethylsilyl group \textit{cis} to the quinazolone ring.
Similarly, aziridination of the vinylsilane (236), prepared from the hydrazone (239) as a mixture of double bond isomers, gave the aziridine (240) in only 11% yield [Scheme 67].

A further product from this aziridination of (236) was the desilylated aziridine (91) which was isolated from the crude reaction product by chromatography in 55% yield and was found to be identical to the aziridine isolated previously from the oxidative addition of (77) to trans-β-methylstyrene [Scheme 67].

An interesting feature in aziridination of (236) was that only one of the double bond isomers appeared to react with (78). Initially, this presented a problem in assigning the configuration at C-2 and C-3 in the aziridine ring of (240) as reaction could have occurred with either double
bond isomer of (236). The solution to this problem, which will be discussed later in this chapter, was only solved when the structures of aziridines derived from the corresponding vinylstannanes were assignable after detailed n.m.r. studies: the N-acetoxyaminoquinazolone (78) has a large preference for reaction with the (Z) isomer over the (E) isomer in both vinylsilanes (236) and the corresponding vinylstannanes (241) and (242).

The desilylated aziridine (91), also produced in this reaction, most probably results from addition of (78) to trans-β-methylstyrene and not from desilylation of aziridine (240) since this was found to be stable to acetic acid. It is likely that the trans-β-methylstyrene in this reaction was produced via the route below where the capture of a proton by (236) results in the β-silicon stabilized carbonium ion (243): this could then undergo acetate assisted desilylation to give (244).

\[
\begin{align*}
\text{Me}_3\text{Si} & \quad \text{Me}_3\text{Si} \quad \text{AcO}^+ \\
\text{Ph} & \quad \text{Me}_3\text{Si} \quad \text{CH}_3
\end{align*}
\]

In common with aziridine (238), the 300 MHz n.m.r. spectrum of (240) also showed the presence of two invertomers: from integration of the two trimethylsilyl signals that resonate at differing chemical shifts in both invertomers, it was estimated that they were present in a 5:1 ratio.

The \(^1\)H n.m.r. spectrum of (240) contained certain features that allowed assignment of (240a) as the major invertomer.

The H-5 proton on the quinazolone ring in the major invertomer (240a) resonates at higher field (§ 7.88) than is usual for this proton at § 8.22 which is where the same proton in the minor invertomer (238b) of (238) resonates: this can be explained in terms of a shielding effect of the
cis-phenyl group. Similarly, the same proton in (238b), the minor invertomer of (238), in which the phenyl and quinazolone ring are now cis to each other was also shielded (δ 7.89) with respect to its position in the major invertomer (δ 8.26).

Assignment of the relative configuration as shown at the 2- and 3-positions of the aziridine ring in (240a) was further supported by the expected shielding of the aziridine ring methyl when cis to the quinazolone, as was found to occur in the minor invertomer of (240). This was consistent with the n.m.r. spectra of other examples that have been examined in which a 2- (or 3-) methyl substituted N-quinazolinonyl aziridine shows a similar shielding of the methyl by the quinazolone in the invertomer in which both are cis. Conversely, the quinazolone ring brings about deshielding of aziridine ring protons which are cis to it (see below).

The presence of a phenyl group cis to the quinazolone in (240a), could also account for some broadened signals in its n.m.r. spectrum which may result from restricted rotation around the N-N bond (see below).61

Aziridinations of vinylsilanes are summarised below in Table 6: the high selectivity for the Z-alkene is intriguing but the yields are disappointing. Aziridination of vinylstannanes was undertaken to try to identify the factors responsible for these low yields and hopefully to
### TABLE 6
Summary of the results from aziridination of vinylsilanes using (78)

<table>
<thead>
<tr>
<th>Vinylsilane</th>
<th>Product isolated</th>
<th>Yield</th>
<th>Invertomer ratio Q/Si cis:trans</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Structure" /></td>
<td><img src="image" alt="Structure" /></td>
<td>25%&lt;sup&gt;a&lt;/sup&gt;</td>
<td>13:1</td>
</tr>
<tr>
<td><img src="image" alt="Structure" /></td>
<td><img src="image" alt="Structure" /></td>
<td>11%&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1:5</td>
</tr>
</tbody>
</table>

<sup>a</sup> Using 3 mol equiv. of the vinylsilane.

<sup>b</sup> This vinylsilane was formed as a 3:1 ratio of geometrical isomers.

<sup>c</sup> The desilylated aziridine (91) is the major product in this reaction.
obtain increased yields of the corresponding stannyl-substituted aziridines.

5.3 AZIRIDINATION OF VINYLSTANNANES

The preparation of vinylstannanes was carried out using the Shapiro reaction and the same procedure employed in the synthesis of vinylsilanes (235) and (236). Thus, double deprotonation of the hydrazones (237) and (239) followed by quenching of the intermediate vinyllithium with tributyl-stannylchloride afforded the vinylstannanes (245) and (241) in 57% and 60% yield respectively [Scheme 68]. The latter was produced as an 3:1 ratio of double bond isomers.

\[
\begin{align*}
&\text{PhSO}_2\text{NHN} = \text{Ph} \\
&\text{Ph} \\
&1. \text{n-BuLi} \\
&\text{2. Bu}_3\text{SnCl} \\
&(237) \ R = \text{H} \\
&(239) \ R = \text{CH}_3
\end{align*}
\]

\[
\begin{align*}
&(245) \ R = \text{H}, \ 57\% \\
&(241) \ R = \text{CH}_3, \ 60\%
\end{align*}
\]

Scheme 68

Using the same procedure as above, trimethyl-1-phenylprop-1-enyl-stannane (242) was obtained as in the case of (241) as a 3:1 ratio of double bond isomers and likewise triphenylstannylpropene (246) was prepared in 76% yield from the hydrazone (247) [Scheme 69].

The results from aziridination of these vinylstannanes (245), (241), (242) and (246) are summarized in Table 7. The yields of aziridines were found in 3 cases to be only slightly greater than those of their silyl analogues and their relative configurations at the aziridine ring carbons (and nitrogens) were easily assigned by n.m.r.: the greater yield for the case of (250) will be discussed later.

Examination of aziridine (248) by \(^1\)H n.m.r. revealed the presence of only one inverting at nitrogen in which the tri-n-butylstannyl group was
TABLE 7
Summary of the results from aziridination of vinylstannanes using (78)

<table>
<thead>
<tr>
<th>Vinylstannanes</th>
<th>Product isolated</th>
<th>Yield</th>
<th>Invertomer ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{SnBu}_3$</td>
<td>$\text{Q}\text{SnBu}_3$</td>
<td>37%$^a$</td>
<td>&gt;50:1</td>
</tr>
<tr>
<td>$\text{Ph}$</td>
<td>$\text{(248)}$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\text{SnBu}_3$</td>
<td>$\text{Q}\text{SnBu}_3$</td>
<td>32%$^a$</td>
<td>4:1</td>
</tr>
<tr>
<td>C</td>
<td>$\text{(249)}$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\text{SnMe}_3$</td>
<td>$\text{Q}\text{SnMe}_3$</td>
<td>64%$^a$</td>
<td>8:1</td>
</tr>
<tr>
<td>C</td>
<td>$\text{(250)}$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\text{SnPh}_3$</td>
<td>$\text{Q}\text{SnPh}_3$</td>
<td>31%$^a$</td>
<td>&gt;50:1</td>
</tr>
<tr>
<td>C</td>
<td>$\text{(251)}$</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$^a$ Using 3 mol equiv. of the vinylstannane.

$^b$ Exists as a 3:1 ratio of double bond isomers.

$^c$ The benzoxazinone (222) was also produced as a by-product in this reaction.

$^d$ Aziridine (91) was also isolated in 11\% yield.
cis to the quinazolone ring since no shielding of the quinazolone H-5 ring proton was observed.

The aziridine (249), however, exists as a 4:1 ratio of invertomers at room temperature in which the major invertomer has the tributylstannyl group cis to the quinazolone. [This differs from the analogous trimethylsilyl substituted aziridine (240), in which the major invertomer has a trans relationship between the silyl group and the quinazolone ring.]

Deducing the relative configuration at nitrogen in aziridine (249) was made easier after examination of the $^1$H n.m.r. spectrum at -40°C of a crystalline sample, dissolved in deuterochloroform at -40°C: at this temperature only signals from the major invertomer at nitrogen were present. From the normal chemical shift of the quinazolone ring H-5 proton it was evident that this major invertomer (249a) has the trialkyltin group cis to this ring. When the temperature was raised from -40°C to ambient, the appearance of the minor invertomer (249b) was observed.

This was identified by the characteristic shielding of the quinazolone H-5 proton (87.98) by the cis-phenyl group. These assignments in (249a) and (249b) were supported by the relative chemical shifts of their
aziridine ring protons and methyl groups: those methyl groups cis to the quinazolone ring were shielded, and those aziridine ring protons cis to the quinazolone ring were deshielded.

Having shown that only one aziridine (albeit as two invertomers) is produced in the aziridination of the vinylstannane (241), it follows that only one of the double bond isomers of the vinylstannane reacts with the N-acetoxyaminoquinazolone (78). An examination of the olefin geometry of the reacting vinylstannane (241) double bond isomer could provide further evidence for the relative configuration at C-2 and C-3 in aziridine (249) if (a) this reacting double bond isomer can be identified and (b) if it is assumed that aziridination is stereospecific with retention of the alkene configuration in the aziridine.

The $^1$H n.m.r. spectrum of $\beta$-methyl-$\alpha$-tributylstannylstylene (241) (which was produced as a 3:1 ratio of double bond isomers) [Figure 27], showed that the major double bond isomer, presumably (241a), exhibited $J$ values for the $^{119}$SnC=CH and $^{117}$SnC=CH coupling of 125Hz and 119Hz respectively, which are typical of trans-vinylstannanes. By contrast, the minor isomer (241b) had $J$ values of 66Hz and 64Hz which are typical for $^{119}$SnC=CH and $^{117}$SnC=CH couplings in cis-vinylstannanes.$^{112-117}$

The aziridination of trimethyl-1-phenylprop-1-enylstannane (242) has also been achieved [Table 7]. Addition of this alkenylstannane (3 mol equiv.) to a solution of (78) at low temperature afforded the two aziri-
dines (250) and (91) after warming to ambient [Scheme 70]: chromatography over silica permitted their isolation in 64% and 11% yields respectively.

The trimethyltin-substituted aziridine (250) exists as an 8:1 ratio of invertomers at room temperature. In common with other examples in Table 7 the major invertomer has the tin cis to the quinazolone. The smaller size of the trimethyltin by comparison with the tri-n-butyltin substituent is consistent with a change in the invertomer ratio from 8:1 to 4:1 in (250) and (249) respectively.

The relative configuration at C-2 and C-3 in aziridine (250) [Figure 28], is supported by a number of factors and these are:

( i) A 64% yield of (250) is such that it can only be derived from the more abundant double bond isomer of (242), which by analogy with (241), should have a Z-configuration (both double bond isomers were produced in a similar ratio from the Shapiro reaction).

( ii) An n.O.e. of 2.2% between the ortho-protons of the aziridine ring phenyl and the aziridine ring proton in (250) supported a cis-relationship between them.
(iii) The familiar pattern of chemical shift changes for the aziridine ring protons and the aziridine ring methyl groups cis and trans to the quinazolone ring referred to previously in both invertomers (250a) and (250b), was consistent with addition to the Z-configurated vinyl-stannane [see Figure 28].

![Chemical structures](image)

**Figure 28**

The addition of 2-triphenylstannylpropene (246) to a solution of the N-acetoxyaminoquinazolone (78) afforded the corresponding stannyl-substituted aziridine (251) [Table 7]. An n.m.r. spectrum of (251) showed only one invertomer in which the triphenyltin group was cis to the quinazolone. This was supported by the upfield shift of H-5 in this aziridine by ca. 0.4 ppm which must be the result of shielding by one of the phenyl rings of the triphenyltin substituent.

It seems likely from comparison of the invertomer ratios in Tables 6 and 7 that there is an attractive interaction between the quinazolone carbonyl oxygen and the tin containing substituents which more than offsets the steric interaction between them.

As in the trimethylsilyl-substituted aziridine (240), the trialkylstannyl-substituted aziridines (249) and (250) show broadened aziridine ring proton signals at room temperature when they (and the phenyl group) are cis to the quinazolone: this can be attributed to retarded N-N bond rotation. It appears also that in those invertomers in which the tin and the quinazolone ring are cis to each other, only one N-N bond rotamer is present which is presumably that which allows the tin-oxygen interaction to
operate.

Intramolecular attractive tin-oxygen interactions have been reported in a number of different cases.\textsuperscript{118,119}

5.4 YIELDS IN AZIRIDINATION OF PHENYLALKENYLSTANNANES AND PHENYLALKENYL-SILANES

One possible explanation for the low yields observed in aziridination of vinylstannanes (245) and (241), and vinylsilanes (235) and (236), may lie in the difficulty in achieving coplanarity of the phenyl ring and alkene double bond. It was suspected that coplanarity of the phenyl ring with the double bond in these alkenes is hindered to an extent that depends firstly upon the size of the substituents on the metal and secondly on the proximity of the substituent on the alkene in relation to the phenyl ring, since coplanarity is known to be required for efficient aziridination of substituted styrenes.\textsuperscript{120} This explanation could account for the increased yield of the aziridine derived from the trimethylstannyl-substituted alkene (242) by comparison with that from the tributylstannyl-substituted alkene (241). To test this hypothesis, the aziridination of trans-trimethyl-2-phenylethenylsilane (252) was examined in which the location of the trans-trimethylsilyl substituent should not spoil the coplanarity of the phenyl ring with the double bond.
5.5 AZIRIDINATION OF TRANS-TRIMETHYL-2-PHENYLETHENYLSILANE (252)

The vinylsilane (252), prepared by the method of Fleming, was aziridinated in the usual way by adding it to a solution of the N-acetoxy-aminoquinazolone (78) at low temperature and allowing the reaction mixture to warm to ambient [Scheme 71].

\[
\begin{align*}
(78) & \quad + \quad \begin{array}{c}
\text{Ph} \\
\text{SiMe}_3
\end{array} \\
\rightarrow & \quad -20^\circ C \rightarrow \text{RT.} \\
(252) & \quad \rightarrow \quad (253)
\end{align*}
\]

Scheme 71

Chromatography of the crude reaction mixture over silica yielded an 86% yield of the corresponding aziridine (253). This excellent yield of aziridine (253) supports the notion that for efficient aziridination, coplanarity of the phenyl ring with the double bond in vinylsilane (252) is mandatory. A 300 MHz $^1$H n.m.r. spectrum of aziridine (253) showed it to exist as two invertomers at nitrogen (ratio 1.8:1) in which the major invertomer has the trimethylsilyl group cis to the quinazolone. This aziridine was found to be unstable in air and completely decomposed over a period of two weeks.

5.6 DESILYLATION OF AZIRIDINES (238), (240) AND (253): FORMATION OF 2H-AZIRINES

Over the past few years, considerable interest has focused on the chemistry of 2H-azirines; the synthesis and reactions of these strained and highly reactive heterocycles have been comprehensively reviewed.\textsuperscript{122,123}

\textsuperscript{†} It was subsequently established that it was possible to achieve aziridination of (252) by simultaneous addition of LTA and the N-aminoquinazolone (77), to a solution of (252) in dichloromethane at room temperature, without any reduction in yield, as the alkenylsilane (252) is stable towards LTA.
Two methods have been widely used for their synthesis; one is a modified Neber reaction of a quaternary hydrazonium salt [Scheme 72], the other procedure is the pyrolysis or photolysis of vinyl azides [Scheme 73].

\[
\begin{align*}
\text{Ph} & \quad \begin{array}{c}
\text{N} \quad \text{N} \\
\text{CH} & \quad \text{CH}
\end{array} \\
\text{Ph} & \quad \begin{array}{c}
\text{CH} & \quad \text{Ph}
\end{array}
\end{align*}
\]

\[
\text{NaOC}_{3}\text{H}_{7-\text{II}}-\text{C}_{3}\text{H}_{2}\text{OH} \quad \text{Ph} \quad \begin{array}{c}
\text{N} \\
\text{CH}
\end{array} \\
\text{Ph} \quad \begin{array}{c}
\text{CH} & \quad \text{Ph}
\end{array}
\]

\[\text{Scheme 72}\]

\[
\text{N}_{3} \quad \text{Ph} \quad \begin{array}{c}
\text{N}
\end{array}
\]

\[
\begin{array}{c}
\text{Ph}
\end{array}
\]

\[\Delta \text{ or } \text{hv}\]

\[\text{Ph} \quad \begin{array}{c}
\text{N}
\end{array}
\]

\[\text{Scheme 73}\]

A preliminary communication by Chan\textsuperscript{126} had reported that treatment of the silyl-substituted cyclopropane (254) with caesium fluoride generated the corresponding cyclopropene (255) by a fluoride ion-promoted elimination of trimethylsilyl and chloride.

\[
\begin{align*}
\text{R'} & = \text{H}, \text{X} = \text{Cl} \\
\text{R'} & = \text{R'} = \text{H}, \text{X} = \text{Br} \\
\text{R'} & = \text{R'} = (\text{CH}_{2})_{4}, \text{X} = \text{Cl}
\end{align*}
\]

Treatment of aziridines (238), (240) and (253) with caesium fluoride was examined as the potential for a similar 1,2 elimination also exists and would provide a new route to 2H-azirines. Thus, to a solution of caesium fluoride in dry DMF was added the aziridine (238) and the reaction was stirred under nitrogen, whilst monitoring the disappearance of the starting
aziridine (238) by t.l.c. After 5h no starting material remained and the crude reaction mixture was chromatographed over silica yielding a 91% yield of the corresponding 2H-azirine (256) [Scheme 74].

Similarly, treatment of aziridine (240) with caesium fluoride under the same conditions gave the azirine (257) in 61% yield after chromatography. The NH-quinazolone (79) was also formed in these desilylation reactions and was subsequently isolated by chromatography in near quantitative yield.

Desilylation of aziridine (253) gave none of the corresponding azirine (258) [Scheme 75]. It is well known that 2H-azirines which are unsubstituted at the 3-position are very reactive and prone to nucleophilic attack at this position and for this reason few azirines of this type have been reported.\textsuperscript{127}
The products from desilylation of aziridine (253) were the two aziridines (259) and (86) which were isolated by chromatography in 58% and 23% yields respectively.

The $^1$H n.m.r. spectrum of aziridine (259) at room temperature showed broadened signals that were attributed to slow inversion at nitrogen (the barrier to inversion is lower than in the quinazolone-substituted aziridines). However, at -55°C both invertomers of (259) were clearly identifiable and the n.m.r. showed the major invertomer (259a) to have the N-H proton trans to the quinazolone [Figure 29].

Assignment of the invertomer identity of (259a) and (259b) was based on the greater $J_{cis}$ over $J_{trans}$ for the HCNH coupling which was found to occur in other N-H aziridines of this type.\textsuperscript{128}

Low temperature nuclear Overhauser effects were also examined in both (259a) and (259b) in an attempt to provide further support for the assigned configurations at nitrogen. However, the results obtained were inconsistent and did not agree with the assignments of (259a) and (259b) based on the magnitude of their coupling constants referred to above.

It was assumed that the azirine (258) was an intermediate in the formation of this aziridine (259) and was attacked at the reactive unsubstituted 3-position by the quinazolone anion (260). Conceivably the minor aziridine product (86) could have resulted from capture of an aziridinyl carbanion intermediate (261) by a proton from adventitious water [Scheme 76].
5.7 AZIRIDINYL CARBANIONS

Previously, aziridinyl carbanions have only been shown to exist as intermediates when they are stabilized by an adjacent carbonyl group.\textsuperscript{129,130} Recently, Seebach\textsuperscript{131} has reported the lithiation of the S-phenylaziridine-carbothioates (262) [Table 8]. In contrast to the corresponding O-alkyl esters, these were cleanly metallated by lithium di-isopropylamide (LDA) and reacted with various electrophiles to give the products (263)-(265).

To test for the existence of the aziridinyl carbanion (261) in Scheme 76, the desilylation of aziridine (253) was carried out in the presence of benzaldehyde (3 mol equiv.) monitoring the reaction by t.l.c. After 5h no starting material remained and a \textsuperscript{1}H n.m.r. spectrum of the crude product after shaking with bisulphite solution to remove excess benzaldehyde showed that alkylation of the aziridinyl carbanion had taken place to give the alcohol (266). This was confirmed by an accurate mass determination which
TABLE 8
C-alkylation of S-phenylaziridinecarbothioates

\[
\begin{array}{c}
\text{RN} \bigcirc \text{COSPh} \\
\text{C-alkylation reaction} \\
\text{RN} \bigcirc \text{COSPh} \\
\text{(262)} \\
\text{1. LDA, THF, } -78^\circ\text{C} \\
\text{2. Electrophile} \\
\text{RN} \bigcirc \text{COSPh} \\
\text{(263)-(265)} \\
\end{array}
\]

<table>
<thead>
<tr>
<th>R</th>
<th>Electrophile</th>
<th>E</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bz</td>
<td>PhCHO</td>
<td>PhCH(OH)</td>
<td>(263)\textsuperscript{a}</td>
<td>71</td>
</tr>
<tr>
<td>Bz</td>
<td>CH\textsubscript{3}I/DMFU\textsuperscript{b}</td>
<td>CH\textsubscript{3}</td>
<td>(264)</td>
<td>61</td>
</tr>
<tr>
<td>Bz</td>
<td>PhCH\textsubscript{2}Br/DMFU\textsuperscript{b}</td>
<td>PhCH\textsubscript{2}</td>
<td>(265)</td>
<td>62</td>
</tr>
</tbody>
</table>

\textsuperscript{a} ratio of diastereoisomers = 77:23;
\textsuperscript{b} DMPU = N,N-dimethylpropyleneurea.
gave a correct molecular ion corresponding to (266) [Scheme 77].

\[
\begin{array}{c}
Q \quad \text{SiMe}_3 \quad \text{H} \\
\text{Ph} \quad \text{H} \\
\text{H}
\end{array}
\quad \xrightarrow{\text{i}} \quad
\begin{array}{c}
Q \quad \text{H} \\
\text{Ph} \quad \text{H}
\end{array}
\quad \xrightarrow{\text{ii}}
\begin{array}{c}
Q \quad \text{CH(OH)Ph} \\
\text{Ph} \quad \text{H}
\end{array}
\]

\[
\begin{array}{c}
Q \quad \text{NH} \quad \text{I}
\end{array}
\quad \xrightarrow{\text{iii}}
\begin{array}{c}
Q \quad \text{O} \\
\text{Ph} \quad \text{H}
\end{array}
\]

\[
\begin{array}{c}
\text{Ph} \\
\text{H}
\end{array}
\]

Scheme 77

Reagents:
(i) CsF, DMF, PhCHO, 5h; (ii) MnO₂, CH₂Cl₂; (iii) LTA, CH₂Cl₂.

Attempts to purify the alcohol (266) by flash chromatography were unsuccessful so it was directly oxidized by manganese dioxide to give the benzoylaziridine (267) in an overall yield from (253) of 85%. This aziridine (267) was found to be identical to that isolated from the oxidative addition of NAQ (77) to benzylidene acetophenone (268).

This reaction sequence strongly suggests that the aziridinyl carbanion is long-lived enough to be captured by benzaldehyde but, in the absence of an electrophile, forms the azirine (258) by expulsion of the quinazolone ring.

Oxiranyl carbanions have been postulated as intermediates in the desilylation of silyloxiranes. Treatment of the α,β-epoxysilane (269) with tetra-n-butyl ammonium fluoride followed by quenching with deuterium oxide gave the styrene oxide (270) (in 33% yield) with retention of con-
The ease of conversion of oxiranyl carbanions to their corresponding isomeric enolate anions may contribute to a reduction in their stability when compared to that of aziridiny1 carbanions.
CHAPTER 6

Aziridination of Alkenes by N-Aminoquinazolones and Lead Tetra-acetate-trifluoroacetic Acid
6.1 INTRODUCTION

Peroxytrifluoroacetic acid has been found to be a more efficient reagent for olefin epoxidation than peracetic acid. In particular, it was observed that yields in epoxidation of terminal alkenes were improved using trifluoroperacetic acid by comparison with peracetic acid.\(^{133}\) As a consequence of this, it was of interest to examine whether the same increased reactivity could also be brought about in aziridination using (78) by exchanging acetoxyl by trifluoroacetoxyl.

It had previously been observed that the LTA oxidation of (111) in the presence of TFA and \(\alpha,\beta\)-unsaturated esters or \(\alpha,\beta\)-unsaturated ketones had a remarkable effect on the reactivity, and particularly on the facial reactivity, of prochiral double bonds in these alkenes.\(^{61}\)

Since the reactive intermediate in aziridinations of alkenes using (111) in the absence of TFA has previously been shown to be the corresponding N-acetoxyaminoquinazolone (110), it was conceivable that the greater reactivity in the presence of TFA could be ascribed to the N-trifluoroacetoxylaminoquinazolone (271) [Scheme 79], where exchange of the acetate ligands on the lead by trifluoroacetate and transfer of the trifluoroacetoxy group to the amino group of (111) takes place in the oxidation (see Scheme 21). Alternatively, TFA could conceivably bring about the exchange of the acetoxy group in (110) by trifluoroacetoxy.

\[\begin{align*}
\text{Scheme 79}
\end{align*}\]
Oxidation of a number of terminal alkenes was therefore examined using (77) in the presence of TFA with the assumption that formation of the protonated trifluoroacetoxyaminoquinazolone (272) takes place in situ.

Monosubstituted alkenes show poor reactivity towards aziridination when using N-acetoxyaminoquinazolones and yields of the corresponding aziridine are little better than 10%. Similar behaviour is also exhibited in epoxidation where the reactivity of alkenes towards the peracid diminishes as the number of alkyl substituents on the double bond is reduced.

6.2 AZIRIDINATION OF TERMINAL ALKENES IN THE PRESENCE OF TFA

In Chapter 2 it was reported that aziridination of hex-1-ene by the simultaneous addition of (77) and LTA to a stirred solution of the alkene resulted in an 11% yield of the corresponding aziridine (85) with the major product being the de-aminated quinazolone (79) (62%). However, when the reaction was repeated in the presence of TFA (3 mol equiv.) using 1.5 mole equivalents of hexene, the isolated yield of aziridine (85) was raised to 64% after chromatography. In addition, the unstable ring-opened trifluoroacetate (273) was also isolated in 11% yield from this chromatography [Scheme 80].

\[
\begin{align*}
&\text{Q} \quad \text{LTA, TFA} \quad \text{Hex-1-ene} \quad \text{NH}_2 \\
&\text{(77)} \quad \rightarrow \quad \text{Q} \quad \text{NH} \quad \text{(CH}_2)_2\text{CH}_3 \\
&\text{Q} \quad \text{NH} \quad \text{(CH}_2)_2\text{CH}_3 \quad \text{OCOCF}_3 \\
&\text{(85) 64%} \quad \text{(273) 11%}
\end{align*}
\]

Scheme 80

Varying the concentration of TFA in this reaction also affected the yields of the products obtained: the use of 6 mole equivalents of TFA resulted in a 35% yield of both (85) and (273), whereas using 1.8 mole equivalents of TFA, the isolated yields of (85) and (273) were only 37% and
5%, respectively, with 27% of the de-aminated quinazolone (79) also obtained.

Oxidation of N-aminoquinazolone (77) in the presence of allyl chloride (1.5 mol equiv.) gave less than 10% of the aziridine (274) from examination of the $^1$H n.m.r. spectrum of the crude reaction product. Even when the oxidation was carried out in neat allyl chloride as solvent, the isolated yield of aziridine (274) was only 20%. However, when the reaction was repeated in the presence of TFA using only 1.5 mole equivalents of allyl chloride the aziridine (274) was isolated in 85% yield [Scheme 81].

\[
\begin{align*}
(77) & \xrightarrow{\text{LTA, TFA, } \text{CH}_2\text{Cl}_2} (274) 85% \\
\text{Scheme 81}
\end{align*}
\]

The structure of (274) followed unambiguously from its $^1$H n.m.r. spectrum in which the protons within each of the chloromethyl and ethyl methylene groups were diastereotopic.

In contrast to (85), aziridine (274) was clearly more stable to attack by TFA and was able to withstand the strongly acidic conditions of the reaction; conceivably this may be due to the combined diversionary effect of protonation of the quinazolone ring and of the electron-withdrawing effect of the $-\text{Cl}$ group. It has previously been shown elsewhere$^{36}$ that aziridine (36) bearing the less basic N-phthalimido substituent was rapidly ring-opened by TFA to give the trifluoroacetate (275) as one regioisomer [Scheme 82].

The stability to TFA of many of the aziridines described in this chapter is surprising. The ready ring-opening of (36) with ca. 3 moles of TFA implies that the stability of the quinazolone-substituted aziridines is not just a consequence of the weak basicity of the aziridine ring nitrogen.
but a function also of the quinazolone ring itself. Presumably, protonation of the quinazolone ring reduces the basicity of the aziridine nitrogen's lone-pair via a resonance-relayed effect; protonation of the aziridine ring nitrogen being assumed as the first step in the ring-opening process. In epoxidation using trifluoroperacetic acid, it is essential to buffer the solution to avoid ring opening of the epoxide.$^{133}$

Allyl acetate is a further example of an alkene which can be aziridinated to give (276) in 82% yield by oxidation of (77) only in the presence of 3 mole equivalents of TFA [Scheme 83].

\[
\begin{align*}
(77) + H_2C=CHCH_2OAc & \xrightarrow{\text{LTA, TFA, } CH_2Cl_2} Q \\
& \xrightarrow{\text{N}} \text{N} \\
& \xrightarrow{\text{QAc}} (276) 82\%
\end{align*}
\]

Scheme 83

Since vinyl acetate is aziridinated in good yield by oxidative addition of NAP (15),$^{134}$ aziridination of the diethoxyphosphoryl-substituted allylchloride (277)$^{135}$ was examined with the intention of finding suitable conditions for rearrangement of the expected product aziridine (278) to the \(\beta\)-lactam (279) [Scheme 84].

Unexpectedly, however, no aziridine (278) was formed under these conditions and only the de-aminated quinazolone (79) was isolated in 68% yield. Repetition of the reaction in the presence of TFA (6 mol equiv.) does presumably bring about aziridination of (277) but the isolated product
was the chloroketone (191) obtained in 71% yield and formed by ring-opening of the (protonated) aziridine (278) with loss of the phosphoryl group.

The factor(s) responsible for enhanced yields in aziridination of terminal alkenes in the presence of TFA were presumably also responsible for bringing about electrophilic amination of toluene. Thus, the simultaneous and portionwise addition of NAQ (77) and LTA to a solution of dichloromethane containing toluene (1.5 mol equiv.) and TFA (3 mol equiv.) resulted in a 34% yield of (280) [Scheme 85].

The product (280) was isolated by chromatography over silica and the para relationship between the substituents on the benzene ring was
identified by the characteristic AA'BB' spin splitting pattern for the benzenoid protons observed in its ¹H n.m.r. spectrum. In the absence of TFA toluene is not attacked by (78).

Clearly, the species formed from oxidation of NAQ (77) in the presence of TFA was different from that formed in its absence and was also remarkably more selective. Thus oxidation of (77) in a mixture of α-methylene-γ-butyrolactone and methyl methacrylate (1:1) gave a 2:1 mixture of the corresponding aziridines (92) and (93) in the absence of TFA.

\[
\begin{align*}
(92) & \quad (93)
\end{align*}
\]

By contrast, in the presence of TFA aziridination of only methyl methacrylate occurred, from examination of the ¹H n.m.r. spectrum of the crude reaction mixture.

6.3 AZIRIDINATION OF ALKENES USING 3-AMINO-2-t-BUTYL-QUINAZOLONE (230) AND LTA-TFA

Aziridinations by oxidative addition of (230) to various alkenes were also examined. Surprisingly, however, no aziridines were obtained in reaction with the electron deficient methyl methacrylate or α-methylene-γ-butyrolactone when the aziridination was carried out in the absence of TFA. The major products obtained in these latter reactions were the benzoxazinone (281) and the de-aminated quinazolone (282) which were isolated by column chromatography in ca. 13% and 38% respectively in both cases.

\[
\begin{align*}
(281) & \quad (282)
\end{align*}
\]
This failure to isolate any aziridine-containing products prompted an examination of the intermediate in the oxidation of (230). Oxidation of (230) at -20°C followed by examination of the low temperature ¹H n.m.r. spectrum at -40°C without any intermediate warming revealed the only product to be the corresponding N-acetoxyaminoquinazolone (231). Addition of styrene (3 mol equiv.) to this solution at -40°C followed by warming to ambient afforded some of the corresponding aziridine (283) which, however, was isolated by chromatography in only 8% yield [Scheme 86].

Although the yield of aziridine (283) was low it was identical to that obtained when LTA oxidation of (230) was carried out at room temperature in the presence of styrene where the major product was the de-aminated material (282). The low yield in this aziridination, therefore, is not the result of inefficient conversion of (230) to the corresponding N-acetoxyaminoquinazolone (231).

If the same transition state is used to rationalize these results as has been proposed previously, then it is possible that these poor yields may be the result of steric interaction that exists either between the olefinic protons and the t-butyl group or between the hydrogen of the NHOAc group and the t-butyl group in the transition state for aziridination [Figure 30] [it is assumed that the H and OAc groups take up the sites indicated in this Figure 30].
An interesting observation was that the presence of TFA (3 mol equiv.) also improved the yields of aziridines when (230) was oxidized in the presence of alkenes.

Thus, simultaneous addition of (230) and LTA to a solution of hex-1-ene containing TFA (3 mol equiv.) afforded the corresponding aziridine (284) in 40% yield after chromatography; a further product isolated in 28% yield was the amino alcohol (285).

Similarly, oxidation of (230) in the presence of E- and Z-but-2-ene using TFA gave their corresponding aziridines. Aziridination of E-but-2-ene at 0°C using TFA gave a 24% yield of (286) along with the ring-opened aziridine (287) which was isolated in 17% yield.
Using Z-but-2-ene and 3 mole equivalents of TFA afforded the aziridine (288) in 46% yield and was accompanied by 10% of the amino alcohol (289).

3-Methylcyclohex-1-ene is a further example of an alkene in which aziridination using (230) was only achieved in the presence of TFA. The major product (290) was isolated by chromatography in 42% yield and included 10% of an impurity (probably the C-2 epimer). Assignment of stereochemistry and the conformation of the six-membered ring in (290) was based on the similar coupling constants to those reported in Table 4 (see chapter 3).
6.4 INVESTIGATION INTO THE MECHANISM OF AZIRIDINATION IN THE PRESENCE OF TFA

Oxidation of N-aminoquinazolone (77) by slow addition of LTA at -20°C gives an almost quantitative yield of the N-acetoxyaminoquinazolone (78) [Scheme 87].

The successful aziridination of allyl chloride described earlier could also be accomplished in 80% yield by dropwise addition of a solution of (78) held at -20°C to a dichloromethane solution of the alkene (3 mol equiv.) containing TFA (6 mol equiv.) at 0°C and then allowing the solution to warm to ambient. Under these conditions it is assumed that aziridination takes place as the solution of (78) is added, a situation with presumably also obtains in the oxidative addition procedure in the presence of TFA. When this experiment was carried out by addition of TFA (3 mol equiv.) to a solution of (78) containing allyl chloride (2 mol equiv.) the aziridine (274) was isolated in only 43% yield after chromatography.

In view of the analogies between epoxidation using peracids and aziridination using (78) referred to earlier, it was surprising to find that exchange of acetoxy by trifluoroacetoxyl in (78) was not necessary for efficient aziridination of terminal alkenes. Thus oxidation of N-aminoquinazolone (77) in deuterochloroform at -20°C followed by separation of lead di-acetate at -40°C and ³H n.m.r. examination of the deuterochloroform solution after addition of TFA (ca. 3 mol equiv.) at -40°C without any intermediate warming of the solution, showed downfield shifts for the
resonances of the quinazolone ring protons and for the (still non-equivalent) methylene protons of the ethyl group. However, the chemical shift of the NH proton was hardly affected and two OOCCH$_3$ methyl signals were visible of similar intensity, presumably from free acetic acid and from the bound acetoxy group. Thus neither the NH nor the acetoxy group appeared to be rapidly exchanging or exchanged. Slow decomposition of the N-acetoxyaminoquinazolone (78) occurred in the presence of TFA even at -40°C and the de-aminated quinazolone (79) was one of the products.

Conceivably, the aziridination could still have been proceeding via the trifluoroacetoxyaminoquinazolone (272) in (undetected) equilibrium with N-acetoxyaminoquinazolone (78) in the presence of TFA. However, oxidation of N-aminoquinazolone (77) with lead tetra-trifluoroacetate (LTTFA)$^{137}$ in the presence of allyl chloride gave (impure) aziridine (274) in only 28% yield.$^{139}$ Likewise, oxidation of NAQ (77) with [bis(trifluoroacetoxy)-iodo]benzene [PhI(OOCF$_3$)$_2$] in the presence of allyl chloride gave aziridine (274) in only 12% yield: the assumption here is that the corresponding trifluoroacetoxyaminoquinazolone (272) was the aziridinating intermediate involved.

Significantly when the latter reaction was carried out in the presence of 1 mole equivalent of TFA, the yield was raised to 78% and in the presence of 2 mole equivalents of TFA a 94% yield of (274) was obtained.

It appears, therefore, that the greatly increased reactivity in addition of N-acetoxyaminoquinazolone (78) or oxidative addition of N-aminoquinazolone (77) to allyl chloride and presumably to other alkenes, brought about by the presence of TFA is the result, for the most part, of protonation of the quinazolone ring and not just the result of exchange of acetoxy by trifluoroacetoxy in the reactive intermediate (78) if, in fact, this occurs at all.

-123-
The same reasoning may also be used to account for the increase in yields of aziridine when oxidation of (230) is carried out in the presence of TFA.

Even some part of the small yields of aziridine (274) produced above when using LTTFA or PhI(OOCF₃)₂ may be the result of the accretion of TFA as a by-product in the oxidation.

Support for this conclusion also comes from the oxidation of N-amino-phthalimide (15) in the presence of hex-1-ene or allyl chloride, either with LTA in the presence of TFA (3 mol equiv.) or using [bis(trifluoro-acetoxy)iodo]benzene: in both cases the only isolated product was phthalimide (50-60%). Clearly N-aminophthalimide lacks the basic site which is present in the quinazolone ring, protonation of which appears to be important in aziridination of some otherwise unreactive alkenes.

6.5 HOW DOES PROTONATION OF THE QUINAZOLONE RING BRING ABOUT INCREASED EFFICIENCY IN AZIRIDINATION?

It is suggested that protonation of the quinazolone ring at N-1 or the carbonyl oxygen or conceivably both these positions facilitates the reaction by reducing the barrier to rotation around the N-N bond and thus lowering the transition state energy for aziridination which resembles Figure 31.

In this transition state (31), eclipsing of the nitrogen lone pairs is
required and the magnitude of this unfavourable interaction will be reduced by delocalization of the N-3 lone pair either via the amidine unit (protonation on N-1) or via the amide (protonation on the carbonyl oxygen). The magnitude of this eclipsing interaction will presumably be a function of the amount of p-character in the orbital containing the lone pair.

At the present time, it is not clear which site (A, B, C or D) on the alkene in Figure (31) is occupied by the alkyl group in addition to terminal alkenes. An attractive syn-interaction between the carbonyl oxygen (at site A in Figure 31) of α,β-unsaturated esters or α,β-unsaturated ketones and C-2 of the quinazolone ring (Figure 32) was proposed to account for the facial selectivity obtained in aziridinations using (111) in the presence of TFA (although the intermediate was thought to have been the corresponding N-nitrene\(^3\))

\[
\begin{align*}
R^\ast = & \text{Bu}^\dagger \text{MeCH}
\end{align*}
\]

\textbf{Figure 32}

A transition state resembling that in Figure (32) in which the alkyl group of the terminal alkene, e.g. CH\(_2\)Cl replaces CO\(_2\)R would be expected to lead to a significantly higher level of asymmetric induction than one in which the CH\(_2\)Cl is located at any other position on the alkene.

In practice aziridination of allyl chloride using (111) gave a 4:1 ratio of aziridine stereoisomers (291) (61%) in the presence of TFA and a 1:1.4 ratio of the same stereoisomers in the absence of TFA (Figure 33).
6.6 AZIRIDINATION OF CYCLOHEXENE AT \(-35^\circ C\) USING (78) IN THE PRESENCE OF TFA

The use of TFA in aziridination of simple alkyl-substituted alkenes now offers a convenient route to many aziridines which previously had been unobtainable due to the poor reactivity of the starting alkene.

Earlier attempts to determine whether such alkenes exhibited an alkyl group-quinazolone syn-selectivity were thwarted by their lack of reactivity towards (78) at the low temperatures necessary to inhibit N-inversion. However, since TFA lowers the temperature at which aziridination occurs,\(^{36}\) it should be possible in its presence to carry out aziridination at a temperature low enough to show whether or not this syn-selectivity obtains. Thus, to a solution of the N-acetoxyaminoquinazolone (78) at \(-35^\circ C\) was added firstly cyclohexene (3 mol equiv.) and then TFA (3 mol equiv.). Examination of the 300 MHz \(^1\)H n.m.r. spectrum of this solution at \(-40^\circ C\) showed only the anti(exo)-aziridine (95) to be present.

The temperature of the probe was raised from \(-40^\circ C\) to ambient over a period of 20 min. but the \(^1\)H n.m.r. spectrum of the solution indicated that
decomposition of aziridine (95) had occurred.

It appeared, therefore, that in this TFA-accelerated aziridination at -35°C, no syn-interaction is present between the quinazolone and the substituents on the alkene.

In order for this conclusion to be valid, it was necessary to show that the presence of TFA at this temperature did not cause a lowering of the inversion barrier at the aziridine ring nitrogen. This could have resulted in conversion of the kinetically-formed syn-aziridine into the thermodynamically preferred (and observed) anti-aziridine (95). To examine this possibility, the effect of TFA on the inversion barrier of aziridine (94) was investigated.

Aziridine (94) exists as a 4:1 ratio of invertomers at room temperature. When a crystalline sample was dissolved in deuterochloroform at -40°C only the major invertomer was observed in which the ester group is syn to the quinazolone. When TFA (3 mol equiv.) was then added at -40°C, no change in the invertomer ratio was observed. When the n.m.r. sample was removed from the probe, maintained at ambient temperature for 10 min., and then the spectrum re-recorded at -40°C an invertomer ratio of 10:1 (CO₂Me and quinaz. syn:anti) was observed. A crystalline sample of this aziridine dissolved in CDCl₃ at room temperature in the absence of TFA showed a 4:1 ratio of the corresponding invertomers when the n.m.r. spectrum of the solution was measured at -40°C. Thus addition of TFA does not significantly lower the inversion barrier in aziridine (94) (although it does affect the equilibrium position between these invertomers): neither would
TFA be expected to have the effect of lowering the inversion barrier in aziridine (95).

It would appear, therefore, that formation of the anti-aziridine (95) in the presence of TFA at -35°C is the result of a transition state for aziridination as shown in Figure 34.

Such a transition state contrasts with that proposed earlier in Figure (32) and in Figure 35 above, where the alkene substituent -CO₂R and the quinazolone ring have a syn-relationship (an endo-type transition state by analogy with the Diels-Alder reaction).

It is possible that, in the absence of a π-electron containing substituent on the alkene, all aziridinations prefer an exo transition state of the type illustrated in Figure 34 whether TFA is present or not.

6.7 ASYMMETRIC INDUCTION IN AZIRIDINATION OF ALKENES

Previous work has shown that oxidation of the chiral (but racemic) N-aminoquinazolone (111) with LTA in the presence of various α,β-unsaturated esters or ketones gives aziridines with significant or even complete asymmetric induction only in the presence of TFA and little asymmetric induction in the absence of TFA, e.g. Scheme 88.³⁶

This effect was interpreted at the time as involving an N-nitrene intermediate which, in TFA, was protonated on the quinazolone N-1 and this resulted in a change in the transition state geometry from (292) (in the
absence of TFA) to (293) in the presence of TFA): the proximity of the existing chiral centre to the developing chiral centre in (293) was assumed to give rise to the asymmetric induction observed [Figure 36].

Figure 36

However, as shown in this thesis, the intermediate in this aziridination is not the \( N \)-nitrene but the \( N \)-acetoxyaminoquinazolone (110) and therefore a re-interpretation of the way in which (110) brings about asymmetric induction in addition to prochiral alkenes in the presence of TFA is required.

It is suggested that rather than bring about chiral induction by a change in the transition state from (292) to (293) above, the effect of
adding TFA in aziridinations using (110) is to accelerate the reaction of the latter with alkenes to the point where aziridination is faster than the interconversion of the two invertomers (stereoisomers) of (110). It is possible that TFA also retards the rate of interconversion between the stereoisomers of (110) by protonation on N-1 raising the inversion barrier at the chiral exo-cyclic ring nitrogen to such an extent that it is effectively stereostable over its reaction time. The facial selectivity observed in aziridination of prochiral alkenes in the presence of TFA using (110) may then be rationalised in terms of double asymmetric induction where the creation of a new chiral centre in the product aziridine takes place under the combined influence of two pre-existing chiral centres.

If this interpretation is correct then it should be possible to bring about chiral aziridination of prochiral alkenes with -NHOAc as the only chiral centre.
EXPERIMENTAL
GENERAL EXPERIMENTAL

All 90 MHz $^1$H n.m.r. spectra were recorded on a Varian EM 390 spectrometer. High-field $^1$H n.m.r. (300 MHz) and $^{13}$C n.m.r. (75 MHz) spectra were recorded on a Bruker AM 300 spectrometer at the University of Leicester. $^1$H n.m.r. (400 MHz) spectra were recorded by courtesy of the high-field n.m.r. service [S.E.R.C] at the University of Warwick. All n.m.r. spectra were recorded at room temperature, unless stated otherwise. Infra-red spectra of crystalline compounds were determined using Nujol mulls and liquids as thin films, using a Perkin-Elmer 298 spectrometer. Accurate mass measurements were made at the S.E.R.C. mass spectrometry centre, University College of Swansea and standard mass spectra were recorded on a Micromass 16B spectrometer. Elemental analysis was carried out by CHN Analysis, Wigston, Leicester or Butterworth Laboratories, Teddington, Middlesex. Melting points were determined on a Kofler hot stage and are uncorrected.

Flash chromatography was carried out according to the method of Still et al. using silica gel manufactured by Merck & Co., Kiesel 60 (230-400 mesh) or basic (pH 9) activated alumina UG1. Purifications by chromatotron were performed using model 7924T and Merck & Co. Kieselgel 60 (PF 254) silica plates. T.l.c. was conducted on pre-coated aluminium sheets (60-254) with a 0.2 mm layer thickness, manufactured by Merck & CO.

The concentration of the n-butyllithium was determined by back-titration with hydrochloric acid (0.1M) from solutions of dibromoethane and water using phenolphthalein as an indicator and was ~2.5M unless otherwise indicated.

Light petroleum refers to the 40-60°C fraction unless otherwise stated and all light petroleum and ethyl acetate was distilled prior to use. Tetrahydrofuran (THF) and benzene were distilled from sodium metal in the
presence of benzophenone. Ether refers to diethyl ether and was initially sodium-dried and then distilled from lithium aluminium hydride. Dichloromethane, pyridine, diisopropylamine and triethylamine were distilled from powdered calcium hydride. Trimethylsilylchloride was distilled immediately prior to use from tributylamine. Methanol and ethanol were dried by distillation from magnesium and iodine.

Lead tetra-acetate was always freed from acetic acid under reduced pressure prior to use. Alkenes used in aziridination were distilled prior to use, all other reactants were reagent grade unless otherwise stated and were used as received. Saturated sodium bicarbonate solution was routinely used in basic washings during work-up.

Filtrations of solutions at low temperatures (-45°C) under gravity were accomplished by carrying out these operations at the bottom of a lagged tank containing shelves lined with solid carbon dioxide with access through a removable top.

**PHYSICAL DATA**

Infra-red (i.r.) spectra are measured in units of cm⁻¹. The abbreviations used in determining i.r. data are:

br-broad; s-strong; m-medium; w-weak.

In nuclear magnetic resonance (n.m.r.) spectra, chemical shifts are expressed in p.p.m. on the $\delta$ scale relative to the internal standard (TMS). If a trimethyl group was already present in a compound then chloroform ($\delta$ 7.28) was used as the internal standard. The following abbreviations are used in recording n.m.r. data:

J-coupling constant (in Hz); s-singlet; d-doublet; t-triplet; q-quartet; m-multiplet; dd-double doublet; ddd-double doublet of doublets; dddd-double double doublet of doublets; dq-doublet of quartets; Ar-aromatic; quinaz.-
quinazolone.

Mass spectra were determined in units of mass relative to charge (M/Z) unless stated otherwise.
EXPERIMENTAL
Chapter 2
Preparation of methyl-N-(propanoyl)anthranilate (294)

This was prepared by a general procedure\textsuperscript{140} for the synthesis of methyl-N-substituted anthranilates. Thus, to methyl anthranilate (20g, 0.132 mol) was added propionic anhydride (18.07g, 0.138 mol). After the addition the mixture was heated at 100°C with stirring for 1h., then cooled and diluted with ether (100 ml). The ether solution was then washed successively with sodium bicarbonate solution and water, dried with magnesium sulphate and evaporated under reduced pressure. After evaporation of the ether solution, the product (294) was obtained as colourless crystals (24.1g, 88%), m.p. 30-31°C (from light petroleum);

$\nu_{\text{max}}$ (Nujol): 3270m, 1680s, 1585s, 1520s, 1430s, 1440s, 1255s, 1180s, 1090s, 965s, 920m, 795m, 745s and 695 cm$^{-1}$;

$\delta_{\text{H}}$ (CDCl$_3$, 90 MHz): 11.0 (br.s, exch. D$_2$O, NH), 8.63 (dd, J8 and 1Hz, ArH$_3$), 7.93 (dd, J7 and 2Hz, ArH$_6$), 7.43 (ddd, J8, 8 and 2Hz, ArH$_4$), 6.96 (ddd, J8, 7 and 1Hz, ArH$_5$), 3.86 (s, CO$_2$CH$_3$), 2.43 (q, J7.5Hz, CH$_2$CH$_3$) and 1.26 (t, J7.5Hz, CH$_2$CH$_3$).
Preparation of 3-amino-2-ethylquinazolin-4(3H)-one (77)

This was prepared by a general procedure, using the methyl N-substituted anthranilate (294) (17g, 0.082 mol) and hydrazine hydrate (95%, 20.55g, 0.41 mol), with ethanol (120 ml) as solvent. After 6h. refluxing the bulk of the ethanol solvent was removed under reduced pressure, the residue dissolved in dichloromethane, which was then washed once with water, dried with magnesium sulphate and evaporated to give the N-aminoquinazolone (77) (88%) as colourless crystals, m.p. 117-118°C (from ethanol) (lit. m.p. 152-153°C);

\[
\nu_{\text{max}} \text{ (Nujol): 3320s, 3220s, 1680s, 1635s, 1600s, 1340m, 1300m, 1250m, 1190m, 1150m, 1020m, 950m, 910m, 800m, 770s, 700s, 665m and 645m cm}^{-1};
\]

\[
\delta_H (\text{CDC}_3, 90 \text{ MHz}): 8.1 \text{ (dd, J8 and 1Hz, ArH}_5\text{)}, 7.7-7.2 \text{ (m, ArH}_6\text{, ArH}_7\text{ and ArH}_8\text{)}, 4.8 \text{ (br.s, exch. D}_2\text{O, NH}_2\text{)}, 2.95 \text{ (q, J7Hz, CH}_2\text{CH}_3\text{)}\text{ and 1.3 (t, J7Hz, CH}_2\text{CH}_3\text{)}.
\]

General procedure (1) for the preparation of N-acetoxyaminoguinaizolones with lead tetra-acetate at low temperature (-20 to -30°C)

The powdered N-aminoquinazolone (1 mol equiv.) and acetic acid-free lead tetra-acetate (LTA) (1.05-1.10 mol equiv.) were added alternately and continuously in very small portions over 15 min. to a vigorously stirred solution of dry deuterochloroform (1 ml/100 mg of N-aminoquinazolone) at -25°C. After stirring for a further 20-30 min. the lead di-acetate was
separated at low temperature (-30°C) and the solution washed with a cold (-25°C) saturated solution of sodium hydrogen carbonate, dried by passing through a small pre-cooled column of magnesium sulphate before recording its n.m.r. spectrum at the temperature indicated and without allowing the temperature to rise above -25°C throughout.

Preparation of N-acetoxyamino-2-ethylquinazolin-4(3H)-one (78)

\[
\begin{align*}
&\begin{array}{c}
N \\
\text{HNOAc} \\
\text{HNOAc} \\
\end{array} \\
&\begin{array}{c}
\text{Q} \\
\text{HNOAc} \\
\end{array} \\
&\begin{array}{c}
\text{H} \\
\text{H} \\
\end{array} \\
(78)
\end{align*}
\]

The foregoing general procedure (1) was followed using the N-aminoquinazolone (77) (0.100g, 5.28x10^-4 mol), LTA (0.246g, 5.55x10^-4 mol) and dry deuterochloroform (1 ml). Inspection of the low temperature \(^1\text{H}\) n.m.r. spectrum at -20°C revealed the major product to be the N-acetoxyamino-2-ethylquinazolin-4(3H)-one (78);

\(\nu_{\text{max}} (\text{CDCl}_3, -20^\circ\text{C}): 1768\text{s}, 1710\text{s} \text{ and } 1626\text{s cm}^{-1};\)

\(\delta_{\text{H}} (\text{CDCl}_3, 300\ \text{MHz, -20°C}): 10.98 \ (\text{s, NH}), \ 8.25 \ (\text{ddd, J8, 1.4 and 0.6Hz, ArH}_5), \ 7.84 \ (\text{ddd, J8, 7.4 and 1.4Hz, ArH}_7), \ 7.71 \ (\text{ddd, J8, 1.4 and 0.6Hz, ArH}_8), \ 7.52 \ (\text{ddd, J8, 7.4 and 1.4Hz, ArH}_9), 3.19 \ (\text{dq, J17 and 7Hz, HCHCH}_3), 3.03 \ (\text{dq, J17 and 7Hz, HCHCH}_3), 2.15 \ (\text{s, COCCH}_3) \text{ and } 1.43 \ (\text{t, J7Hz, CH}_2\text{CH}_3);\)

\(\delta_{\text{C}} (\text{CDCl}_3, 75\ \text{MHz, -20°C}): 169.46(\text{s}), 159.9(\text{s}), 158.52(\text{s}), 146.56(\text{s}), 135.48(\text{d}), 127.29(\text{d}), 126.97(\text{d}), 124.44(\text{d}), 119.56(\text{s}), 27.02(\text{t}), 18.98(\text{q}) \text{ and } 11.29(\text{q}).\)
A minor product (<5%) in this reaction was 2-ethylquinazolin-4(3H)-one (79) identified by its observable signals at 6 11.6 (s, NH), 8.23 (d, J8Hz, ArH₅) and 2.8 (q, J7.2Hz, CH₂CH₃).

When the foregoing solution was allowed to warm to ambient temperature 2-ethylquinazolin-4(3H)-one (79) was the major product which was subsequently isolated by chromatography of the crude reaction mixture over silica, with ethyl acetate-light petroleum (1:1) as eluant. The de-aminated quinazolone (79) was obtained as colourless crystals (0.062g, 68%), m.p. 235-237°C (from ethanol);

νₘₕₐₓ (Nujol): 3170m, 1680s, 1620s, 1340m, 1270m, 1250m, 1200m, 1140m, 1070w, 1015w, 955m, 900s, 805m, 795m, 770s, 690m and 625m cm⁻¹;

δₓ (CDCl₃, 90 MHz): 11.6 (br.s, exch. D₂O, NH), 8.2 (dd, J8 and 1Hz, ArH₅), 7.8-7.2 (m, ArH₆, ArH₇ and ArH₈), 2.8 (q, J7Hz, CH₂CH₃) and 1.4 (t, J7Hz, CH₂CH₃).

M/Z (%): 174(M⁺,89), 173(100), 146(14) and 119(37).

De-amination of N-amino-2-ethylquinazolin-4(3H)-one

The N-aminoquinazoline (77) (1g, 5.28x10⁻³ mol) was suspended in aqueous hydrochloric acid (4M, 27.5 ml) and was stirred magnetically at room temperature. Sodium nitrite solution (1.65g, in 8.75 ml of water) was added dropwise over 30 min. After setting aside overnight, the resulting
solution was neutralised using saturated sodium bicarbonate solution and the crude reaction mixture was extracted with dichloromethane (2x50 ml). The extracts were combined, dried with MgSO₄, and the solvent evaporated under reduced pressure to yield 2-ethylquinazolin-4(3H)-one (79) as colourless crystals (6.99g, 76%), m.p. 235-237°C (from ethanol) (lit. m.p. not quoted).

**Reaction of 3-acetoxyamino-2-methylquinazolone (82) with 3-amino-2-ethylquinazolone (77)**

$$\text{NH}_2 \quad \text{(81)} \quad \text{HNOAc} \quad \text{(82)} \quad (77) \quad \text{H} \quad (79) \quad \text{H} \quad (84)$$

2-Methyl-3-acetoxyaminoquinazolone (82) was prepared in solution by alternate and continuous addition of very small portions of the N-amino-quinazolone (81) (0.1g, 5.71x10⁻⁴ mol) and LTA (0.259g, 5.83x10⁻⁴ mol) over 20 min. to a dichloromethane solution (1 ml) maintained at -20°C. The solution was stirred for a further 20 min. at this temperature and then 3-amino-2-ethylquinazolone (77) (0.216g, 1.14x10⁻³ mol) was added in one portion. After allowing the solution to warm to room temperature, with continuous stirring, dichloromethane (5 ml) was added, the solution washed with saturated sodium hydrogen carbonate, dried over magnesium sulphate and evaporated under reduced pressure. Examination of the crude product by 300 MHz n.m.r. shows the presence of 2-methylquinazolone (84), 2-ethylquinazolone (79) and 3-amino-2-ethylquinazolone (77) in the ratio of 1:1:1 respectively from which it was concluded that efficient reaction according to the
The absence of any residual 3-amino-2-methylquinazolone (81) in the above n.m.r. spectrum shows that this compound was completely consumed in the original LTA oxidation.

General procedure (2) for the aziridination of alkenes using pre-formed N-acetoxyaminquinazolone (at -20 to -25°C) followed by the subsequent addition of the alkene(s)

The powdered N-aminoquinazolone (1 mol equiv.) and acetic acid-free lead tetra-acetate (LTA) (1.05-1.1 mol equiv.) were added alternately and continuously in very small portions over 15 min. to a vigorously stirred solution of dry dichloromethane (1 ml/100 mg of N-aminoquinazolone) cooled at -20 to -25°C with a dry ice-acetone bath. The mixture was then stirred for a further 30 min. at low temperature, before addition of the alkene(s) (1.5-3.5 mol equiv.) and allowing to warm to ambient temperature. The insoluble lead di-acetate was then separated, washed with dichloromethane and the total filtrate washed successively with sodium bicarbonate solution and water, dried with magnesium sulphate and the solvent removed by evaporation under reduced pressure.

General procedure (3) for the aziridination of alkenes at room temperature by oxidative (LTA) addition of N-aminoquinazolones in the presence of alkenes

Powdered N-aminoquinazolone (1 mol equiv.) and acetic acid-free lead tetra-acetate (1.05-1.10 mol equiv.) were added alternately and continuously in very small portions over 15 min. to a vigorously stirred solution
of dry dichloromethane (1 ml/100 mg of N-aminoquinazolone) and the alkene (1.5-3.5 mol equiv.) at room temperature. The mixture was then stirred for 30 min. at room temperature. The insoluble lead di-acetate was then separated and washed with dichloromethane and the total filtrate washed successively with sodium bicarbonate solution and water, dried with magnesium sulphate and the solvent removed by evaporation under reduced pressure.

**Aziridination of hex-1-ene**

![Chemical structure of 1-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-2-n-butylaziridine (85)](attachment:image)

The general procedure (2) was followed using N-aminoquinazolone (77) (1.00 g, 5.28 x 10^-3 mol), LTA (2.46 g, 5.55 x 10^-3 mol) and hex-1-ene (1.33 g, 0.0158 mol) in dry dichloromethane (10 ml). Chromatography of the crude product over silica, with ethyl acetate-light petroleum (1:3) as eluant, gave 1-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-2-n-butylaziridine (85) (Rf = 0.45) as colourless crystals (0.157 g, 11%), m.p. 65-66°C (from ethanol) (Found: C, 70.7; H, 8.1; N, 15.3. C_{16}H_{21}N_{5}O requires C, 70.8; H, 7.8; N, 15.5%);

ν_{max} (Nujol): 1665 s, 1595 s, 1450 s, 1335 m, 1250 m, 1230 m, 1220 m, 1170 m, 1135 m, 1065 m, 950 m, 915 w, 840 m, 770 s, 730 w, 695 m, 685 m and 645 m cm⁻¹;

δ_{H} (CDCl₃, 300 MHz): 8.18 (ddd, J8, 1.5 and 0.6 Hz, ArH₅), 7.67 (ddd, J8.2, 6.8 and 1.5 Hz, ArH₇), 7.62 (ddd, J8.2, 1.5 and 0.61 Hz, ArH₆), 7.40 (ddd, J8, 6.8 and 1.5 Hz, ArH₆), 3.11 (dq, J16.5 and 7.4 Hz, H₇CH₃), 3.02 (dq,
J16.5 and 7.4 Hz, HCHCH₃), 2.82 (m, azir. ring H-2 gem. to (CH₂)₃CH₃), 2.43 (dd, J5.8 and 1.8 Hz, azir. ring H-3 cis to (CH₂)₃CH₃), 2.38 (dd, J7.8 and 1.8 Hz, azir. ring H-3 trans to (CH₂)₃CH₃), 2.3-1.3 (m, (CH₂)₃), 1.43 (t, J7.4 Hz, CH₂CH₃) and 0.95 (t, J7 Hz, (CH₂)₃CH₃);

M/Z (%): 271(M⁺, 31), 228(14), 202(10), 201(9), 186(8), 175(50), 174(100), 173(64), 146(11), 131(30), 130(30), 119(17) and 103(14).

Further elution using the same solvent mixture gave the 2-ethylquinazolin-4(3H)-one (79) as the major product from this reaction (62%) as colourless crystals (from ethanol).

When this experiment was repeated using general procedure (3) and identical amounts of all the reactants, the aziridine (85) was obtained in 13% yield after chromatography. The de-aminated quinazolone (79) was also isolated (64%) after chromatography.

Aziridination of styrene

```
N
Q
Ph
```

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.1 g, 5.28x10⁻⁴ mol), LTA (0.246 g, 5.55x10⁻⁴ mol) and styrene (0.082 g, 7.93x10⁻⁴ mol) in dry dichloromethane (1 ml). After work-up the excess styrene was removed under high vacuum and 1-(4-oxo-2-ethyl-3(4H)-quinazoliny1)-2-phenylaziridine (86) was isolated as colourless crystals (0.116 g, 76%), m.p. 102-105°C (from ethanol) (Found: C, 74.1; H, 6.0; N, 14.4. C₁₆H₁₆N₃O requires C, 74.2; H, 5.9; N, 14.4%).
$\nu_{\text{max}}$ (Nujol): 1665s, 1597s, 1345m, 1290m, 1170w, 1070w, 780m, 775m, 760s, 710m and 700s cm$^{-1}$;

$\delta_{\text{H}}$ (CDCl$_3$, 300 MHz): 8.2 (ddd, J8.0, 1.5 and 0.6Hz, ArH$_q$), 7.67 (ddd, J8.0, 7.45 and 1.5Hz, ArH$_q$), 7.62 (ddd, J8.0, 1.3 and 0.6Hz, ArH$_q$), 7.42–7.34 (m, 6 x ArH), 3.69 (dd, J8.0 and 5.5Hz, azir. ring H-2), 3.12 (dd, J8.0 and 2.26Hz, azir. ring H-3 trans to Ph), 2.99 (q, J7.3Hz, CH$_2$CH$_3$), 2.87 (dd, J5.5 and 2.26Hz, azir. ring H-3 cis to Ph) and 1.35 (t, J7.3Hz, CH$_2$CH$_3$);

M/Z (%): 291(M$^+$, 27), 262(22), 200(100), 174(50), 173(60), 172(80), 118(72), 117(73), 104(58) and 103(59).

Aziridination of styrene using preformed N-acetoxyaminoquinazolone (7): formation of syn-aziridine (86a)

![Diagram of aziridination reaction]

Powdered N-aminoquinazolone (77) (0.1g, 5.28x10^{-4} mol) and acetic acid-free lead tetra-acetate (0.246g, 5.55x10^{-4} mol) were added alternately and continuously in very small portions over 15 min. to a vigorously stirred solution of dry deuterochloroform (1 ml) containing styrene (0.165g, 1.58x10^{-3} mol) at -30°C. After stirring for a further 20-30 min. the insoluble lead di-acetate was separated at low temperature and the solution transferred to a pre-cooled n.m.r. tube which was supported in a dewar containing dry ice-acetone at -40°C, all operations being carried out at less than -40°C.

The low temperature $^1$H n.m.r. spectrum at -40°C showed that the major product was the N-acetoxyaminoquinazolone (78). A minor product (~10%) was
assigned the syn-aziridine structure (86a) from its n.m.r. signals at;
$\delta_H$ (CDCl$_3$, 300 MHz, -40°C): 3.81 (t, J6Hz, azir. ring CHPh), 3.7 (dd, J6 and 3.8Hz, azir. ring HCH cis to quinaz. and Ph) and 3.45 (dd, J6 and 3.8Hz, azir. ring HCH trans to quinaz. and Ph).

When the temperature was raised gradually from -40°C to room tempera­
ture signals from the anti-aziridine, i.e. the major invertomer (86b), were
also observed by n.m.r. and grew in intensity whilst those of the syn-
invertomer (86a) disappeared: disappearance of signals from the N-acetoxy-
aminoquinazolone (78) was also observed.

Spectra were recorded at -40°C, -30°C, -25°C, -20°C, -15°C, -5°C and
room temperature with intervals of approximately 20 min. Apart from the
spectrum recorded at room temperature all spectra showed signals from the
N-acetoxyaminoquinazolone (78) to be present whose intensity diminished
with increase in temperature. The ratio of syn:anti aziridines were
measured by n.m.r. and the following data were recorded. At -40°C, 
>100:<1; at -30°C, 90:10; at -25°C, 65:35; at -20°C, 30:70; at -15°C, 
10:90; and at -5°C 100% anti-invertomer was observed with no syn-invertomer
present.

Aziridination of $\alpha$-methylstyrene

The general procedure (2) was followed using the N-aminoquinazolone
(77) (0.4g, 2.11x10$^{-3}$ mol), LTA (0.986, 2.22x10$^{-3}$ mol) and $\alpha$-methylstyrene
(0.74g, 6.34x10^-3 mol) in dry dichloromethane (4 ml). Chromatography of the crude product over silica, with ethyl acetate-light petroleum (1:2) as eluant, afforded 1-(4-oxo-2-ethyl-3(4H)-quinazoliny1)-2-methyl-2-phenyl-aziridine (87) as colourless crystals (0.374g, 58%), m.p. 117-120°C (from ethanol) (Found: C, 74.55; H, 6.45; N, 13.7. C_{19}H_{23}N_{3}O requires C, 74.7; H, 6.25; N, 13.75%);

$\nu_{\text{max}}$ (Nujol): 1665s, 1590s, 1280m, 1220m, 790m, 780m and 695m cm^-1;

$\delta_H$ (CDCl$_3$, 300 MHz): 8.22 (ddd, J7.9, 1.4 and 0.6Hz, ArH$_5$), 7.7 (ddd, J8.0, 7.4 and 1.4Hz, ArH$_7$), 7.64 (ddd, J8.0, 1.2 and 0.6Hz, ArH$_9$), 7.44 (ddd, J7.9, 7.4 and 1.2Hz, ArH$_8$), 7.55-7.1 (m, 5 x PhH), 3.31 (br.s, azir. ring H-3 cis to quinaz.), 3.1 (d, J2Hz, azir. ring H-3 trans to quinaz.), 2.86 (dq, J16 and 7.5Hz, HCHCH$_3$), 2.62 (br.dq, J16 and 7.5Hz, HCHCH$_3$), 1.54 (s, azir. ring CH$_3$) and 1.26 (t, J7.5Hz, CH$_2$CH$_3$);

M/Z (%): 305(M^+,12), 202(19), 201(36), 200(70), 175(100), 174(90), 173(80), 146(47), 133(37), 132(92), 131(80), 130(95), 129(21), 119(78), 117(41), 115(23), 105(25), 104(39), 103(74) and 102(29).

Aziridination of indene

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.245g, 1.29x10^-3 mol), LTA (0.604, 1.36x10^-3 mol) and indene (0.225g, 1.94x10^-3 mol) in dry dichloromethane (2.5 ml). Chromatography of the crude reaction product over silica with ethyl acetate-light petroleum (1:2) as eluant, gave 2,3-benzo-6-(4-oxo-2-ethyl-3(4H)-quinazoliny1)-6-aza-
bicyclo[3.1.0]hexane (88) as colourless crystals (0.24g, 62%), m.p. 151-153°C (from ethyl acetate) (Found: C, 75.15; H, 5.75; N, 13.8. C_{19}H_{17}N_{3}O requires C, 75.2; H, 5.65; N, 13.85%);

ν_{max} (Nujol): 1660s, 1595s, 1290m, 1235m, 1220m, 1010w, 840w, 800w, 780m, 760m, 725m and 685m cm^{-1};

δ_{H} (CDCl_{3}, 300 MHz): 8.22 (dd, J8.2 and 1.6Hz, ArH_{6}), 7.8-7.1 (m, ArH_{6}, ArH_{7}, ArH_{8} and 4 x ArH), 4.2 (d, J6Hz, azir. ring H-1 cis to quinaz.), 3.89 (t, J6Hz, azir. ring H-5, cis to quinaz.), 3.53 (d, J17Hz, H-4), 3.34 (dd, J17 and 6Hz, H-4), 3.12 (dq, J7 and 2.3Hz, CH_{2}CH_{3}) and 1.42 (t, J7Hz, CH_{2}CH_{3});

M/Z (%): 303(M^{+},10), 174(14), 173(17), 130(25), 129(100), 119(15), 103(19) and 102(11).

Aziridination of indene: formation of the syn-aziridine

Powdered N-aminooquinazolone (77) (0.1g, 5.28x10^{-4} mol) and acetic acid-free lead tetra-acetate (0.246g, 5.55x10^{-4} mol) were added alternately and continuously in very small portions over 15 min. to a vigorously stirred solution of dry deuterochloroform (1 ml) containing 3 mole equivalents of indene (0.184g, 1.58x10^{-3} mol) at -30°C. After stirring for 20-30 min. the insoluble lead di-acetate was separated at low temperature and the solution was transferred to a pre-cooled n.m.r. tube which was supported in a dewar maintained at -40°C, all operations being carried out at less than -40°C.

Examination of the n.m.r. spectrum at -30°C showed two sets of aziridine ring protons neither of which corresponded to the foregoing aziridine (88) and were assigned to the 2 rotameric forms (88a) and (88b)
of the kinetically-formed syn-aziridine. The ratio of rotamers at -30°C was 1:1.3. Aziridination of indene was incomplete under these conditions and unreacted N-acetoxyaminoquinazolone was also present which reacted further with indene as the temperature was raised to ambient (see below).

[Diagram of 88a and 88b]

$\delta_H$ (CDCl$_3$, 300 MHz, -40°C, major rotamer): 4.72 (d, J4.5Hz, azir. ring H-1) and 3.74 (t, J4.5Hz, azir. ring H-5);

$\delta_H$ (CDCl$_3$, 300 MHz, -40°C, minor rotamer): 4.33 (d, J4.5Hz, azir. ring H-1) and 4.15 (t, J4.5Hz, azir. ring H-5).

When the temperature was raised gradually from -40°C to ambient broadening of the aziridine ring protons at 0°C was observed and growth of signals from the foregoing aziridine (88) occurred at the expense of broadened signals from the minor invertomer rotamers.

Spectra were obtained at -30°C, -20°C, -10°C, 0°C, +10°C and +20°C after -20 min. at each temperature and the ratio of syn:anti aziridines were recorded. At -30°C and -20°C this ratio was >100:1, at -10°C 90:10, at 0°C 50:50 (with broadening of the ring protons in the syn-aziridine invertomers), at +10°C 40:60 and at +20°C only signals from the anti-aziridine invertomer were observed.
Aziridination of methyl acrylate

\[ \text{Q} \]

\[ \text{CO}_2\text{Me} \]

(89)

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.15g, 7.93x10^-4 mol), LTA (0.369g, 8.32x10^-4 mol) and methyl acrylate (0.102g, 1.189x10^-3 mol) in dry dichloromethane (1.5 ml). After work-up methyl-1-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-azidine-2-carboxylate (89) was obtained as colourless crystals (0.175g, 81%), m.p. 116-118°C (from ethanol) (Found: C, 61.6; H, 5.6; N, 15.25. \( C_{14}H_{15}N_3O_3 \) requires C, 61.5; H, 5.55; N, 15.35%);

\( \nu_{\max} \) (Nujol): 1755s, 1670s, 1595s, 1440s, 1335m, 1290m, 1240s, 1205s, 975m, 930m, 770s, 755m, 695s and 635m cm^{-1};

\( \delta_H \) (CDCl\(_3\), 300 MHz): 8.17 (ddd, J8, 1.4 and 0.6Hz, Ar\(_H_5\)), 7.72 (ddd, J8.1, 7.4 and 1.4Hz, Ar\(_H_7\)), 7.62 (ddd, J8.1, 1.3 and 0.6Hz, Ar\(_H_8\)), 7.42 (ddd, J8, 7.4 and 1.3Hz, Ar\(_H_6\)), 3.86 (s, \( CO_2CH_3 \)), 3.65 (dd, J7.5 and 5.4Hz, azir. ring \( H-2 \)), 3.18 (dd, J7.5 and 1.5Hz, azir. ring \( H-3 \) trans to \( CO_2CH_3 \)), 3.08 (2 x dq, J17 and 6.6Hz, \( CH_2CH_3 \)), 2.92 (dd, J5.4 and 1.5Hz, azir. ring \( H-3 \) cis to \( CO_2CH_3 \)) and 1.42 (t, J6.6Hz, \( CH_2CH_3 \));

M/Z (%): 273(M\(^+\), 81), 175(21), 174(19), 173(19), 131(100), 130(52) and 103(22).
Aziridination of trans-but-2-ene

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.2g, 1.05x10^-3 mol), LTA (0.493g, 1.11x10^-3 mol) and trans-but-2-ene (0.088g, 1.58x10^-3 mol) in dry dichloromethane (2 ml). The alkene trans-but-2-ene which is a gas at room temperature and atmospheric pressure was used as a solution in dichloromethane (1 ml) obtained by passing trans-but-2-ene into a known weight of dichloromethane cooled in ice so as to minimise evaporation. After work-up 1-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-E-2,3-dimethylaziridine (90) was obtained as colourless crystals (0.179g, 70%), m.p. 57-59°C (from acetonitrile) (Found: C, 69.2; H, 7.0; N, 17.2. C_{14}H_{17}N_{3}O requires C, 69.1; H, 7.05; N, 17.25%);

ν_max (Nujol): 1672s, 1610m, 1590s, 1570m, 1365m, 1335m, 1300m, 1285m, 1220m, 1145m, 1050m, 765m, 700m, 695m and 650m cm⁻¹;

$\delta_H$ (CDCl₃, 300 MHz): 8.18 (ddd, J8, 1.4 and 0.6Hz, ArH₅), 7.69 (ddd, J8, 7.2 and 1.4Hz, ArH₇), 7.63 (ddd, J8, 1.2 and 0.6Hz, ArH₉), 7.41 (ddd, J8, 7.2 and 1.2Hz, ArH₉), 3.15 (dq, J16 and 7.5Hz, HCHCH₃), 2.89 (quintet, J5.9Hz, azir. ring H-2 cis to quinaz.), 2.87 (dq, J16 and 7.5Hz, HCHCH₃), 2.51 (quintet, J5.9Hz, azir. ring H-3 trans to quinaz.), 1.54 (d, J5.9Hz, CHCH₃ trans to quinaz.), 1.4 (t, J7.5Hz, CH₂CH₃) and 1.1 (d, J5.9Hz, CHCH₃ cis to quinaz.);

M/Z (%): 243(M⁺,14), 228(13), 214(11), 200(5), 174(20), 173(18), 131(21), 130(18), 119(8), 103(11), 90(7), 78(12), 77(24) and 70(100).
Aziridination of trans-β-methylstyrene

The general procedure (2) was followed using the N-aminooquinazolone (77) (0.5g, 2.64x10^{-3} mol), LTA (1.232g, 2.77x10^{-3} mol) and trans-β-methylstyrene (0.937g, 7.93x10^{-3} mol) in dry dichloromethane (5 ml). Chromatography of the crude product over silica with ethyl acetate-light petroleum (1:2) as eluant, gave 1-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-E-2-methyl-3-phenylaziridine (91) as colourless crystals (0.49g, 61%), m.p. 98-101°C (from ethanol) (Found: C, 74.55; H, 6.35; N, 13.7. C_{19}H_{19}N_{3}O requires C, 74.7; H, 6.25; N, 13.75%);

ν_{max} (Nujol): 2985m, 1670s, 1595s, 1470s, 1365m, 1335m, 1220m, 915m, 770s and 695s cm^{-1};

^{1}H n.m.r. spectrum of aziridine (91) showed that the ratio of invertomers at room temperature was 1.5:1.

M/Z (%): 305(M^{+},5), 290(7), 276(9), 214(10), 200(5), 173(12), 157(13),
Aziridination of α-methylene-γ-butyrolactone

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.25g, 1.32x10^{-3} mol), LTA (0.616g, 1.38x10^{-3} mol) and α-methylene-γ-butyrolactone (0.194g, 1.98x10^{-3} mol) in dry dichloromethane (2.5 ml). Chromatography of the crude product over alumina with ethyl acetate-light petroleum (2:1) as eluant, gave 7-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-2-oxa-7-aza-spiro[4.2]heptan-1-one (92) as colourless crystals (0.23g, 62%), m.p. 168-171°C (from ethanol) (Found: C, 63.1; H, 5.4; N, 14.6. C_{16}H_{15}N_{3}O_{3} requires C, 63.1; H, 5.3; N, 14.7%);

ν_{max} (Nujol): 1765s, 1680s, 1598s, 1330m, 1290m, 1230m, 1130m, 1110m, 1025m, 775s, 740m and 700m cm^{-1};

δ_{H} (CDCl_{3}, 300 MHz): 8.16 (ddd, J8.0, 1.5 and 0.6Hz, ArH_{6}), 7.69 (ddd, J8.2, 6.7 and 1.5Hz, ArH_{7}), 7.53 (ddd, J8.2, 1.5 and 0.6Hz, ArH_{6}), 7.40 (ddd, J8.2, 6.7 and 1.5Hz, ArH_{7}), 4.98 (br.ddd, J8, 8 and 8Hz, CHCOO), 4.55 (ddd, J9.3, 8 and 3.8Hz, HCHCOO), 3.05 (br.s, azir. ring H-6 cis to quinaz.), 3.00 (q, J7.4Hz, CH_{2}CH_{3}), 2.97 (br.s, azir. ring H-6 proton trans to quinaz.), 2.87 (ddd, J14, 8 and 3.8Hz, HCHCH_{2}COO), 2.62 (ddd, J14, 9.3 and 8Hz, HCHCH_{2}COO) and 1.45 (t, J7.4Hz, CH_{2}CH_{3});

M/Z (%): 285(M^{+},57), 187(11), 175(32), 174(25), 173(24), 132(11), 131(100), 130(49), 119(10), 112(10) and 103(19).
Aziridination of methyl methacrylate

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.4g, 2.11x10^-3 mol), LTA (0.986g, 2.22x10^-3 mol) and methyl methacrylate (0.741g, 7.4x10^-3 mol) in dry dichloromethane (4 ml). Chromatography of the crude reaction product over silica with ethyl acetate-light petroleum (1:1) as eluant, gave methyl-1-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-2-methylaziridine-2-carboxylate (93) as colourless crystals (0.41g, 67%), m.p. 90-93°C (from ethanol) (Found: C, 62.7; H, 6.0; N, 14.6. C_{15}H_{17}N_{2}O_{3} requires C, 62.7; H, 5.95; N, 14.6%);

νmax (Nujol): 1730s, 1665s, 1595s, 1450m, 1380m, 1330m, 1310m, 1205s, 1170s, 1060w, 990w, 785m, 760m and 700m cm^-1;

$^1$H (CDCl$_3$, 300 MHz, major invertomer, CO$_2$Me cis to quinaz.): 8.15 (ddd, J8.0, 1.5 and 0.6Hz, ArH$_5$), 7.7 (dd, J8.0 and 7.3Hz, ArH$_7$), 7.64 (ArH$_8$, obscured), 7.39 (ddd, J8.0, 7.3 and 1.3Hz, ArH$_6$), 3.56 (s, CO$_2$CH$_3$), 3.26 (br.s, azir. ring H-3 cis to CO$_2$CH$_3$), 2.98 (2 x dq, J17 and 7.3Hz, CH$_2$CH$_3$), 2.85 (d, J1.5Hz, azir. ring H-3 trans to CO$_2$CH$_3$), 1.77 (s, CH$_3$) and 1.42 (t, J7.3Hz, CH$_2$CH$_3$);

$^1$H (CDCl$_3$, 300 MHz, minor invertomer, CO$_2$Me trans to quinaz.): 8.19 (dd, J8 and 1.5Hz, ArH$_5$), 7.7 (dd, J8.1 and 7.3Hz, ArH$_7$), 7.64 (ArH$_9$, obscured), 7.42 (dd, J8.0 and 7.3Hz, ArH$_6$), 3.84 (s, CO$_2$CH$_3$), 3.4 (br.s, azir. ring H-3 trans to CO$_2$CH$_3$), 2.77 (2 x dq, J17 and 7.3Hz, CH$_2$CH$_3$), 1.73 (s, CH$_3$) and 1.39 (t, J7.3Hz, CH$_2$CH$_3$): the aziridine ring proton cis to CO$_2$CH$_3$ was obscured. The ratio of the two invertomers was 2:1 at room temperature.

M/Z (%): 287(M^+,42), 200(46), 175(50), 174(47), 173(51), 158(16), 157(16), 131(100), 130(73), 119(14), 114(37), 104(10) and 103(25).
Aziridination of methyl crotonate

\[
\begin{align*}
\text{CO}_2\text{Me} & \\
\text{N} & \\
\text{CH}_3
\end{align*}
\]

(94)

The general procedure (3) was followed using the N-aminoquinazolone (77) (0.5g, 2.64x10^{-3} mol), LTA (1.23g, 2.77x10^{-3} mol) and methyl crotonate (0.79g, 7.93x10^{-3} mol) in dry dichloromethane (5 ml). Crystallisation of the crude product gave E-methyl-1-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-2-methylaziridine-3-carboxylate (94) as colourless crystals (0.44g, 58%), m.p. 93-95°C (from ethanol) (Found: C, 62.55; H, 6.0; N, 14.55. \(\text{C}_{15}\text{H}_{17}\text{N}_3\text{O}\) requires C, 62.7; H, 5.95; N, 14.6%);

\(\nu_{\text{max}}\) (Nujol): 1728s, 1665s, 1590s, 1435s, 1330s, 1200s, 1130m, 1055m, 1010m, 770m and 690m cm^{-1};

\(\delta_H\) (CDCl\(_3\), 300 MHz, major invertomer, CO\(_2\)Me cis to quinaz.): 8.17 (ddd, J7.9, 1.4 and 0.5Hz, ArH\(_5\)), 7.68 (ddd, J8, 7.3 and 1.4Hz, ArH\(_7\)), 7.62 (ddd, J8, 1.2 and 0.5Hz, ArH\(_8\)), 7.40 (ddd, J7.9, 7.3 and 1.2Hz, ArH\(_6\)), 3.63 (s, CO\(_2\)CH\(_3\)), 3.44 (q, J5Hz, azir. ring H-2 trans to quinaz.), 3.24 (d, J5Hz, azir. ring H-3 cis to quinaz.), 3.0 (dq, J17 and 7.5Hz, HCHCH\(_3\)), 2.82 (dq, J17 and 7.5Hz, HCHCH\(_3\)), 1.6 (d, J5Hz, CHCH\(_3\)) and 1.42 (t, J7.5Hz, \(\text{CH}_2\text{CH}_3\));

\(\delta_H\) (CDCl\(_3\), 300 MHz, minor invertomer, CO\(_2\)Me trans to quinaz.): 8.2-7.4 (4 x ArH, quinazolone ring protons obscured by major invertomer), 3.88 (s, CO\(_2\)CH\(_3\)), 3.69 (d, J5Hz, azir. ring H-3 cis to quinaz.), 3.19 (dq, J17 and 7.5Hz, HCHCH\(_3\)), 2.88 (dq, J17 and 7.5Hz, HCHCH\(_3\)), 1.42 (t, \(\text{CH}_2\text{CH}_3\), obscured by triplet from major invertomer) and 1.25 (d, J5Hz, CHCH\(_3\)). The other aziridine ring proton in the minor invertomer was obscured. The ratio of major : minor invertomers at room temperature was 4:1.

M/Z (%): 287(M^+,30), 272(14), 228(31), 175(10), 174(41), 173(33), 132(13), 131(100), 130(52), 119(10), 114(30) and 103(22).
Aziridination of cyclohexene

The general procedure (3) was followed using the N-aminoquinazolone (77) (0.3g, 1.58x10⁻³ mol), LTA (0.739g, 1.66x10⁻³ mol) and cyclohexene (0.391g, 4.75x10⁻³ mol) in dry dichloromethane (3 ml). Chromatography of the crude product over silica with ethyl acetate-light petroleum (1:2) as eluant, gave 7-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-7-azabicyclo[4.1.0]heptane (95) (Rf = 0.51) as colourless crystals (0.187g, 44%), m.p. 85-88°C (from ethyl acetate-light petroleum) (Found: C, 71.15; H, 7.1; N, 15.57. C₁₆H₁₉N₃O requires C, 71.35; H, 7.1; N, 15.6%);

νmax (Nujol): 1665s, 1595s, 1335s, 1300m, 1285m, 1220m, 810w, 765m and 695m cm⁻¹;

S H (CDCl₃, 300 MHz): 8.18 (ddd, J₈, 1.4 and 0.6Hz, ArH₅), 7.67 (ddd, J₈, 1, 7.4 and 1.4Hz, ArH₇), 7.61 (ddd, J₈, 1.3 and 0.6Hz, ArH₆), 7.39 (ddd, J₈, 7.4 and 1.3Hz, ArH₆), 3.01 (q, J7.5Hz, CH₂CH₃), 2.74 (m, azir. ring H-1 and H-6), 2.35-2.2 (m, CH₂), 2.05-1.9 (m, CH₂), 1.55-1.40 (m, CH₂), 1.4-1.25 (m, CH₂) and 1.43 (t, J7.5Hz, CH₂CH₃);

M/Z (%): 269(M⁺,24), 226(37), 213(12), 201(11), 200(95), 187(11), 175(22), 174(47), 173(64), 158(14), 157(15), 146(12), 132(15), 131(84), 130(92), 129(19), 119(19), 104(13), 103(47) and 102(15).
Oxidation of 3-amino-2-ethylquinazolin-4(3H)-one (77) with lead tetraacetate at room temperature in methanol

\[
\begin{array}{c}
\text{O} \\
\text{N} \\
\text{H} \\
\text{OMe}
\end{array}
\quad (96)
\]

The general procedure (3) was followed using methanol as both the solvent and reactant. The N-aminoquinazolone (77) (0.25g, 1.32x10^{-3} mol) was oxidized using LTA (0.616g, 1.38x10^{-3} mol) in methanol (5 ml). The crude product [which by n.m.r. contained 50% of the de-aminated quinazolone (79)] was then diluted with dichloromethane (10 ml) and washed with sodium hydroxide solution (2M, 5x10 ml) to remove the de-aminated quinazolone, dried (MgSO\(_4\)) and the solvent removed by evaporation under reduced pressure to yield 2-ethyl-3-methoxyaminquinazolin-4(3H)-one (96) as a colourless solid (0.067g, 23%), m.p. 109-111°C (from ethanol) (Found: C, 60.45; H, 6.0; N, 19.2. \(\text{C}_{11}\text{H}_{13}\text{N}_{3}\text{O}_{2}\) requires C, 60.25; H, 5.95; N, 19.15%);

\(\nu_{\text{max}}\) (Nujol): 3200s, 1680s, 1600s, 1490s, 1330m, 1300m, 1245s, 1190m, 1020s, 920s, 820m, 770s, 735m, 695s, 665m and 645m cm\(^{-1}\);

\(\delta_{\text{H}}\) (CDCl\(_3\), 300 MHz): 9.32 (s, exch. D\(_2\)O, NH), 8.23 (ddd, J8.0, 1.5 and 0.6Hz, Ar\(_{H_3}\)), 7.73 (ddd, J8.2, 6.8 and 1.5Hz, Ar\(_{H_7}\)), 7.65 (ddd, J8.2, 1.4 and 0.6Hz, Ar\(_{H_6}\)), 7.42 (ddd, J8.0, 6.8 and 1.4Hz, Ar\(_{H_6}\)), 3.72 (s, OCH\(_3\)), 3.09 (br.m, CH\(_2\)CH\(_3\)) and 1.40 (t, J7.5Hz, CH\(_2\)CH\(_3\));

M/Z (%): 219(M\(^+\),5), 189(30), 174(80), 173(100), 146(6), 131(48), 119(50) and 103(5).

Attempted exchange of the NH and acetoxy groups in N-acetoxyamino-2-ethylquinazolin-4(3H)-one (78) using d\(_4\)-acetic acid

Powdered 3-amino-2-ethylquinazolin-4(3H)-one (77) (0.4g, 2.11x10^{-3} mol)
and acetic acid-free lead tetra-acetate (0.98 g, 2.2 x 10^{-3} mol) were added alternately and continuously in very small portions over 15 min. to a vigorously stirred solution of deuterochloroform (4 ml) cooled to -30°C with a dry ice-acetone bath. The mixture was then stirred for a further 20 min. at -30°C then the insoluble lead di-acetate was filtered off and the deuterochloroform solution was washed with cold saturated sodium bicarbonate solution and dried (MgSO₄); all these processes being carried out at <-30°C. The low temperature ^{1}H n.m.r. spectrum at -20°C showed only N-acetoxyamino-2-ethylquinazolin-4(3H)-one (78) to be present with no contamination from acetic acid. The deuterochloroform solution was then stirred for a further 20 min. with d₄-acetic acid (4 mol equiv.) at -30°C. After this time the low temperature ^{1}H n.m.r. spectrum was then re-recorded at -20°C and only the starting N-acetoxyaminoquinazolone (78) was found to be present, hence no deuterium incorporation into (78) had occurred.

Oxidation of N-aminocruinazolone (44) with lead tetra-acetate at -40°C

Over a period of 30 min., very small portions of the N-aminocruinazolone (44) (0.15 g, 6.96 x 10^{-4} mol) and dry LTA (0.32 g, 7.31 x 10^{-4} mol) were added alternately and continuously to magnetically stirred deuterochloroform (1.5 ml) maintained at -40°C with a dry ice-acetone bath. The mixture was
stirred for a further 20 min. and then lead di-acetate separated and a portion of the solution transferred to an n.m.r. tube; all operations being carried out at <-40°C. The n.m.r. spectrum of this solution at -40°C showed the presence of N-acetoxyaminoquinazolone (102) and the aziridine (45)\textsuperscript{38} in a 65:35 ratio respectively. For N-acetoxyaminoquinazolone (102); \( ^6 \text{H} (\text{CDCl}_3, 300 \text{ MHz}, -40^\circ \text{C}): 10.98 (s, \text{NH}), 8.24 (dd, J8 and 1.4Hz, ArH\textsubscript{6}), 7.84 (ddd, J8, 7.4 and 1.43 Hz, ArH\textsubscript{7}), 7.72 (d, J8Hz, ArH\textsubscript{9}), 7.53 (ddd, J8, 7.4 and 1.5Hz, ArH\textsubscript{6}), 5.98 (m, CH=CH\textsubscript{2}), 5.17 (dd, J17 and 2Hz, CH=CHH (cis)), 5.07 (dd, J10 and 2Hz, CH=CHH (trans)), 3.27 (ddd, J16, 8 and 6Hz, HCHCH\textsubscript{2}CH=CH\textsubscript{2}), 3.16-3.03 (m, HCHCH\textsubscript{2}CH=CH\textsubscript{2} and HCHHCHCH=CH\textsubscript{2}), 2.64 (br.q, J7Hz, HCHCH=CH\textsubscript{2}) and 2.14 (s, OCOC\textsubscript{3}).

The aziridine (45)\textsuperscript{38} was identified by its characteristic aziridine ring proton signals at 3.00 (dd, J5.5 and 2Hz) and 1.96 (dd, J6.5 and 2Hz).

Oxidation of N-aminoquinazolone (103) with lead tetra-acetate at -40°C

\[
\text{N} \quad \text{HNOAc}
\]

The oxidation of N-aminoquinazolone (103)\textsuperscript{60} was carried out as described for (44) by adding the N-aminoquinazolone (103) (0.1g, 4.36x10\textsuperscript{-4} mol) and LTA (0.203g, 4.57x10\textsuperscript{-4} mol) to deuterochloroform (1 ml) at -40°C. Examination of the n.m.r. spectrum of the solution at -40°C showed that quantitative conversion to the N-acetoxyaminoquinazolone (104) had occurred.
with;

$^6_H (CDCl_3, 300 MHz, -40^\circ C): 10.96 (s, NH), 8.26 (dd, J8.0 and 1.5Hz, ArH_5), 7.84 (ddd, J8.0, 7.4 and 1.5Hz, ArH_7), 7.71 (dd, J8.0 and 1.5Hz, ArH_6), 7.52 (ddd, J8, 7.4 and 1.5Hz, ArH_6), 5.82 (m, CH=CH_2), 5.1 (dd, J16.5 and 2Hz, CH=CHH (cis)), 5.03 (dd, J10 and 2Hz, CH=CHH (trans)), 3.16 (ddd, J17, 8 and 7Hz, HCHCH_2CH=CH_2), 2.99 (ddd, J17, 8 and 7Hz, HCHCH_2CH=CH_2), 2.16 (s, OCOCH_3) and 2.31-1.82 (m, CH_2CH_2CH=CH_2).

**Oxidation of N-aminoguiazolone (106) with lead tetra-acetate at -30^\circ C**

![Chemical structure](image)

The oxidation was carried out by dissolving the N-aminoguiazolone (106) (0.1g, 3.36x10^-4 mol) in deuterochloroform (5 ml), dissolving LTA (0.156g, 3.55x10^-4 mol) in deuterochloroform (5 ml) and adding both solutions at the same rate over 30 min. from separate dropping funnels to a stirred deuterochloroform solution (2 ml) maintained at -30^\circ C. After stirring for a further 20 min. the lead di-acetate was separated and the solution examined by n.m.r. at -30^\circ C without any intermediate warming of the solution to give the N-acetoxyaminoguiazolone (107) as a 1:1 mixture of stereoisomers.

$^6_H (CDCl_3, 300 MHz, -30^\circ C): 10.97 (s, NH), 10.94 (s, NH), 8.25 (dd, J8 and...
1.5Hz, ArH₅), 7.85 (ddd, J₈, 7.4 and 1.5Hz, ArH₇), 7.72 (d, J₈Hz, ArH₈),
7.53 (ddd, J₈, 7.4 and 1.5Hz, ArH₉), 5.4 (m, CH=CHCH₂), 4.73 (m, =CHCH₂),
3.12 (ddd, J₁₅, 9 and 6Hz, CHH-quinaz.), 2.76 (ddd, J₁₆, 16 and 7.5Hz,
CHH-quinaz.), 1.82 (s, CH₃C=CH), 1.70 (s, CH₃C=CH), 1.6 (d, J₅.5Hz,
CH=CHCH₃), 1.55 (d, J₅.5Hz, CH=CHCH₃); other signals were obscured by
CH₃CO₂H.

Oxidation of N-aminoquinazolone (108) with lead tetra-acetate at -40°C

Oxidation was carried out by dissolving the N-aminoquinazolone (108)
(0.1g, 3.52x10⁻⁴ mol)⁶⁰ in deuterochloroform (5 ml) and dissolving LTA
(0.164g, 3.7x10⁻⁴ mol) in deuterochloroform (5 ml) and adding both
solutions at the same rate over 30 min. from separate dropping funnels to a
stirred deuterochloroform solution (2 ml) maintained at -40°C by means of a
dry ice-acetone bath. After stirring for a further 20 min. the lead
di-acetate was separated and the solution examined by ¹H n.m.r. at -30°C
without any intermediate warming of the solution: only signals from
aziridine (107) were present which corresponded closely to those previously
reported⁶⁰ for this compound.
Preparation of N-acetoxyamino-2-(1,2,2-trimethylpropyl)-quinazolin-4(3H)-one (110) in solution

\[
\text{Bu}^+ \quad \begin{array}{c}
\text{Me} \\
\text{HNOAc}
\end{array} \quad \text{N} \quad \text{N} \\
\text{(110)}
\]

The general oxidation procedure (1) was followed using the N-aminoquinazolone (111) (0.15g, 6.12x10^{-4} mol), \textsuperscript{61} LTA (0.285g, 6.42x10^{-4} mol) and dry deuterochloroform (1.5 ml). Examination of the solution by \textsuperscript{1}H n.m.r. at -40°C showed only (110) as a 4:1 mixture of stereoisomers.

\textsuperscript{61} S\textsubscript{H} (CDCl\textsubscript{3}, 300 MHz, -40°C, major stereoisomer): 11.1 (s, NH), 8.26 (ddd, J\textsubscript{8}, 1.4 and 0.6Hz, Ar\textsubscript{H\textsubscript{5}}), 7.84 (ddd, J\textsubscript{8}, 7.5 and 1.4Hz, Ar\textsubscript{H\textsubscript{7}}), 7.72 (ddd, J\textsubscript{8}, 1.4 and 0.6Hz, Ar\textsubscript{H\textsubscript{6}}), 7.51 (ddd, J\textsubscript{8}, 7.5 and 1.4Hz, Ar\textsubscript{H\textsubscript{5}}), 3.78 (q, J\textsubscript{7.1Hz}, tBuCH\textsubscript{Me}), 2.13 (s, OOC\textsubscript{OCH\textsubscript{3}}), 1.38 (d, J\textsubscript{7.1Hz}, tBuCH\textsubscript{CH\textsubscript{3}}) and 0.99 (s, tBu);

\textsuperscript{61} S\textsubscript{H} (CDCl\textsubscript{3}, 300 MHz, -40°C, minor stereoisomer): 10.89 (s, NH), 3.67 (q, J\textsubscript{7Hz}, tBuCH\textsubscript{Me}), 2.17 (s, OOC\textsubscript{OCH\textsubscript{3}}), 1.31 (d, J\textsubscript{7Hz}, tBuCHCH\textsubscript{3}) and 1.11 (s, tBu); the quinazolone ring protons signals are coincident with those of the major stereoisomer.

Preparation of N-chloroacetyl anthranilic acid

This was prepared\textsuperscript{143} from anthranilic acid and chloroacetyl chloride, the product was recrystallised from 50% glacial acetic acid, yielding N-chloroacetyl anthranilic acid, m.p. 181-184°C (lit.\textsuperscript{143} 183-187°C).
Preparation of 4,1-benzoxazepine-2,5-(1H,3H)-dione

This preparation follows the method of Uskokovic et al. but the change in conditions as described below resulted in an improved yield of the title compound from 20% to 86%.

A solution of N-chloroacetyl anthanilic acid (5.65g) at triethylamine (1 mol equiv.) in dry DMF (250 ml) were added dropwise to a refluxing solution of DMF (70 ml) under nitrogen. The addition was carried out over 3h and after the addition was complete the solution was refluxed for a further 6h, after which the DMF was removed under reduced pressure. The solid which remained was triturated with water (70 ml) then filtered and the solid product which was isolated in 86% yield, was shown to be pure by 1H n.m.r. and used directly without further purification.

$\nu_{\text{max}}$ (Nujol): 1750s, 1715s, 1220s, 1245s and 1280s cm$^{-1}$;  
it. $\nu_{\text{max}}$ (CDCl$_3$): 1728, 1710, 1216, 1242 and 1278 cm$^{-1}$;  
$\delta_H$ (d$_6$-DMSO, 90 MHz): 10.65 (s, NH), 7.9-7.1 (m, 4 x ArH) and 4.6 (s, CH$_2$);  
it. 1H n.m.r. not quoted.

Preparation of 3-amino-2-(hydroxymethyl)-quinazolin-4(3H)-one (112)

\[
\begin{align*}
\text{HO} & \quad \text{N} \quad \text{O} \\
\text{NH}_2 & \\
\text{(112)}
\end{align*}
\]

A solution of the foregoing 4,1-benzoxazepine-2,5-(1H,3H)-dione (6g, 0.038 mol) and hydrazine hydrate (8.48g, 0.1694 mol) in ethanol (80 ml) was refluxed for 8h, after which the bulk of the ethanol was removed under
reduced pressure, the residue was triturated with water to remove any excess hydrazine and then filtered. The N-aminoquinazolone (112) was obtained as pale yellow crystals (91%), m.p. 210-212°C (from glacial acetic acid) (lit.\textsuperscript{143} m.p. 216-220°C).

**Aziridination of styrene using (112) and procedure (2)**

\[
\begin{align*}
\text{HO} & \quad \text{AcO} \\
\text{N} & \quad \text{N} \\
\text{Ph} & \quad \text{Ph}
\end{align*}
\]

(114) (115)

The general procedure (2) was followed using the N-aminoquinazolone (112) (0.25g, 1.31x10^{-3} mol), LTA (0.61g, 1.37x10^{-3} mol) and styrene (0.41g, 3.93x10^{-3} mol) in dry dichloromethane (2.5 ml). Examination of the \textsuperscript{1}H n.m.r. of the crude reaction product showed it to contain the aziridines (114) and (115) present in a 3:1 ratio respectively from comparison of the integral resonances at s 3.96 and s 4.2.

Chromatography of the crude reaction product over silica with ethyl acetate-light petroleum (1:3) as eluant, gave the aziridine (115) as colourless crystals (0.059g, 13%), m.p. 87-90°C (from ethanol);

\[\nu_{\text{max}}\text{ (Nujol): 1745s, 1675s, 1600s, 1365s, 1335m, 1330m, 1225s, 1130m, 1080s, 1030s, 910s, 775s, 735s and 695m cm}^{-1};\]

\[\delta_{\text{H}}\text{ (CDCl}_3\text{, 300 MHz): 8.19 (d, J8.1Hz, ArH}_5\text{), 7.7 (t, J8.1Hz, ArH}_7\text{), 7.64 (d, J8.1Hz, ArH}_6\text{), 7.44 (t, J8.1Hz, ArH}_6\text{), 7.7 (t, J8.1Hz, ArH}_7\text{), 7.64 (d, J8.1Hz, ArH}_5\text{), 7.44 (t, J8.1Hz, ArH}_6\text{), 7.36 (m, 5 x PhH), 5.41 (d, J14.7Hz,}...\]
$\text{HCHOAc}$, 5.31 (d, J14.7 Hz, HCHOAc), 4.2 (dd, J7.9 and 5.4 Hz, azir. ring H-2 cis to quinaz.), 3.65 (dd, J7.9 and 2 Hz, azir. ring H-3, trans to Ph and cis to quinaz.), 2.71 (dd, J5.4 and 2 Hz, azir. ring H-3 cis to Ph and trans to quinaz.) and 2.13 (s, CH$_2$);

$\delta$C (CDCl$_3$, 75 MHz): 170.2(s), 160.1(s), 151.4(s), 145.5(s), 136.4(s), 133.9(d), 128.5(d), 128.0(d), 127.3(d), 126.9(d), 126.3(d), 126.1(d), 121.8(s), 62.1(t), 43.9(d), 40.4(t) and 20.6(q);

M/Z (%): 335(M+,1), 273(5), 245(15), 244(100), 176(20), 175(22), 172(18), 147(15) and 116(12).

Further elution using the same solvent system afforded the aziridine (114) (0.13g, 32%) which was identical to that isolated from a subsequent experiment.

**Acetylation of aziridine (114)**

Aziridine (114) (0.255g, 8.70x10$^{-4}$ mol) was stirred overnight at room temperature in a solution of pyridine (0.44g, 5.22x10$^{-3}$ mol) and acetic anhydride (0.177g, 1.74x10$^{-3}$ mol). The reaction mixture was poured into water (10 ml) and extracted with dichloromethane (2x10 ml). The organic extracts were combined and washed successively with hydrochloric acid (2M) and sodium bicarbonate solution, dried (MgSO$_4$) and the solvent removed by evaporation under reduced pressure to yield the acetylated aziridine (115) as colourless crystals (0.166g, 57%) (from ethanol). This aziridine (115) was identical to that isolated from the previous experiment.
Aziridination of styrene using (112) and procedure (3)

The general procedure (3) was followed using the N-aminoquinazolone (112) (0.6g, 3.14x10^{-3} mol), LTA (1.46g, 3.29x10^{-3} mol) and styrene (0.98g, 9.42x10^{-3} mol) in dry dichloromethane (6 ml). Chromatography of the crude oxidation product over silica with ethyl acetate-light petroleum (1:2) as eluant, gave 1-(4-oxo-2-hydroxymethyl-3(4H)-quinazolinyl)-2-phenylaziridine (114) (Rf = 0.52) as colourless crystals (0.44g, 47%), m.p. 112-114°C (from ethanol) (Found: C, 69.25; H, 5.3; N, 14.15. C_{17}H_{15}N_{3}O_{2} requires C, 69.7; H, 5.15; N, 14.3%);

ν_{max} (Nujol): 3150br.m, 1675s, 1600s, 1430s, 1300m, 1240m, 1190w, 1125m, 770s, 725s, 685s and 670m cm^{-1};

$\delta_{H}$ (CDCl$_3$, 300 MHz): 8.15 (ddd, J7.9, 1.3 and 0.6Hz, ArH$_5$), 7.67 (ddd, J8.0, 7.2 and 1.3Hz, ArH$_7$), 7.58 (ddd, J8.0, 1.3 and 0.6Hz, ArH$_8$), 7.4 (ddd, J7.9, 7.2 and 1.3Hz, ArH$_9$), 7.34 (m, 5 x ArH), 4.77 (br.s, CH$_2$OH), 4.3 (m, exch. D$_2$O, CH$_2$OH), 3.96 (dd, J8 and 5.3Hz, azir. ring H-2, cis to quinaz.), 3.45 (dd, J8 and 1.9Hz, azir. ring H-3, trans to Ph and cis to quinaz.) and 2.68 (dd, J5.3 and 1.9Hz, azir. ring H cis to Ph and trans to quinaz.);

$\delta_{C}$ (CDCl$_3$, 75 MHz): 159.7(s), 155.7(s), 144.7(s), 136.1(s), 134(d), 128.5(d), 128.0(d), 126.6(d), 126.3(d), 126.25(d), 126.22(d), 121.2(s), 60.1(t), 44.3(d) and 40.6(t);

M/Z (%): 293(M^+,16), 262(30), 202(100), 186(21), 185(20), 174(26), 172(29), 118(40) and 117(42).
Preparation of N-acetoxyaminoquinazolone (117)

The general procedure (1) was followed using the N-aminoquinazolone (116) (0.25g, 8.89x10^-4 mol), \( \text{LTA} \) (0.414g, 9.34x10^-3 mol) and dry deuterochloroform (2.5 ml). Inspection of the low temperature \(^1\text{H} \) n.m.r. (-40°C) revealed that the major product was N-acetoxyamino-2-benzyloxy-methylquinazolin-4(3H)-one (117), with a characteristic NH signal at \( \delta \) 10.75 in the n.m.r. spectrum. It was evident from the integral value for this NH signal in the n.m.r. spectrum that the N-acetoxyaminoquinazolone (117) was present in only 50% yield. The solution was then allowed to warm to room temperature and worked up in the usual way. Chromatography of the crude reaction product over silica with ethyl acetate-light petroleum (1:2) as eluant, gave the benzoxazinone (295) as a colourless oil (0.028g, 12%) (Found: M+H/Z 268.0976. \( \text{C}_{16}\text{H}_{14}\text{NO}_3 \) requires M+H, 268.0973, a M+H ion was observed under the chemical ionisation conditions used);

\[ \nu_{\max} \text{(Film): } 1755\text{s}, 1605\text{s}, 1415\text{s} \text{ and } 1210\text{s } \text{cm}^{-1}; \]

\( \delta \text{H} \) (CDCl\(_3\), 300 MHz): 8.21 (dd, J8 and 1.5Hz, ArH\(_6\)), 7.83 (ddd, J8.1, 7.4 and 1.5Hz, ArH\(_7\)), 7.68 (d, J8.1Hz, ArH\(_8\)), 7.54 (ddd, J8, 7.4 and 1.2Hz, ArH\(_6\)), 7.45-7.3 (m, 5 x PhH), 4.77 (s, CH\(_2\)) and 4.45 (s, CH\(_2\));

M/Z (%): 268(M+H\(^+\),2), 161(100), 146(25), 133(20), 119(55) and 105(20).
Further elution using the same solvent system afforded 2-benzyloxy-
methylquinazolin-4(3H)-one (296) as a colourless solid (0.144g, 61%), m.p.
167-169°C;
$\delta_H$ (CDCl$_3$, 90 MHz): 9.9 (s, exch. D$_2$O, NH), 8.2 (d, J8Hz, ArH$_5$), 7.7-7.2
(m, ArH$_6$, ArH$_7$, ArH$_8$ and 5 x PhH), 4.6 (s, CH$_2$) and 4.5 (s, CH$_2$).

Aziridination of styrene using N-aminoquinazolone (116) and procedure (3)

The general procedure (3) was followed using the N-aminoquinazolone
(116) (0.155g, 5.51x10^{-3} mol), LTA (0.257g, 5.79x10^{-4} mol) and styrene
(0.086g, 8.27x10^{-4} mol) in dry dichloromethane (1.5 ml). Crystallisation
of the crude reaction product gave 1-(4-oxo-2-benzyloxymethyl-3(4H)-quin-
azolinyl)-2-phenylaziridine (118) which was isolated as colourless crystals
(0.149g, 71%), m.p. 103-105°C (from ethanol) (Found: C, 75.05; H, 5.65; N,
10.9. C$_{24}$H$_{21}$N$_3$O$_2$ requires C, 75.15; H, 5.5; N, 10.95%);
$\nu_{max}$ (Nujol): 1665s, 1595s, 1450s, 1290s, 1230m, 1135m, 1100m, 1020m, 890m,
770m, 740s and 690m cm$^{-1}$;
$\delta_H$ (CDCl$_3$, 300 MHz): 8.23 (ddd, J7.9, 1.2 and 0.5Hz, ArH$_5$), 7.75 (ddd, J8,
1.3 and 0.5Hz, ArH$_6$), 7.73 (ddd, J8, 8 and 1.2Hz, ArH$_7$), 7.47 (ddd, J7.9, 8
and 1.3Hz, ArH$_8$), 7.4-7.2 (m, 10 x ArH), 4.76 (s, CH$_2$), 4.65 (s, CH$_2$), 3.88
(dd, J8 and 5Hz, azir. ring H-2 cis to quinaz.), 3.35 (dd, J8 and 2Hz,
azir. ring H-3 trans to Ph and cis to quinaz.) and 2.75 (ddd, J5 and 2Hz, azir. ring H-3 cis to Ph and trans to quinaz.);

M/Z (%): 383(M+,13), 293(49), 292(100), 277(95), 262(52), 235(23), 187(33), 186(92), 175(57), 160(90), 145(22), 144(22), 132(28), 129(18), 120(32), 119(74), 117(78), 116(95), 105(27), 104(32), 103(22) and 102(37).

Aziridination of styrene using N-aminoquinazolone (116) and procedure (2)

The general procedure (2) was followed using the N-aminoquinazolone (116) (0.2g, 7.11x10^{-4} mol), LTA (0.332g, 7.47x10^{-4} mol) and styrene (0.22g, 2.13x10^{-3} mol) in dry dichloromethane (2 ml). Chromatography of the crude reaction product over silica with ethyl acetate-light petroleum (1:2) as eluant, gave the aziridine (118) as colourless crystals (53%) which was identical in all respects to that isolated from the previous experiment. Further elution using the same solvent gave the de-aminated quinazolone (296) in 28% yield.

Preparation of N-aminophthalimide (15)

![Chemical Structure]

N-aminophthalimide was prepared by the method of Drew and Hatt in 52% yield from hydrazine hydrate and phthalimide. The crude material was
crystallised from acetonitrile, m.p. 196-200°C (decomp.) (lit.**14** 200-205°C).

Evidence for N-acetoxyaminophthalimide as an intermediate: oxidation of N-aminophthalimide with LTA at low temperature followed by addition (aziridination) of styrene

To a rapidly stirred suspension of N-aminophthalimide (0.3g, 1.85x10^-3 mol) in dry dichloromethane (5 ml) at -60°C (dry ice-acetone) was added under nitrogen a solution of LTA (0.863g, 1.94x10^-3 mol) dissolved in dry dichloromethane (35 ml) over 3h.

After the reaction had been stirred for a further 30 min. the precipitated lead di-acetate was separated off and styrene (0.577g, 5.55x10^-3 mol) was added to the filtrate; all operations were carried out at <-50°C.

The filtrate was then allowed to warm to ambient temperature with stirring, washed successively with aqueous sodium hydrogen carbonate and water, dried (MgSO_4) and evaporated under reduced pressure. Rapid chromatography on silica using ethyl acetate-light petroleum (1:2) as eluant, gave the aziridine (37)\(^{17}\) as colourless crystals (41%) (from dichloromethane-light petroleum), m.p. 150-153°C (lit.\(^{17}\) m.p. 152°C).

Competitive aziridination of methyl methacrylate and \(\alpha\)-methylene-\(\gamma\)-butyrolactone using NAP (15)

\[
\text{Phthal} \quad \text{Phthal} \\
\begin{array}{c}
\text{N} \\
\text{O} \\
\text{O}
\end{array} \\
(120) \\
\begin{array}{c}
\text{N} \\
\text{O} \\
\text{CO}_2\text{CH}_3
\end{array} \\
(121)
\]

Powdered N-aminophthalimide (15) (0.1g, 6.17x10^-4 mol) and lead tetra-
acetate (0.28g, 6.48x10^{-4} mol) were added alternately and in very small portions over 15 min. to a stirred solution of dry dichloromethane (1 ml), containing equimolar amounts of methyl methacrylate (0.123g, 1.23x10^{-3} mol) and α-methylene-γ-butyrolactone (0.121g, 1.23x10^{-3} mol) at room temperature. Work-up was carried out as detailed in the general procedure (3). The 300 MHz n.m.r. spectrum of the crude product revealed that the aziridines (120) and (121) were formed in a 2:1 ratio respectively from comparison of the integration values of the signals at δ 3.36^a and δ 3.19. No attempt at isolation of the aziridines was made: both have been previously characterised.

Competitive aziridination of methyl methacrylate and α-methylene-γ-butyrolactone using NAQ (77)

See experimental relating to Chapter 6.

Competitive aziridination of styrene and methyl acrylate using oxidative (LTA) addition of N-aminophthalimide

\[
\text{Phtal} \quad \text{Phtal}
\]

(37) \quad (36)

Powdered N-aminophthalimide (0.15g, 9.25x10^{-4} mol) and acetic acid-free lead tetra-acetate (0.432g, 9.72x10^{-4} mol) were added alternately and continuously in very small portions over 15 min. to a vigorously stirred solution of dry dichloromethane (1.5 ml) containing styrene (0.288g,
2.77x10^{-3} \text{ mol}) and methyl acrylate (0.239g, 2.77x10^{-3} \text{ mol}) at room temperature. The mixture was then stirred for a further 30 min. at room temperature. The insoluble lead di-acetate was then separated and washed with dichloromethane and the total filtrate washed successively with sodium bicarbonate solution and water, dried with magnesium sulphate and the solvent removed by evaporation under reduced pressure.

Examination of the $^1$H n.m.r. spectrum of the crude product revealed the presence of the aziridines (37) and (36) from comparison with the spectra of authentic samples. From integration of the signals at $\delta$ 3.6 (37) and $\delta$ 3.19 (36) the ratio of these aziridines (37) and (36) was ca. 10:1 respectively.

Competitive aziridination of styrene and methyl acrylate using NAQ and procedure (2)

\[
\begin{align*}
\text{Q} & \text{N} & \text{Ph} \\
(86) \\
\text{Q} & \text{N} & \text{CO}_2\text{Me} \\
(89)
\end{align*}
\]

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.2g, 1.057x10^{-3} \text{ mol}), LTA (0.493g, 1.11x10^{-3} \text{ mol}) in dry dichloromethane (2 ml). Styrene (0.33g, 3.17x10^{-3} \text{ mol}) and methyl acrylate (0.273g, 3.17x10^{-3} \text{ mol}) were added together.

Examination of the $^1$H n.m.r. spectrum of the crude reaction product revealed the presence of the aziridines (86) and (89) which were identified by comparison with spectra of authentic samples. From integration of the signals at $\delta$ 3.69 (86) and $\delta$ 3.65 (89) the ratio of (86) and (89) was 9:1 respectively.
Competitive aziridination of styrene and methyl acrylate at room temperature

When the previous reaction was repeated at room temperature using the general procedure (3) the ratio of aziridines (86) and (89) was 12:1 respectively, as similarly measured by high-field n.m.r. spectroscopy.

Preparation of 2-acetylbenzofuran (123)

2-Acetylbenzofuran was prepared\textsuperscript{146} from salicylaldehyde and chloroacetone. Recrystallisation of the crude product from ethanol gave 2-acetylbenzofuran (5.23g, 72%) as a colourless solid, m.p. 70-72°C (lit.\textsuperscript{147} m.p. 87°C).

Aziridination of 2-acetylbenzofuran by oxidative (LTA) addition of N-aminophthalimide

![Diagram](33)

2-Acetylbenzofuran (4.72g, 2.95x10\textsuperscript{-2} mol) was dissolved in CH\textsubscript{2}Cl\textsubscript{2} (50 ml) and N-aminophthalimide (3.68g, 2.27x10\textsuperscript{-2} mol) and lead tetra-acetate (10.5g, 2.36x10\textsuperscript{-2} moles) were added in portions over 1h with stirring. After the addition was complete the reaction mixture was stirred for a further 20 min. and the lead di-acetate filtered off. The filtrate was then washed with saturated sodium bicarbonate solution (2x60 ml), water (2x50 ml), dried (MgSO\textsubscript{4}) and evaporated to yield a pale yellow solid. The product (33) was crystallised from ethyl acetate-light petroleum, m.p. 135-139°C (lit.\textsuperscript{26} m.p. 136-140°C);
$\nu_{\text{max}}$ (Nujol): 3070\,m, 1720\,s, 1245\,s, 1145\,s, 1115\,s, 1095\,s, 990\,m, 970\,m, 900\,m, 780\,m, 770\,m, 750\,m, 705\,s and 650\,s cm$^{-1}$;

$\delta_H$ (CDCl$_3$, 90 MHz): 7.6-6.6 (m, 8 x ArH, major and minor invertomers), 5.23 (s, azir. ring H, major invertomer), 5.0 (s, azir. ring H, major invertomer), 2.63 (s, COCH$_3$, minor invertomer), 2.53 (s, COCH$_3$, major invertomer). The ratio of invertomers at room temperature is 3:1.

The decomposition of aziridine (33) in the presence of equimolar amounts of styrene and methyl acrylate at 80°C

Aziridine (33) (0.1g, 3.12x10$^{-4}$ mol) was heated under reflux in the presence of styrene (0.097g, 9.36x10$^{-4}$ mol) and methyl acrylate (0.081g, 9.36x10$^{-4}$ mol) for 5h in dry benzene (3 ml) at 80°C. The reaction mixture was then allowed to cool to room temperature and the solvent was removed by evaporation under reduced pressure.

Examination of the crude reaction product by 300 MHz n.m.r. showed the two aziridines (37) and (36) to be present in a 1:3 ratio respectively from integration of signals at $\delta$ 3.6 (37) and $\delta$ 3.19 (36).

Competitive aziridination of styrene and methyl acrylate by oxidative (LTA) addition of N-aminophthalimide at 80°C

Solid N-aminophthalimide (15) (0.25g, 1.52x10$^{-3}$ mol) and LTA (0.71g, 1.6x10$^{-3}$ mol) were intimately mixed and added in very small portions over 10 min. to a refluxing solution of dry benzene (3 ml) containing styrene (0.475g, 4.57x10$^{-3}$ mol) and methyl acrylate (0.393g, 4.57x10$^{-3}$ mol). The reaction mixture was refluxed for a further 10 min. and was then allowed to cool to room temperature. The lead di-acetate was filtered off and the
filtrate was diluted with dichloromethane (10 ml), washed with sodium bicarbonate solution, dried with magnesium sulphate and the solvent removed by evaporation under reduced pressure. Examination of the 300 MHz n.m.r. spectrum of the crude reaction product showed the two aziridines (37) and (36) to be present in a 1.5:1 ratio respectively. In control experiments a benzene solution of aziridines (37) and (36) in a 1:1 ratio was heated with and without the presence of 2 mole equivalents of acetic acid. In both cases, no change in ratio was detected by $^1$H n.m.r. examination of the product after the same work-up described above.

Preparation of 2-[^2H$_3$]acetylbenezofuran (125)

2-Acetylbenezofuran (1g, 6.25x10$^{-3}$ mol) was placed in a dry 100 ml 2-necked flask under nitrogen, dry THF (20 ml) was added and the solution magnetically stirred at room temperature. When the 2-acetylbenezofuran had dissolved, D$_2$O (20 ml) into which a very small pellet of sodium (~10 mg) had been dissolved was added and the solution was stirred at room temperature for 1h. The crude reaction mixture was then poured into D$_2$O (10 ml) and the aqueous solution was extracted with dichloromethane (2x30 ml). The combined organic extracts were dried with magnesium sulphate and the solvent removed by evaporation under reduced pressure to give 2-[^2H$_3$]-acetylbenezofuran (125) as yellow crystals (0.74g, 73%), m.p. 76-78°C (from ethanol);

$\nu_{\text{max}}$ (Nujol): 3120m, 1665s, 1610s, 1550s, 1445m, 1330s, 1175s, 1115m, 1005s, 920m, 885m, 865m, 847m, 760m and 750s cm$^{-1}$;

$\delta_{H}$ (CDCl$_3$, 90 MHz): 7.7-7.2 (m, 5 x H);

M/Z (%): 163(M$^+$,44), 145(100), 89(45) and 63(19).
Aziridination of 2-[\textsuperscript{2}H\textsubscript{3}]acetylbenzofuran by oxidative (LTA) addition of NAP

![Chemical Structure](image)

(124)

Powdered N-aminophthalimide (15) (0.478g, 2.95x10\textsuperscript{-3} mol) and acetic acid-free lead tetra-acetate (1.37g, 3.09x10\textsuperscript{-3} mol) were intimately mixed and added alternately and continuously in very small portions over 15 min. to a vigorously stirred solution of dry dichloromethane (5 ml) and 2-[\textsuperscript{2}H\textsubscript{3}]acetylbenzofuran (125) (0.53g, 3.24x10\textsuperscript{-3} mol) at room temperature. The mixture was then stirred for a further 30 min., the insoluble lead di-acetate was separated off and washed with dichloromethane and the total filtrate washed successively with sodium bicarbonate solution and water, dried with magnesium sulphate and the solvent removed by evaporation under reduced pressure. Crystallisation of the crude reaction product from ethyl acetate-light petroleum gave the aziridine (124) (0.58g, 61%), m.p. 132-136°C;

\(\nu_{\text{max}}\) (Nujol): 1723s cm\textsuperscript{-1};

\(\delta_{H}\) (CDCl\textsubscript{3}, 90 MHz): 7.7-6.7 (m, ArH, major and minor invertomers), 5.3(s, azir. ring H, minor invertomer) and 5.05 (s, azir. ring H, major invertomer).

This aziridine exists as a 3:1 ratio of invertomers at room temperature.

M/Z (%): 323(M\textsuperscript{+},56), 279(100), 277(21), 163(18), 147(10), 145(37), 133(29), 132(25), 131(20), 130(16), 105(17), 104(75), 103(28) and 102(13).
Thermolysis of the aziridine (124) in the presence of 2-acetylbenzofuran

The deuterium labelled aziridine (124) (0.05g, 1.54x10^{-4} mol) and 2-acetylbenzofuran (0.024g, 1.54x10^{-4} mol) were dissolved in dry d_6-benzene (0.75 ml) and the decomposition of aziridine (124) was monitored at 80°C by 1H n.m.r. by integration of the aziridine ring proton at δ 4.62 (major invertomer).

When 50% of the starting material (124) had disappeared the complete 1H n.m.r. spectrum was recorded and showed only the aziridines (124) and (33) to be present in a 1:1 ratio. The formation of aziridine (33) was supported by the appearance of 2 signals at δ 2.37 and δ 2.53 which correspond to the acetyl methyl groups in the minor and major invertomers respectively of aziridine (33).

Competitive aziridination of 2-acetylbenzofuran and methyl acrylate by thermolysis of aziridine (124)

Aziridine (124) (0.05g, 1.54x10^{-4} mol) and 2-acetylbenzofuran (0.024g, 1.54x10^{-4} mol) were dissolved in dry d_6-benzene (0.75 ml). To this solution was added methyl acrylate (0.053g, 6.19x10^{-4} mol, 4 mol equiv.) and the disappearance of the aziridine (124) at 80°C was monitored by 1H n.m.r. as described previously.

After 50% of the starting material had disappeared the complete 1H n.m.r. spectrum was recorded and showed aziridines (36) and (33) to be present in a 1:2.5 ratio respectively. From this it is clear that (124) brings about the aziridination of 2-acetylbenzofuran at a rate at least 10 times faster than aziridination of methyl acrylate allowing for the different concentrations of alkene used.
Preparation of pyruvoyl chloride

This was prepared\textsuperscript{148} by the treatment of pyruvic acid with \(\alpha,\alpha\)-dichloromethyl methyl ether. Final distillation of the product, b.p. 52-55\(^\circ\)C at 100 mmHg (lit.\textsuperscript{148} b.p. 43-45\(^\circ\)C at 120 mmHg), gave a 40% yield of the pure pyruvoyl chloride.

Preparation of 2-acetyl-5-nitrobenzofuran (128)

Details of this experiment are given because the original reference\textsuperscript{149} does not report the use of a base in this reaction.

To a suspension of 2-hydroxy-5-nitrobenzyl triphenylphosphoniumchloride (10g, 0.022 moles)\textsuperscript{149} and triethylamine (4.49g, 0.044 moles), in refluxing xylene (100 mls) was added dropwise pyruvoyl chloride (2.83g, 0.026 moles) and the reaction was refluxed for a further 30 min. The crude reaction mixture was then filtered while hot and the filtrate was cooled and evaporated to dryness by removal of the solvent under reduced pressure. Chromatography over silica, with ethyl acetate-light petroleum (1:2) as eluant, gave the 2-acetyl-5-nitrobenzofuran (128) as yellow crystals (1.16g, 26%), m.p. 168-171\(^\circ\)C (from ethanol) (lit.\textsuperscript{149} m.p. 170\(^\circ\)C).

Aziridination of 2-acetyl-5-nitrobenzofuran (128) by oxidative (LTA) addition of NAP

![Diagram of N-aminophthalimide](image)

(129)

Powdered \(\text{N-aminophthalimide (15)}\) (0.327g, 2.01\times10^{-3} \text{mol}) and acetic
acid-free lead tetra-acetate (0.941g, 2.12x10^{-3} mol) were mixed and added alternately and continuously in very small portions over 15 min. to a vigorously stirred solution of dry dichloromethane (3 ml) and 2-acetyl-5-nitrobenzofuran (128) (0.620g, 3.027x10^{-3} mol) at room temperature. The mixture was then stirred for a further 30 min. at room temperature, the insoluble lead di-acetate was separated off and washed with dichloromethane and the total filtrate washed successively with sodium bicarbonate solution and water, dried with magnesium sulphate and the solvent removed by evaporation under reduced pressure. Direct crystallisation of the crude oxidation product from ethyl acetate-light petroleum gave the aziridine (129) (0.405g, 55%), m.p. 160-162°C (from ethyl acetate-light petroleum) (Found: M+1/Z, 366.0742. C_{16}H_{11}N_{3}O_{6} requires M+1, 366.0726 (FAB resulting in a (M+1) molecular ion);

ν_{max} (Nujol): 1730s, 1530s, 1350s, 1255s, 1140s, 1100m, 1070m, 935m, 795m, 710s and 690s cm^{-1};

\( \delta_{H} (CDCl_{3}, 300 MHz, major invertomer): 8.55 (d, J2.4Hz, ArH_{4}), 8.17 (dd, J9 and 2.4Hz, ArH_{5}), 7.65 (m, 4 \times ArH), 7.02 (d, J9Hz, ArH_{7}), 5.15 (s, azir. ring H cis to COCH_{3}) \) and 2.61 (s, COCH_{3});

\( \delta_{H} (CDCl_{3}, 300 MHz, minor invertomer): 8.6 (d, J2.4Hz, ArH_{4}), 8.33 (dd, J9 and 2.4Hz, ArH_{5}), 7.76 (m, 4 \times ArH), 7.2 (d, J9Hz, ArH_{7}), 5.39 (s, azir. ring H cis to COCH_{3}) \) and 2.75 (s, COCH_{3}).

This aziridine exists as a 4:1 ratio of invertomers at room temperature.

M/Z (%): 365(M^{+},1), 323(54), 205(74), 190(72), 147(14), 144(12), 104(28), 86(60), 84(100) and 76(25).
Competitive aziridination of styrene and methyl acrylate using thermolysis of aziridine (129)

Aziridine (129) (0.1g, 2.73x10^{-4} mol) was heated under reflux in the presence of styrene (0.085g, 8.21x10^{-4} mol) and methyl acrylate (0.07g, 8.21x10^{-4} mol) for 5h in dry benzene (3 ml) at 80°C. The reaction mixture was then allowed to cool to room temperature and the solvent was removed by evaporation under reduced pressure.

Examination of the crude reaction product by 300 MHz n.m.r. showed the two aziridines (37) and (36) to be present in a 1:3 ratio respectively from integration of peaks at δ 3.6 (37) and δ 3.19 (36) as before.

Preparation of N-trimethylsilylaminophthalimide (133)

\[
\begin{align*}
\text{N-aminophthalimide (15) (5g, 0.0308 mol) was suspended in dichloromethane (80 ml) containing triethylamine (4.73 ml, 0.0339 mol) and stirred at room temperature. Trimethylsilylchloride (4.3 ml, 0.0339 mol) was added over a 10 min. period and the mixture stirred overnight; it was then filtered to remove unchanged N-aminophthalimide, dried with magnesium sulphate and the solvent removed by evaporation under reduced pressure to give N-trimethylsilylaminophthalimide (133) as a light yellow oil (6.18g, 84%);}
\end{align*}
\]

\[\nu_{\text{max}}\text{ (Film): 3350br.m, 1720s, 1465w, 1250m, 1220m, 1110m, 1025m, 1000m,}\]
Oxidation of N-trimethylsilylaminophthalimide (133) with lead tetra-acetate at low temperature (−50°C) in the presence of methyl acrylate

N-trimethylsilylaminophthalimide (133) (0.13g, 5.55x10⁻⁴ mol) was dissolved in dichloromethane (5 ml), LTA (0.259g, 5.83x10⁻⁴ mol) was also dissolved in dichloromethane (5 ml) and both solutions were added at the same rate over 20 min. from separate dropping funnels to a stirred solution of dichloromethane (1 ml) containing methyl acrylate (0.143g, 1.66x10⁻³ mol) at -50°C. After stirring for a further 10 min. the reaction was warmed to ambient temperature and worked-up according to general procedure (3). Chromatography of the crude oxidation product over silica, with ethyl acetate-light petroleum (1:1) as eluant, afforded the N-methylaminophthalimide (134) as colourless crystals (0.045g, 46%), m.p. 210-213°C (from ethanol);

$\nu_{\text{max}}$ (Nujol): 3290m, 1700s, 1255s, 1080s, 880, 785s and 710s cm⁻¹;

$\delta_H$ (CDCl₃, 90 MHz): 7.7 (m, 4 x ArH), 4.55 (q, J=6Hz, exch. D₂O, NH) and 2.8 (d, J=6Hz, HNCH₃);
M/Z (%): 176(M⁺, 29), 149(11), 148(79), 147(27), 131(11), 130(100), 105(56), 104(68) and 102(13).

Oxidation of N-aminophthalimide with lead tetra-benzoate at room temperature in the presence of styrene

Powdered N-aminophthalimide (15) (0.1g, 6.17x10⁻⁴ mol) and lead tetra-benzoate (0.449g, 6.48x10⁻⁴ mol) were added alternately and in very small portions over 15 min. to a stirred solution of dichloromethane (1 ml), containing styrene (0.192g, 1.85x10⁻³ mol) at room temperature. Work-up was as outlined in the general procedure (3) and crystallisation of the crude oxidation product from dichloromethane-light petroleum gave the aziridine (37) in 47% yield, m.p. 150-153°C (lit. 152°C).

Preparation of N-benzoyloxyamino-2-ethylquinazolin-4(3H)-one in solution

\[
\begin{align*}
\text{N} & \quad \text{N} \\
\text{H} & \quad \text{OCOPh}
\end{align*}
\]

(136)

The general procedure (1) was followed using the N-aminquinazolone (77) (0.1g, 5.28x10⁻⁴ mol), lead tetra-benzoate (0.383g, 5.55x10⁻⁴ mol) in place of LTA, and dry deuterochloroform (1 ml). Examination of the low temperature \(^1\)H n.m.r. (-30°C) revealed the major product besides lead
di-benzoate and benzoic acid to be the N-benzoyloxyamino-2-ethylquinazolin-4(3H)-one (136);

$\delta_H$ (CDCl$_3$, 300 MHz, -30°C): 11.32 (s, NH), 8.22 (d, J8Hz, ArH$_6$), 7.0-8.0 (m, ArH$_6$, ArH$_7$, ArH$_8$ and 5 x PhH), 3.25 (dq, J15 and 6.8Hz, HCHCH$_3$), 3.17 (dq, J15 and 6.8Hz, HCHCH$_3$) and 1.47 (t, J6.8Hz, CH$_2$CH$_3$).

The signals at 8.00-7.00 ppm are obscured by benzoic acid and lead di-benzoate resonances.
EXPERIMENTAL
Chapter 3
Aziridination of geraniol

\[
{\text{Q}} \quad N \quad \begin{array}{c}
\text{Me} \\
\text{Me} \\
\text{Me}
\end{array}
\quad \begin{array}{c}
\text{OH}
\end{array}
\quad \begin{array}{c}
\text{Q} \\
\text{Me}
\end{array}
\quad \begin{array}{c}
\text{Me} \\
\text{Me}
\end{array}
\quad \begin{array}{c}
\text{OH}
\end{array}
\quad \begin{array}{c}
\text{Q}
\end{array}
\]

(137)  
(138)

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.5g, 2.64x10^{-3} mol), LTA (1.23g, 2.77x10^{-3} mol) and geraniol (1.22g, 7.93x10^{-3} mol) in dry dichloromethane (5 ml). Chromatography of the crude oxidation product over silica with ethyl acetate-light petroleum (1:2) as eluant, gave the aziridine (137) (Rf = 0.45) as colourless crystals (0.7g, 78%), m.p. 128-130°C (from ethanol) (Found: C, 70.45; H, 7.95; N, 12.3.

\[
C_{20}H_{27}N_{3}O_{2}
\]

requires C, 70.35; H, 7.95; N, 12.3%);

\[\nu_{\text{max}}\text{ (Nujol): 3400br.s, 1670s, 1595s, 1335s, 1210s, 1000s, 770s, 735s and 695s cm}^{-1};\]

\[\delta_{\text{H}}\text{ (CDCl}_{3}\text{, 300 MHz, (137)): 8.16 (ddd, J8.0, 1.6 and 0.6Hz, ArH}_{5}\text{), 7.70 (ddd, J8.1, 7.3 and 1.6Hz, ArH}_{7}\text{), 7.64 (ddd, J8.1, 1.4 and 0.6Hz, ArH}_{8}\text{), 7.42 (ddd, J8.0, 7.3 and 1.4Hz, ArH}_{6}\text{), 4.92 (m, CH}_{2}\text{CH=C(CH}_{3}\text{)_{2}}\text{), 4.58 (br.s, exch. D}_{2}\text{O, OH), 4.04 (ddd, J10.5, 6 and 3Hz, HCHOH), 3.75 (m, HCHOH), 3.09 (dq, J16 and 7.5Hz, HCHCH}_{3}\text{), 3.02 (dd, J9 and 3Hz, azir. ring H), 2.79 (dq, J16 and 7.5Hz, HCHCH}_{3}\text{), 2.19 (m, HCHCH=CHC=Me}_{2}\text{), 1.99 (m, HCHCH=CHC=Me}_{2}\text{), 1.72 (ddd, J12, 9 and 4.5Hz, HCHCH=CHC=Me}_{2}\text{), 1.63 (s, CH}_{3}\text{), 1.54 (s, CH}_{3}\text{), 1.46 (s, CH}_{3}\text{), 1.4 (t, J7Hz, CH}_{2}\text{CH}_{3}\text{) and 0.85 (ddd, J12, 9 and 6Hz, HCHCH=CHC=Me}_{2}\text{);}\]

\[\delta_{\text{C}}\text{ (CDCl}_{3}\text{, 75 MHz): 161(s), 157.7(s), 145.8(s), 134.9(d), 133(d), 126.9(d), 126.2(s), 126.1(d), 122.2(d), 120.9(s), 61.6(t), 54.5(d), 54.3(s), 34.6(t), 27.7(t), 25.7(q), 25.4(t), 17.7(q), 17.7(q) and 10.7(q);}\]

\[\text{M/Z (%): 341 (M}^{+},1), 310(16), 242(70), 229(21), 200(90), 175(95),\]

-181-
Further elution with ethyl acetate-light petroleum (1:2) yielded the aziridine (138) \((R_f = 0.38)\) as a colourless oil (0.063g, 7%); 
\[\nu_{\text{max}}^\text{(Nujol): 3400m, 1675s, 1595s, 1470m, 1220m, 1100w, 1010w and 770m cm}^{-1};\]
\[\delta H (CDCl_3, 300 MHz, (138)): 8.16 (ddd, J8.1, 1.6 and 0.6Hz, ArH_8), 7.67 (ddd, J8.1, 7.2 and 1.6Hz, ArH_7), 7.62 (ddd, J8.1, 1.4 and 0.6Hz, ArH_6), 7.40 (ddd, J8.1, 7.2 and 1.4Hz, ArH_5), 5.49 (m, CHCH_2OH), 4.18 (d, J7Hz, CH_2OH), 3.08 (dq, J16 and 7Hz, HCHCH_3), 2.87 (m, azir. ring H), 2.76 (dq, J16 and 7Hz, HCHCH_3), 2.30 (m, CH_2CH_2), 1.76 (s, CH_3=CHCH_2OH), 1.59 (m, HCHCH_2), 1.42 (s, azir. ring CH_3, trans to quinaz.), 1.40 (t, J7Hz, CH_2CH_3), 1.14 (s, azir. ring CH_3, cis to quinaz.) and 0.87 (m, HCHCH_2).\]

Examination of the 300 MHz \(^1\)H n.m.r. spectrum of the crude aziridination product showed aziridines (137) and (138) to be present in greater than 10:1 ratio respectively from integration of the signals at \(\delta 4.92\) and \(\delta 5.49\).

**Aziridination of geraniol using oxidative (LTA) addition of NAP (15)**

![](image.png)

Powdered \(N\)-aminophthalimide (15) (0.25g, 1.54\times10^{-3} \text{ mol}) and LTA (0.719g, 1.62\times10^{-3} \text{ mol}) were added alternately and in very small portions over 15 min. to a stirred solution of dry dichloromethane (2.5 ml),
containing geraniol (0.714g, 4.62x10^-3 mol) at room temperature. After working-up as described in the general procedure (3), purification of the crude oxidation product by chromatography with ethyl acetate-light petroleum (1:2) as eluant, gave the aziridine (139) (R_f = 0.44) as a colourless oil (0.295g, 61%) (Found: M/Z 314.1613. C_{18}H_{22}N_{2}O_{3} requires M, 314.1630);

\[ \nu_{\text{max}} \text{ (Film): } 3460\text{br.m, 1710s, 1465m, 1375m, 1185m, 1150m, 1080w, 1040m, 985w, 890w, 785w and 705m cm}^{-1}; \]

\[ \delta_{H} \text{ (CDCl}_3, 300 \text{ MHz): } 7.82-7.63 \text{ (m, 4 x ArH), 5.02 (m, CH=CMe}_2\text{), 3.95 (dd, J12 and 3.5Hz, HCHOH), 3.70 (dd, J12 and 9Hz, HCHOH), 3.48 (br.s, exch. D}_2\text{O, OH), 2.75 (dd, J9 and 3.5Hz, azir. ring H), 2.3-1.9 (m, HCHCH}_2\text{), 1.65 (s, CH=C(CH}_3\text{)} \text{CH}_3\text{), 1.57 (s, CH=C(CH}_3\text{)} \text{CH}_3\text{), 1.4 (s, CH}_3\text{) and 1.12 (m, HCHCH}_2\text{); } \]

\[ M/Z \text{ (M): } 314(M^+,2), 296(2), 283(34), 215(14), 203(11), 202(30), 163(19), 162(95), 153(10), 148(41), 147(30), 136(32), 134(15), 132(12), 130(40), 122(17), 121(66), 119(26), 109(19), 107(16), 105(42) \text{ and 104(71).} \]

Further elution with ethyl acetate-light petroleum (1:2) yielded aziridine (140) (R_f = 0.22) as a colourless oil (0.053g, 11%) (Found: M/Z 314.1625. C_{18}H_{22}N_{2}O_{3} requires M, 314.1630);

\[ \nu_{\text{max}} \text{ (Film): } 3400\text{br.m, 2920m, 1710s, 1465w, 1375m, 1145w, 890w, 790w and 710m cm}^{-1}; \]

\[ \delta_{H} \text{ (CDCl}_3, 300 \text{ MHz): } 7.9-7.7 \text{ (m, 4 x ArH), 5.5 (m, CHCH}_2\text{OH), 4.18 (d, J7Hz, CH}_2\text{OH), 2.78 (t, J6.5Hz, azir. ring H), 2.33 (m, CH}_2\text{CH}_2\text{), 1.96 (m, HCHCH}_2\text{), 1.74 (s, CH}_3\text{C=CH), 1.66 (m, HCHCH}_2\text{), 1.40 (s, azir. ring CH}_3\text{, trans to quinaz.) and 1.28 (s, azir. ring CH}_3\text{, cis to quinaz.)}. \]

The 300 MHz ^1H n.m.r. spectrum of the crude aziridination product showed aziridines (139) and (140) to be present in a 6:1 ratio respectively from integration of the signals at 85.02 and 85.5.
Preparation of geranyl chloride

A dry, 250 ml, three-necked flask was equipped with a magnetic stirring bar and reflux condenser (to which was attached a calcium chloride drying tube) and charged with carbon tetrachloride (90 ml) and geraniol (15.42g, 0.1 mol). To this solution was added triphenylphosphine (34.09g, 0.13 mol) and the reaction mixture was refluxed with stirring for 1h. The mixture was then allowed to cool to room temperature, dry light-petroleum (100 ml) was added and stirring was continued for a further 5 min. The precipitated triphenylphosphine oxide was filtered and washed with 50 ml of light petroleum. The solvent was then removed from the combined filtrates by evaporation under reduced pressure. Distillation of the resultant oil afforded geranyl chloride (70%) (b.p. 45-50°C at 1 mmHg) (lit.150 b.p. 47-49°C at 0.4 mmHg);

\[ \nu_{\text{max}} \text{ (Film): 1660m, 1445s, 1380m, 1253s and 840m cm}^{-1}; \]

\[ \delta_H (\text{CDCl}_3, 90 \text{ MHz}): 5.39 \text{ (m, CH}_2\text{Cl)}, 5.02 \text{ (m, CH}=\text{CH}_2\text{)}, 3.98 \text{ (d, J8Hz, CH}_2\text{Cl)}, 2.05 \text{ (m, CH}_2\text{CH}_2\text{)}, 1.71 \text{ (d, J1.4Hz, C=C(CH}_3\text{)CH}_2\text{)}, 1.67 \text{ (s, C=C(CH}_3\text{)CH}_3\text{)} \text{ and 1.61 (s, C}=\text{C(CH}_3\text{)CH}_3\text{).} \]

Aziridination of geranyl chloride

The general procedure (2) was followed using the N-aminoquinazalone (77) (0.5g, 2.64x10^{-3} mol), LTA (1.23g, 2.77x10^{-3} mol) and geranyl chloride...
(1.37g, 7.93×10^{-3} \text{ mol}) \text{ in dry dichloromethane (5 ml)}. A 300 MHz \textsuperscript{1}H n.m.r. spectrum of the crude aziridination product revealed a 6:1 ratio of the respective aziridines (141) and (142). Chromatography of this mixture over silica, with ethyl acetate-light petroleum (1:3) as eluant, gave the aziridine (142) (R_f = 0.35) as a colourless oil (0.077g, 8.1%) (Found: M/Z 359.1759. \text{C}_{20}\text{H}_{26}\text{N}_3\text{OCl requires M, 359.1764});

ν_{max} (Film): 1680s, 1590s, 1380m, 1285m, 1220m, 1160w, 1110w, 930w, 800w, 770s, 690m and 645m cm^{-1};

ν_{max} (CDCl_{3}, 300 MHz): 8.17 (ddd, J7.9, 1.3 and 0.55Hz, ArH_{5}), 7.69 (ddd, J8, 7.2 and 1.3Hz, ArH_{7}), 7.63 (ddd, J8, 1.3 and 0.55Hz, ArH_{6}), 7.42 (ddd, J7.9, 7.2 and 1.3Hz, ArH_{8}), 4.97 (m, CH=CH_{2}), 4.5 (dd, J10.5 and 3.6Hz, HCHCl), 3.34 (t, J10.5Hz, azir. ring H), 3.23 (dd, J10.5 and 3.36Hz, HCHCl), 3.02 (dq, J16 and 7.5Hz, HCHCH_{3}), 2.75 (dq, J16 and 7.5Hz, HCHCH_{3}), 2.22 (m, HCHCH_{2}), 2.05 (m, HCHCH_{2}), 1.6 (s, C=C(CH_{3})CH_{3}), 1.55 (s, C=C(CH_{3})CH_{3}), 1.52 (s, azir. ring CH_{3}), 1.39 (t, J7.5Hz, CH\textsubscript{2}CH_{3} obscuring CH_{2}HCH) and 0.85 (m, CH\textsubscript{2}HCH);

M/Z (%): 359(M^{+}, 1), 324(17), 242(73), 200(30), 186(30), 175(50), 174(76), 173(65), 150(100), 146(13), 134(26), 131(24), 130(39) and 119(27). Further elution with ethyl acetate-light petroleum (1:3) gave the aziridine (141) (R_f = 0.17) as colourless crystals (0.54g, 57%), m.p. 74-76^\circ C \text{ (from ethanol)} \text{ (Found: C, 66.95; H, 7.35; N, 11.7; Cl, 9.75. \text{C}_{20}\text{H}_{26}\text{N}_3\text{OCl requires C, 66.75; H, 7.3; N, 11.65; Cl, 9.85%});}

ν_{max} (Nujol): 1670s, 1595s, 1335s, 1280s, 1220s, 1165s, 1105s, 925s, 800m, 770s, 735s, 690s and 650s cm^{-1};

ν_{max} (CDCl_{3}, 300 MHz): 8.17 (ddd, J8, 1.4 and 0.6Hz, ArH_{5}), 7.68 (ddd, J8.1, 7.4 and 1.4Hz, ArH_{7}), 7.62 (ddd, J8.1, 1.3 and 0.6Hz, ArH_{6}), 7.40 (ddd, J8, 7.4 and 1.3Hz, ArH_{8}), 5.51 (m, CHCH_{2}Cl), 4.11 (d, J8Hz, CH_{2}Cl), 3.08 (dq, J16.5 and 7.5Hz, HCHCH_{3}), 2.85 (br.s, azir. ring H), 2.76 (dq, J16.5 and
7.5Hz, HCHCH₃), 2.45-2.2 (m, CH₂HCH), 1.81 (s, =C(CH₃)), 1.65-1.5 (m, HCHCH₂), 1.43 (s, azir. ring CH₃, trans to quinaz.), 1.40 (t, J7.5Hz, CH₂CH₃) and 1.14 (s, azir. ring CH₃, cis to quinaz.).

Aziridination of geranyl chloride using oxidative (LTA) addition of NAP (15)

\[
\begin{align*}
\text{Phthal} & \quad \text{M} \\
\text{N} & \quad \text{N} \\
\text{Me} & \quad \text{Me} \\
\text{Cl} & \quad \text{Cl}
\end{align*}
\]

Powdered N-aminophthalimide (15) (0.15g, 9.25x10⁻⁴ mol) and LTA (0.431g, 9.72x10⁻⁴ mol) were added alternately and in very small portions over 15 min. to a stirred solution of dry dichloromethane (1.5 ml), containing geranyl chloride (0.479g, 2.77x10⁻³ mol) at room temperature. After working-up as described in the general procedure (3), purification of the crude aziridination product by chromatography with ethyl acetate-light petroleum (1:9) as eluant, gave the aziridine (144) as a colourless oil (0.043g, 14%) (Found: M/Z 332.1285. C₁₁H₂₁N₂O₂Cl requires M, 332.1291);

\[
\begin{align*}
\nu_{\text{max}} \text{ (Film):} & \quad 1710s, 1450s, 1370s, 1250s, 1185s, 1135s, 1050m, 980m, 890s, 780s \text{ and } 710s \text{ cm}^{-1}; \\
S_{\text{H}} \text{ (CDCl₃, 300 MHz):} & \quad 7.73 \text{ (m, 4 x ArH)}, 5.05 \text{ (m, CH=CHMe₂)}, 4.23 \text{ (dd, J10 and 5Hz, HCHCl)}, 3.35 \text{ (dd, J10 and 9.2Hz, HCHCl)}, 3.08 \text{ (dd, J9.2 and 5Hz, azir. ring H)}, 2.4-1.0 \text{ (m, CH₂CH₂)}, 1.63 \text{ (s, CH=C(CH₃)CH₃)}, 1.57 \text{ (s, CH=CH(CH₃)CH₃) and 1.46 (s, azir. ring CH₃);} \\
M/Z (\%): & \quad 332(M⁺,1), 297(40), 281(27), 255(67), 214(100), 203(26), 163(57), 150(38), 147(36), 135(28), 134(37), 130(55), 108(23), 105(28), 104(63) \text{ and}
\end{align*}
\]
Further elution with ethyl acetate-light petroleum (1:9) afforded the aziridine (143) as colourless crystals (0.144g, 47%), m.p. 74-77°C (from ethanol) (Found: M/Z 332.1289. C₁₈H₂₁N₂O₂Cl requires M, 332.1291); 

ν_max (Nujol): 1690s, 1250s, 1150s, 1075s, 890s, 825m, 780m, 710s and 700s cm⁻¹;

£_H (CDCl₃, 300 MHz): 7.73 (m, 4 x ArH), 5.53 (tq, J8.2 and 1Hz, CHCH₂Cl), 4.11 (d, J8.2Hz, CH₂Cl), 2.75 (t, J6.2Hz, azir. ring H), 2.38 (m, CHCH₂CH₂), 1.97 (m, CHHCHCH₂), 1.79 (d, J1Hz, (CH₃)C=CH), 1.67 (m, CHHCHCH₂), 1.4 (s, azir. ring CH₃, trans to quinaz.), 1.29 (s, azir. ring CH₃, cis to quinaz.).

From a 300 MHz ¹H n.m.r. spectrum of the crude aziridination product the ratio of aziridines (143) and (144) was found to be 7:1 respectively from integration of signals at δ5.05 and δ5.53.

Aziridination of linalool

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.5g, 2.64×10⁻³ mol), LTA (1.23g, 2.77×10⁻³ mol) and linalool (145) (1.22g, 7.93×10⁻³ mol) in dry dichloromethane (5 ml). Chromatography of the crude oxidation product over silica with ethyl acetate-light petroleum (1:4) as eluant, gave the aziridine (146) (R₇ = 0.34) as a colourless oil (0.65g, 73%) as a 1:1 mixture of stereoisomers.
The high resolution accurate mass scan showed no molecular ion at 341 however, a (M+H⁺) ion was present at 342, Found: M+H/Z 342.2184. C₂₀H₂₈N₃O₂ requires M, 342.2181;

ν_max (Film): 3460br.m, 2970m, 1665s, 1590s, 1465s, 1365s, 1220m, 990m, 820s, 770s, 730s, 690m and 645m cm⁻¹;

S_H (CDCl₃, 300 MHz): 8.17 (d, J8.0Hz, ArH₅), 7.7-7.3 (m, ArH₇, ArH₈ and ArH₉), 6.05-5.9 (m, CH=CH₂), 5.33, 5.27 (2 x dd, J8.0 and 1Hz, CH=CHH (cis)), 5.08 (dd, J10.0 and 1Hz, CH=CHH (trans)), 3.05 (dq, J17.0 and 7.5Hz, HCH₃), 3.03 (d, J3.0Hz, exch. D₂O, OH), 2.95 (br.s, azir. ring H), 2.77 (dq, J17.0 and 7.5Hz, HCH₃), 2.25-1.5 (m, CH₂CH₂), 1.4 (m, 4 x CH₃ and CH₂CH₃) and 1.1 (s, 2 x CH₃);

M/Z (%): 341(M⁺,1), 242(29), 231(54), 230(100), 215(10), 214(10), 200(41), 190(41), 189(17), 175(95), 174(82), 173(60), 168(26), 152(14), 130(26), 121(34), 119(54) and 110(33).

**Aziridination of cyclohex-2-en-1-ol**

![Q](image)

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.5g, 2.64x10⁻³ mol), LTA (1.23g, 2.77x10⁻³ mol) and cyclohex-2-en-1-ol (0.77g, 7.93x10⁻³ mol) in dry dichloromethane (5 ml). Chromatography of the crude oxidation product over silica with ethyl acetate-light petroleum (1:1) as eluant, gave 7-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-2α-hydroxy-7-azabicyclo[4.1.0]heptane (153) (R_f = 0.35) as colourless crystals (0.58g,
77%), m.p. 99-102°C (from ethanol) (Found: C, 67.3; H, 6.8; N, 14.7.
\[C_6H_{19}N_3O_2\] requires C, 67.35; H, 6.7; N, 14.7%);

\(\nu_{\text{max}}\) (Nujol): 3480s, 1655s, 1595s, 1335m, 1285m, 1220w, 1060s, 970w, 940w,
830w, 780s and 695m cm\(^{-1}\);

\(\delta_H\) (CDCl\(_3\), 300 MHz): 8.17 (ddd, J8.2, 1.5 and 0.7Hz, ArH\(_5\)), 7.7 (ddd,
J8.1, 7.5 and 1.5Hz, ArH\(_7\)), 7.63 (ddd, J8.1, 1.4 and 0.7Hz, ArH\(_9\)), 7.41
(ddd, J8.2, 7.5 and 1.4Hz, ArH\(_8\)), 5.21 (d, J4Hz, exch. D\(_2\)O, OH), 4.19 (ddd,
J9, 6, 4.5 and 4Hz, CH\(_{\text{OCH}}\)), 3.18 (dd, J7.5 and 4.0Hz, azir. ring H-1), 3.09
(dq, J18 and 7.5Hz, HCH\(_2\)CH\(_3\)), 2.91 (dq, J18 and 7.5Hz, HCH\(_2\)CH\(_3\)), 2.77 (ddd,
J7.5, 6 and 1.5Hz, azir. ring H-6), 1.45 (t, J7.5Hz, CH\(_2\)CH\(_3\)) and 2.15-1.15
(m, 6 x aliphatic H);

M/Z (\%) : 285(M\(^+\),45), 226(18), 200(41), 189(11), 175(44), 174(100),
173(75), 146(11), 131(30), 130(31), 119(24), 112(13) and 103(15).

Preparation of cyclohex-2-enyl acetate

Cyclohex-2-enyl acetate was prepared from cyclohex-2-en-l-ol using
pyridine (6 mol equiv.) and acetic anhydride (2 mol equiv.) in the usual
way (see p.191) and was distilled prior to use, b.p. 66-70°C (lit.\(^{147}\)
68-71°C).
Aziridination of cyclohex-2-enyl acetate

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.30g, 1.58x10^{-3} mol), LTA (0.739g, 1.66x10^{-3} mol) and cyclohex-2-enyl acetate (150) (0.66g, 4.75x10^{-3} mol) in dry dichloromethane (3 ml). The crude oxidation product was triturated with cold ether and the insoluble de-aminated quinazolone (79) was separated off. The ether was evaporated and the product chromatographed over silica with ethyl acetate-light petroleum (1:2) as eluant and afforded 2β-acetoxy-7-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-7-azabicyclo[4.1.0]heptane (156) as colourless crystals (0.036g, 7%), m.p. 120-123°C (from ethanol) (Found: M/Z 327.1586. C_{18}H_{21}N_{3}O_{3} requires M, 327.1582);

ν_{max} (Nujol): 1725s, 1675s, 1595s, 1470s, 1365s, 1250s, 1180w, 1110w, 1040m, 925m, 850w, 810w, 775m, 690m and 650m cm^{-1};

ν_{H} (CDCl_{3}, 300 MHz): 8.16 (ddd, J8.1, 1.5 and 0.6Hz, ArH_{5}), 7.68 (ddd, J8.2, 7.6 and 1.5Hz, ArH_{7}), 7.61 (ddd, J8.2, 1.5 and 0.6Hz, ArH_{8}), 7.4 (ddd, J8.1, 7.6 and 1.5Hz, ArH_{6}), 5.43 (dd (with broadening), J=5 and 5Hz, CHOAc), 3.05 (q, J7Hz, CH2CH3 obscuring H-6), 2.93 (d, J7.5Hz, H-1), 2.11 (s, OOCCH3), 2.35-1.25 (m, 6 x aliphatic H) and 1.43 (t, J7Hz, CH2CH3);

M/Z (%): 327(M^{+},35), 284(12), 268(100), 239(15), 226(30), 213(10), 200(32), 189(20), 175(40), 174(30), 173(45), 157(12), 138(15), 130(50), 119(20), 112(17) and 103(23).
Acetylation of aziridine (153)

To a solution of pyridine (0.43g, 5.47x10^{-3} mol) and acetic anhydride (0.187g, 1.82x10^{-3} mol) was added the aziridine (153) (0.26g, 9.12x10^{-4} mol). The reaction mixture was stirred overnight at room temperature and was then poured into water and extracted with dichloromethane. The dichloromethane was then washed successively with hydrochloric acid (2M), sodium bicarbonate solution and water, dried with magnesium sulphate and evaporated under reduced pressure to give 2x-acetoxy-7-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-7-azabicyclo[4.1.0]heptane (155) as colourless crystals (0.26g, 83%), m.p. 93-95°C (from ethanol) (Found: C, 65.0; H, 6.95; N, 12.0. C_{19}H_{21}N_{3}O_{3}.\frac{1}{2}C_{2}H_{5}OH requires C, 65.1; H, 6.90; N, 12.0%);

$\nu_{\text{max}}$ (Nujol): 3470m, 1735s, 1710s, 1670s, 1590s, 1240s, 1160m, 1035s, 990m, 970m, 920m, 860m, 780m, 770m and 695s cm^{-1};

$\delta_{\text{H}}$ (CDCl$_3$, 300 MHz): 8.15 (ddd, J=8.1, 1.5 and 0.5Hz, Ar$_5$), 7.66 (ddd, J=8.2, 7.5 and 1.5Hz, Ar$_7$), 7.59 (ddd, J=8.2, 1.6 and 0.5Hz, Ar$_6$), 7.38 (ddd, J=8.1, 7.5 and 1.6Hz, Ar$_8$), 5.18 (m, CHOAc), 3.71 (m, OCH$_2$CH$_3$), 3.52 (dd, J=7.5 and 4Hz, H-1), 3.1 (H-6) obscured by 3.08 (q, J=7Hz, CH$_2$CH$_3$), 2.23 (s, OOCCCH$_3$), 2.2-1.25 (m, 6 x aliphatic H), 1.43 (t, J=7Hz, CH$_2$CH$_3$) and 1.23 (t, J=7Hz, OCH$_2$CH$_3$);

M/Z (%): 327(M^+,45), 284(18), 268(52), 267(39), 239(27), 226(26), 201(16), 200(52), 175(57), 174(100), 173(69), 157(10), 154(23), 146(11), 131(48), 130(41), 119(20), 112(55) and 103(18).
Stereoselectivity in aziridination of cyclohex-2-en-1-ol

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.25g, 1.32x10^{-3} mol), LTA (0.616g, 1.38x10^{-3} mol) and cyclohex-2-ene-1-ol (147) (0.389g, 3.96x10^{-3} mol) in dry dichloromethane (3 ml). The crude reaction mixture was then directly acetylated using pyridine (2.3g, 0.029 mol) and acetic anhydride (1g, 9.70x10^{-3} mol) by stirring overnight at room temperature. The mixture was then poured into water (50 ml) and extracted with dichloromethane (2x25 ml), the extracts combined and washed successively with hydrochloric acid (2M, 50 ml), sodium bicarbonate solution (50 ml) and water, dried with magnesium sulphate and the solvent evaporated under reduced pressure.

Examination by 300 MHz n.m.r. of the crude reaction product showed that it contained a mixture of the acetates (155) and (156). The ratio of syn-acetate (155) to anti-acetate (156) was measured and found to be 20:1 respectively from integration of the signals at δ 2.11 and δ 2.23.

When the experiment was repeated using procedure (3) with benzene as the solvent during the aziridination, the ratio of syn- to anti-acetates was measured and found to be 10:1 respectively.

Aziridination of cyclohex-2-enyl acetate in the presence of TFA

The general procedure (4) was followed using the N-aminoquinazolone (77) (0.5g, 2.64x10^{-3} mol), LTA (1.23g, 2.77x10^{-3} mol), cyclohex-2-enyl
acetate (1.11g, 7.93x10⁻³ mol) and trifluoroacetic acid (0.90g, 7.93x10⁻³ mol) in dry dichloromethane (5 ml). Chromatography of the crude oxidation product [which from n.m.r. comprised a 1.2:1 ratio of aziridines (155) and (156)] over silica, with ethyl acetate-light petroleum (1:1) as eluant, gave a mixture of epimeric aziridines (155) and (156) as a crystalline solid (0.57g, 66%).

Preparation of cyclohex-2-enyl methyl ether (160)

To a stirred solution of sodium hydride (0.73g, 0.03 mol) in DMF (10 ml) was added cyclohex-2-en-1-ol (2g, 0.02 mol) and the solution was stirred for 4h at room temperature. Methyl iodide (4.34g, 0.03 mol) was then added and the solution was stirred for a further 2h after which time the crude reaction mixture was poured into water and extracted with ether and the ether dried with magnesium sulphate. The solvent was removed by evaporation under reduced pressure to give the cyclohex-2-enyl methyl ether (160) as a colourless oil b.p. 135-137°C (lit.¹⁴⁷ b.p. 140°C);

$\delta_H$ (CDCl₃, 90 MHz): 5.8 (m, HC=CH), 3.7 (m, CHOCH₃), 3.3 (s, OMe) and 2.1-1.4 (m, 6 x aliphatic H).
Aziridination of cyclohex-2-enyl methyl ether

\[
\begin{array}{c}
\text{N} \\
\text{O} \\
\text{CH}_3 \\
\text{C} \\
\text{H}_2 \\
\text{N} \\
\text{O} \\
\end{array}
\]

(161)

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.3g, 1.58x10^{-3} mol), LTA (0.739g, 1.66x10^{-3} mol) and cyclohex-2-enyl methyl ether (160) (0.533g, 4.75x10^{-3} mol) in dry dichloromethane (3 ml). Chromatography of the crude oxidation product over silica with ethyl acetate-light petroleum (1:2) as eluant, gave 7-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-28-methoxy-7-azabicyclo[4.1.0]heptane (161) (R_f = 0.27) as colourless crystals (0.091g, 19%), m.p. 107-109°C (from ethanol) (Found: C, 68.1; H, 7.1; N, 14.05. C_{17}H_{21}N_{3}O_{2} requires C, 68.2; H, 7.05; N, 14.05%);

\( \nu_{\text{max}} \) (Nujol): 1670s, 1597s, 1285m, 1097s, 735w, 720w, 780m, 770s and 695m cm^{-1};

\( \delta_{\text{H}} \) (CDCl₃, 400 MHz): 8.18 (ddd, J8.1, 7.35 and 1.4Hz, ArH₅), 7.67 (ddd, J8.1, 7.35 and 1.4Hz, ArH₇), 7.62 (ddd, J8.1, 1.3 and 0.6Hz, ArH₉), 7.39 (ddd, J8.1, 7.35 and 1.3Hz, ArH₉), 3.94 (br.dd, J7.6 and 5.4Hz, CHOCH₃), 3.57 (s, OCH₃), 3.04 (dq, J16 and 7.5Hz, HCHCH₃), 2.95 (dq, J16 and 7.5Hz, HCHCH₃), 2.89 (dd, J7.8 and 0.8Hz, H-1), 2.78 (ddd, J7.8, 4.7 and 1.2Hz, H-6), 2.27 (ddd, J14, 6 and 5Hz, 1 x aliphatic H), 1.95-1.25 (m, 5 x aliphatic H) and 1.43 (t, J7.5Hz, CH₂CH₃);

M/Z (%): 299(M⁺,25), 284(24), 228(20), 226(11), 200(100), 175(66), 174(84), 173(87), 158(11), 157(14), 146(15), 132(15), 131(40), 130(57), 126(53), 119(27), 112(11), 111(75), 110(17), 104(11) and 103(26).
Aziridination of 3-methylcyclohex-2-en-1-ol

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.4 g, 2.11x10^{-3} mol), LTA (0.986 g, 2.22x10^{-3} mol) and 3-methylcyclohex-2-en-1-ol (0.711 g, 6.34x10^{-3} mol) in dry dichloromethane (4 ml). Chromatography of the crude oxidation product over silica with ethyl acetate-light petroleum (1:1) as eluant, gave 7-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-5α-hydroxy-1-methyl-7-azabicyclo[4.1.0]heptane (163) (R_f = 0.33) as colourless crystals (0.449 g, 71%), m.p. 125-126°C (from di-isopropyl ether) (Found: C, 68.3; H, 7.0; N, 14.0. C_{17}H_{21}N_{3}O_{2} requires C, 68.2; H, 7.05; N, 14.05%);

\[ \nu_{max} (\text{Nujol}) : 3450\text{br.s}, 1665\text{s}, 1595\text{s}, 1470\text{s}, 1210\text{m}, 1080\text{m}, 930\text{m}, 735\text{m} \text{ and } 695\text{m cm}^{-1}; \]

\[ \delta_{H} (\text{CDCl}_3, 400 \text{ MHz}) : 8.13 \text{ (ddd, J8, 1.4 and 0.5 Hz, ArH_5)}, 7.68 \text{ (ddd, J8.1, 7.4 and 1.4 Hz, ArH_7)}, 7.65 \text{ (ddd, J8.1, 1.3 and 0.5 Hz, ArH_9)}, 7.4 \text{ (ddd, J8, 7.4 and 1.3 Hz, ArH_8)}, 4.97 \text{ (d, J3Hz, excl. D}_2\text{O, OH)}, 4.2 \text{ (ddd, J7.8, 5.6, 4.4 and 3Hz, H-5β)}, 3.06 \text{ (d, J4.4Hz, H-6)}, 3.05 \text{ (dq, J16 and 7.5Hz, HCHCH}_3\text{)}, 2.78 \text{ (dq, J16 and 7.5Hz, HCHCH}_3\text{)}, 2.05 \text{ (ddd, J14, 10 and 5Hz, H-2α)}, 1.8-1.2 \text{ (m, 5 x aliphatic H)}, 1.39 \text{ (t, J7.5Hz, CH}_2\text{CH}_3\text{)} \text{ and } 1.19 \text{ (s, CH}_3\text{);}

M/Z (%): 299(M^+17), 242(11), 240(8), 226(9), 200(90), 190(17), 189(100), 188(16), 173(75), 174(84), 173(99), 172(10), 160(27), 158(15), 146(15), 145(11), 144(14), 132(20), 131(19), 130(42), 127(35), 119(78), 117(12) and 103(18).
Preparation of 3-phenylcyclohex-2-ene-1-one

This was prepared by the method adopted by Walker using ethyl benzoyl acetate, methyl vinyl ketone and aqueous triton B in t-butanol. Hydrolysis of the product gave 3-phenylcyclohex-2-ene-1-one as colourless crystals from ether m.p. 64-66°C (lit. m.p. 64.5-66°C);
$\delta_H (\text{CDCl}_3, 90 \text{ MHz}):$ 7.6-7.2 (m, 5 x PhH), 6.4 (s, =CH) and 2.8-2.0 (m, 3 x CH$_2$).

Preparation of 3-phenylcyclohex-2-en-1-ol (164)

Sodium borohydride (0.968g, 0.025 mol) was added in small portions to a solution of 3-phenylcyclohex-2-ene-1-one (10.19g, 0.0679 mol) in methanol (5 ml) at room temperature and the reaction was monitored by t.l.c. After the disappearance (t.l.c.) of starting material (ca. 6h.) the reaction was quenched with water (100 ml) and extracted with ether (2 x 100 ml). The combined organic extracts were dried (MgSO$_4$) and the solvent was removed by evaporation under reduced pressure. The crude product was purified by crystallization from light petroleum to yield 3-phenylcyclohex-2-ene-1-ol (164) as colourless crystals (11.92g, 87%), m.p. 59-62°C (lit. m.p. 60-61°C);
$\nu_{\text{max}}$ (Film): 3320br.s, 2920s, 2850s, 1490s, 1440m, 1340m, 1260m, 1165w, 1050s, 970s, 910m, 755s and 690s cm$^{-1}$;
$\delta_H (\text{CDCl}_3, 90 \text{ MHz}):$ 7.2 (m, 5 x PhH), 6.1 (m, C=CH), 4.3 (m, CHOH) and 2.4-1.4 (m, 3 x CH$_2$).
Aziridination of 3-phenylcyclohex-2-en-1-ol (164)

The general procedure (2) was followed using the N-aminooquinazolone (77) (0.3g, 1.58x10^{-3} mol), LTA (0.739g, 1.66x10^{-3} mol) and 3-phenylcyclohex-2-ene-1-ol (164) (0.828g, 4.75x10^{-3} mol) in dry dichloromethane (3 ml). Chromatography of the crude oxidation product over silica with ethyl acetate-light petroleum (1:2) as eluant, gave 7-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-5α-hydroxy-1-phenyl-7-azabicyclo[4.1.0]heptane (165) as colourless crystals (0.42g, 74%), m.p. 171-174°C (from ethanol) (Found: C, 73.45; H, 6.5; N, 11.65. C_{22}H_{23}N_{3}O_{2} requires C, 73.1; H, 6.4; N, 11.6%);

ν_max (Nujol): 3420m, 1645s, 1590s, 1295w, 1280w, 1240w, 1080w, 1060w, 910w, 770m, 740w and 690w cm^{-1};

$^1$H (CDCl$_3$, 300 MHz): 8.2 (dd, J7.9 and 1.3Hz, ArH$_5$), 7.65 (ddd, J8, 7.3 and 1.3Hz, ArH$_7$), 7.45 (dd, J8 and 1.3Hz, ArH$_8$), 7.42 (ddd, J7.9, 7.3 and 1.3Hz, ArH$_6$), 7.25-7.05 (m, 5 x PhH), 5.01 (d, J2.5Hz, exch. D$_2$O, OH), 4.45 (dddd, J5.6, 5.5, 5 and 2.5Hz, CHOH), 4.34 (d, J5Hz, H-6), 2.87 (dq, J16.5 and 7.5Hz, HCHCH$_3$), 2.71 (ddd, J14.1, 7.5 and 5.1Hz, 1 x H), 2.40 (m, 1 x H), 2.34 (dq, J16.5 and 7.5Hz, HCHCH$_3$), 1.93 (m, HCHCH$_2$), 1.78 (m, HCHCH$_2$), 1.68 (m, CH$_2$CH), 1.5 (m, CH$_2$HCH) and 1.14 (t, J7.5Hz, CH$_2$CH$_3$);

M/Z (%): 361(M^+,8), 343(5), 304(7), 200(100), 189(12), 188(22), 175(30), 174(38), 173(37), 160(10), 144(11), 143(10), 130(21), 119(14) and 103(11).
Preparation of 3-phenylcyclohex-2-enyl acetate (166)

3-Phenylcyclohex-2-ene-1-ol (164) (4.31g, 0.0287 mol) was added to a solution of pyridine (13.63g, 0.172 mol), and acetic anhydride (5.91g, 0.057 mol) and the mixture was stirred at room temperature for 4h. The reaction mixture was then added to water (100 ml) and extracted with dichloromethane (2x50 ml). The dichloromethane extracts were combined and washed with hydrochloric acid (2M, 100 ml), sodium bicarbonate solution (100 ml) and water (100 ml), dried with magnesium sulphate and the solvent removed by evaporation under reduced pressure. After distillation 3-phenylcyclohex-2-enyl acetate (166) was obtained as a colourless oil (4.35g, 79%), b.p. 150°C at 0.1 mmHg (lit.\textsuperscript{153} b.p. not quoted);

$\nu_{\text{max}}$ (Film): 2935s, 1720s, 1440m, 1360m, 1240s, 1020s, 955m, 905m, 750m and 695m cm$^-1$;

$\delta_H$ (CDCl$_3$, 90 MHz): 7.3 (m, 5 x PhH), 6.0 (m, C=CH), 5.4 (m, CHOAc), 2.0 (s, OOCH$_3$) and 2.6-1.6 (m, 6 x aliphatic H).

Aziridination of 3-phenylcyclohex-2-enyl acetate (166)

![Aziridination of 3-phenylcyclohex-2-enyl acetate (166)](image)

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.3g, 1.58x10$^{-3}$ mol), LTA (0.739g, 1.66x10$^{-3}$ mol) and 3-phenylcyclohex-2-enyl acetate (166) (1.028g, 4.75x10$^{-3}$ mol) in dry dichloromethane (3 ml). Chromatography of the crude oxidation product over silica with ethyl acetate-light petroleum (1:2) as eluant, gave 5S-acetoxy-7-(4-oxo-2-ethyl-
3(4H)-quinazolinyl)-1-phenyl-7-azabicyclo[4.1.0]heptane (167) as colourless crystals (0.276g, 44%), m.p. 132-134°C (from ethanol) (Found: C, 71.35; H, 6.4; N, 10.25. C_{24}H_{25}N_{3}O_{3} requires C, 71.45; H, 6.25; N, 10.4%);

ν\text{max} (Nujol): 1735s, 1670s, 1585s, 1235s, 1215m, 1190m, 1155w, 1055m, 1040m, 1030m, 765s, 750m, 700m and 690m cm\textsuperscript{-1};

δ\text{H} (CDCl\textsubscript{3}, 300 MHz): 8.14 (br.d, J7.9Hz, ArHg), 7.59 (ddd, J8.1, 7.4 and 1.3Hz, ArH\textsubscript{8}), 7.43 (dd, J8.1 and 1.3Hz, ArH\textsubscript{6}), 7.34 (ddd, J7.9, 7.4 and 1.3Hz, ArH\textsubscript{6}), 7.25-7.05 (m, 5 x PhH), 5.62 (pseudo t, J6Hz, CHO\textsubscript{Ac}), 4.6 (br.s, H-6), 2.94 (dq, J16 and 7Hz, HCH\textsubscript{CH\textsubscript{3}}), 2.83 (br.m, HCH\textsubscript{CH\textsubscript{3}}), 2.5-1.4 (m, 6 x aliphatic H), 2.15 (s, OCOCH\textsubscript{3}) and 1.22 (t, J7Hz, CH\textsubscript{2}CH\textsubscript{3});

M/Z (%): 403(M\textsuperscript{+},1), 343(9), 341(6), 230(100), 201(35), 200(30), 175(47), 174(55), 173(64), 170(88), 169(69), 168(38), 167(21), 155(72), 154(60), 143(22), 129(38), 119(25), 115(19) and 103(12).

The other product isolated in this experiment was the de-aminated quinazolone (79) (0.063g, 23%).

Aziridination of 3-methylcyclohex-1-ene (168)

\[\begin{align*}
3& \quad 1 \quad 2 \quad \text{CH}_3 \\
5 & \quad 4 & \quad 6 \\
\text{(170)}
\end{align*}\]

\[\begin{align*}
3& \quad 1 \quad 2 \quad \text{CH}_3 \\
5 & \quad 4 & \quad 6 \\
\text{(169)}
\end{align*}\]

The general procedure (3) was followed using the N-aminoquinazolone (77) (0.5g, 2.64x10\textsuperscript{-3} mol), LTA (1.232g, 2.77x10\textsuperscript{-3} mol) and 3-methylcyclohex-1-ene (0.763g, 7.93x10\textsuperscript{-3} mol) in dry dichloromethane (5 ml). A high-field \textsuperscript{1}H n.m.r. spectrum of the crude oxidation product showed the presence of two stereoisomeric aziridines (169) and (170) which were present in a
ratio of 5:1 respectively. Chromatography over silica, with ethyl acetate-light petroleum (1:4) as eluant, gave 7-(4-oxo-2-ethyl-3(4H)-quinazolin-yl)-2α-methyl-7-azabicyclo[4.1.0]heptane (170) as a colourless oil (0.024g, 4%) (Rf = 0.5) (Found: M/Z 283.1675. C17H21N3O requires M, 283.1684);
νmax (Nujol): 1665s, 1585s, 1520m, 1440s, 1365m, 1330m, 1280m, 1220s, 1155m, 1080m, 1040m, 925w, 765s and 690m cm⁻¹;
δH (CDCl3, 400 MHz): 8.15 (dd, J8.0 and 1.5Hz, ArH5), 7.65 (ddd, J8.2, 6.9 and 1.5Hz, ArH7), 7.59 (dd, J8.2 and 1.3Hz, ArH8), 7.37 (ddd, J8.0, 6.9 and 1.3Hz, ArH6), 3.38 (dd, J8.0 and 3.9Hz, azir. ring, H-1), 3.12 (dq, J16.4 and 7.4Hz, HCHCH3), 2.96 (dq, J16.4 and 7.4Hz, HCHCH3), 2.62 (ddd, J8, 6.7 and 1.3Hz, azir. ring, H-6), 2.14-2.04 (m, H-5α), 2.04-1.96 (m, H-2β), 1.95 (ddddd, J15, 11, 5.6 and 1.3Hz, H-5α), 1.56 (m, H-3β), 1.43 (t, J7.4Hz, CH2CH3 obscuring H-4α or H-4β), 1.41 (d, J6.8Hz, CHCH3) and 1.30-1.05 (m, H-4α or H-4β and H-3α).

![Chemical Structure](image)

Nuclear Overhauser effects were observed as follows:
3.38 (H-1) shows a n.O.e. with 2.68 (H-6, 4.3%) and 2.04-1.96 (H-2β, 5.5%);
2.96 (HCHCH3) shows a n.O.e. with 3.12 (HCHCH3, 4.6%), 2.62 (H-6, 1.6%) and 1.95 (H-5α, 1.2%);
2.62 (H-6) shows a n.O.e. with 3.38 (H-1, 4.8%), 3.12 (HCHCH3, 1.2%), 2.96 (HCHCH3, 2.5%), 2.14-2.04 (H-5β, 4.3%) and 1.95 (H-5α, 1.2%);
1.41 (CHCH3) shows a n.O.e. with 3.12 (HCHCH3, 1.1%) and 2.96 (HCHCH3, 1%);
M/Z (%): 283(M⁺,30), 268(5), 254(10), 240(15), 226(20), 200(52), 175(30), 174(52), 173(58), 158(10), 157(11), 131(37), 130(56), 119(17), 110(100), 109(11) and 103(25).
Further elution with ethyl acetate-light petroleum (1:4) gave 7-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-2β-methyl-7-azabicyclo[4.1.0]heptane (169) (Rf = 0.44) as colourless crystals (0.103g, 14%), m.p. 75-76°C (from light petroleum) (Found: C, 72.05; H, 7.5; N, 14.8. \( \text{C}_{17}\text{H}_{21}\text{N}_{3} \text{O} \) requires C, 72.05; H, 7.45; N, 14.85%);

\( \nu_{\text{max}} \) (Nujol): 1660s, 1585s, 1450s, 1330m, 1280m, 1215s, 1160m, 1040m, 995m, 925m, 765s, 690m and 645m cm\(^{-1}\);

\( \delta_{\text{H}} \) (CDCl\(_3\), 400 MHz): 8.15 (dd, J8.0 and 1.3Hz, ArH\(_6\)), 7.63 (ddd, J8.0, 6.9 and 1.3Hz, ArH\(_7\)), 7.57 (d, J8.0Hz, ArH\(_8\)), 7.36 (ddd, J8.0, 6.9 and 1.2Hz, ArH\(_6\)), 2.99 (dq, J11.3 and 7.3Hz, HCHCH\(_3\)), 2.94 (dq, J11.3 and 7.3Hz, HCHCH\(_3\)), 2.76 (dd, J7.9 and 4.0Hz, azir. ring, H-6), 2.38 (ddd, J14, 4.8 and 4.7Hz, H-5α), 2.37 (d, J7.9Hz, azir. ring, H-1), 2.3-2.21 (m, H-2α), 1.75 (dddd, J15, 10, 4.6 and 4.0Hz, H-5β), 1.64 (dddd, J13, 6, 6 and 2.4Hz, H-3α), 1.48 (m, H-4β), 1.41 (t, J7.3Hz, CH\(_2\)CH\(_3\)), 1.34 (m, H-4α), 1.18 (d, J7.3Hz, CHCH\(_3\)) and 0.85 (dddd, J13, 11.5, 10.5 and 2.8Hz, H-3β).

\[ \text{Q} \]

\[ \text{N} \]

\[ \text{H}^{2\alpha} \]

\[ \text{Me} \]

\[ \text{H}^{5\alpha} \]

\[ \text{H}^{5\beta} \]

\[ \text{H}_{5\beta} \]

Nuclear Overhauser effects were observed as follows:

2.97 (HCHCH\(_3\) and HCHCH\(_3\)) shows a n.o.e. with 2.76 (H-6, 1.4%), 2.38 (H-1 and H-5α, 3.5%), 2.3-2.21 (H-2α, 2.3%) and 1.41 (CH\(_2\)CH\(_3\), 4.9%);

2.76 (H-6) shows a n.o.e. with 2.97 (HCHCH\(_3\) and HCHCH\(_3\), 1.6%), 2.38 (H-5α, 6.2%) and 1.75 (H-5β, 3.7%);

1.18 (CHCH\(_3\)) shows a n.o.e. with 2.37 (H-1, 2.6%), 2.3-2.21 (H-2α, 2.6%) and 0.85 (H-3β, 1.2%);

0.85 (H-3β) shows a n.o.e. with 1.75 (H-5β, 1.7%), 1.48 (H-4β, 3.4%) and 1.18 (CHCH\(_3\), 2.7%).
Preparation of cyclohex-3-en-1-ol (172)

This was prepared by distillation of cyclohexane-1,4-diol in the presence of a few drops of concentrated sulphuric acid and gave cyclohex-3-en-1-ol in 65% yield, b.p. 164-165°C (lit. 147 164-166°C);

\[ \delta_H (\text{CDCl}_3, 90 \text{ MHz}): \text{ 5.6 (m, } \text{HC=CH), 4.9 (m, } \text{CHOH) and 2.6-1.3 (m, 6 x aliphatic H).} \]

Aziridination of cyclohex-3-ene-1-ol (172)

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.35g, 1.85x10^{-3} mol), LTA (0.863g, 1.94x10^{-3} mol) and cyclohex-3-ene-1-ol (172) (0.54g, 5.55x10^{-3} mol) in dry dichloromethane (3.5 ml). Chromatography of the crude oxidation product over silica with ethyl acetate as eluant, gave 7-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-3α-hydroxy-7-azabicyclo[4.1.0]heptane (157) (R_f = 0.26) as colourless crystals (0.41g, 77%), m.p. 130-133°C (from methanol) (Found: M/Z 285.1472. C_{16}H_{19}N_{2}O_{2} requires M, 285.1477);

\[ \nu_{\text{max}} (\text{Nujol}: \text{ 3260s, 1673s, 1580s, 1560s, 1330m, 1280m, 1215m, 1175m, 1120m, 1060s, 1045m, 760s, 700m and 690m cm}^{-1}; \]

\[ \delta_H (\text{CDCl}_3, 300 \text{ MHz}): \text{ 8.17 (ddd, J7.5, 1.2 and 0.6Hz, ArH}_5), \text{ 7.68 (ddd, J8.1, 7.4 and 1.2Hz, ArH}_7), \text{ 7.63 (ddd, J8.1, 1.5 and 0.6Hz, ArH}_5), \text{ 7.42 (ddd, J7.5, 7.4 and 1.5Hz, ArH}_8), \text{ 3.89 (ddd, J6.8, 5.3, 5 and 2.4Hz, CHOCH), 3.02 (q, J7.6Hz, CH}_2CH}_3), \text{ 2.84 (m, H-1 and H-6), 2.51 (ddd, J15, 9} \]
and 7Hz, H-5x), 2.44 (dd, J14.5 and 4.9Hz, H-2x), 2.2 (ddd, J14.5, 5 and 4.5Hz, H-2β), 2.16 (m, H-5β), 1.75 (ddd, J13.5, 7.5, 7 and 4.5Hz, H-4x), 1.53 (dddd, J13.5, 9, 7.2 and 2.4Hz, H-4β) and 1.45 (t, J7.6Hz, CH2CH3);

SC (CDCl3, 75 MHz): 159.7(s), 156.8(s), 145.8(s), 133.6(d), 126.9(d), 126.2(d), 126.0(d), 121.1(s), 65.65(d), 47.1(d), 46.4(d), 30.3(t), 27.8(t), 27.6(t), 19.5(t) and 10.6(q);

M/Z (%): 285(M+,74), 268(20), 256(10), 242(19), 228(10), 227(17), 226(82), 213(25), 201(27), 200(60), 187(19), 175(57), 174(100), 173(83), 158(18), 157(14), 146(12), 132(10), 131(80), 130(76), 119(19), 112(34), 103(31) and 102(12).

Acetylation of aziridine (157) using sodium acetate and acetic anhydride

\[
\begin{align*}
N & \quad \text{H}_{2\alpha} \\
H_{5\alpha} & \quad \text{H}_{5\beta} \\
H_{2\alpha} & \quad \text{OAc}
\end{align*}
\]

(158)

To a solution of acetic anhydride (18 ml, 0.189 mol) and sodium acetate (4.172g, 0.051 mol) was added the alcohol (157) (1.04g, 3.65x10^{-3} mol). The reaction mixture was then heated under reflux for 1 min., allowed to cool and then poured into water (50 ml). After allowing the acetic anhydride to decompose, the solution obtained was then extracted with ether (2x50 ml), the ether layers combined, washed with sodium bicarbonate solution (100 ml), dried (MgSO4) and the solvent removed by evaporation under reduced pressure to give 3α-acetoxy-7-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-7-azabicyclo[4.1.0]heptane (158) (65%) as colourless crystals,
m.p. 167-169°C (from ethanol) (Found: C, 66.15; H, 6.55; N, 12.9.
C_{16}H_{21}N_3O_3 requires C, 66.05; H, 6.45; N, 12.85%);

ν_{\text{max}} (Nujol): 1725s, 1670s, 1595s, 1245s, 1220m, 1170w, 1030s, 925m, 765s
and 690s cm^{-1};

{\delta}_{H} (CDCl_3, 400 MHz): 8.14 (dd, J 8 and 1.4Hz, ArH_{5}), 7.66 (ddd, J8.1, 7.0
and 1.4Hz, ArH_{7}), 7.6 (dd, J8.1 and 1.3Hz, ArH_{8}), 7.39 (ddd, J8, 7 and
1.3Hz, ArH_{6}), 4.67 (dddd (width 36Hz), J11.8, 10.2, 6.6 and 3.6Hz, COAc),
3.0 (dq, J15 and 7.1Hz, H\text{CHCH}_3), 2.94 (dq, J15 and 7.1Hz, H\text{CHCH}_3), 2.85
(ddd, J7.4, 3.6 and 1.2Hz, H-6), 2.67 (dd, J7.4 and 7.4Hz, H-1), 2.65-2.58
(m, H-2β and H-5α), 2.05 (dd, J13.8 and 10.2Hz, H-2α), 2.03 (c, H\text{OCCH}_3),
1.96 (dddd, J14.6, 12.5, 5.2 and 3.6Hz, H-5β), 1.71 (m, H-4β), 1.58 (dddd,
J12.6, 12.5, 11.8 and 4.6Hz, H-4α) and 1.42 (t, J7.3Hz, CH_2CH_3).

Nuclear Overhauser effects were observed as follows:
2.97 (CH_2\text{CH}_3) shows a n.O.e. with 2.67 (h-1, 1.4%), 2.61 (H-5α, 2.0%) and
2.05 (H-2α, 1.7%);
1.71 (H-4β) shows a n.O.e. with 4.67 (H-3β, 5.1%), 2.6 (H-5α, 2.3%) and
1.96 (H-5β, 2%);
1.58 (H-4α) shows a n.O.e. with 2.6 (H-5α, 4.3%) and 2.05 (H-2α, 2.8%);
1.96 (H-5β) shows a n.O.e. with 4.67 (H-3β, 4.6%) and 2.85 (H-6, 6.5%);
4.66 (H-3β) shows a n.O.e. with 2.63 (H-2β, 1.8%) and 1.96 (H-5β, 3.5%).

M/Z (%): 327(M^+,39), 268(48), 226(43), 200(40), 175(42), 174(68), 173(57),
158(12), 157(14), 154(10), 132(12), 131(60), 130(54), 119(17), 112(21),
103(24), 94(100) and 90(15).

Examination of the crude reaction product from the above acetylation
showed the presence of the epimeric acetate (159) (ratio of (158):(159) =
3:1). When the pure acetate (158) was subjected to the above acetylation
conditions it was recovered unchanged in 70% yield.
Aziridination of cyclohex-3-enyl acetate (177)

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.5 g, 2.64 x 10^-3 mol), LTA (1.23 g, 2.77 x 10^-3 mol) and cyclohex-3-enyl acetate (177) (1.11 g, 7.93 x 10^-3 mol) in dry dichloromethane (5 ml). Chromatography of the crude oxidation product over silica with ethyl acetate-light petroleum (1:1) as eluant, gave the aziridines (158) and (159) (0.157 g, 18%) as a 1:1 mixture of epimers.

The 1H n.m.r. spectrum of the crude reaction product also showed a 1:1 mixture of aziridines (158) and (159) identical with that obtained from an authentic 1:1 mixture of the latter.

Synthesis of 3β-acetoxy-7-(4-oxo-2-ethyl-3(4H)-quinazoliny1)-7-azabicyclo[4.1.0]heptane (159) using the Mitsunobu reaction

Following the procedure given by Bartlett,\textsuperscript{155} diethylazodicarboxylate (0.304 g, 1.74 x 10^-3 mol) in dry THF (2 ml) was added dropwise with stirring to a solution of the alcohol (157) (0.333 g, 1.16 x 10^-3 mol), triphenylphosphine (0.458 g, 1.74 x 10^-3 mol) and acetic acid (0.0913 g, 1.52 x 10^-3 mol) in dry THF (4 ml). After setting aside overnight, the bulk of the solvent was
removed at room temperature under reduced pressure and the residue chromatographed over Kieselgel using ethyl acetate-light petroleum (1:1) as eluant. The first fraction eluted gave 3β-acetoxy-7-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-7-azabicyclo[4.1.0]heptane (159) as a colourless solid (0.148g, 42%), m.p. 145-148°C (from ethanol) (Found: M/Z 327.1585. C_{16}H_{21}N_{3}O_{3} requires M, 327.1582);

$\nu_{\text{max}}$ (Nujol): 1730br.s and 1665s cm$^{-1}$;

$\delta_h$ (CDCl$_3$, 400 MHz): 8.16 (dd, J8.0 and 1.5Hz, ArH$_g$), 7.67 (ddd, J8.2, 7.0 and 1.5Hz, ArH$_e$), 7.61 (d, J8.2Hz, ArH$_h$), 7.4 (ddd, J8.0, 7.0 and 1.2Hz, ArH$_d$), 4.95 (m, (width 23Hz), H-3α), 2.97 (q, J7.4Hz, CH$_2$CH$_3$), 2.84 (ddd, J7.9, 4.5 and 1.6Hz, H-6), 2.78 (ddd, J7.9, 6 and 1.2Hz, H-1), 2.5 (dd, J15.5 and 4.8Hz, H-2α), 2.34 (ddd, J14.9, 5.8, 5.8 and 1.6Hz, H-5α), 2.18-2.1 (m, H-2β and H-5β), 1.74-1.62 (m, H-4α and H-4β) and 1.43 (t, J7.4Hz, CH$_2$CH$_3$).

Irradiation at $\delta$ 2.5 caused the multiplet at $\delta$ 4.95 (H-3α) to collapse to a multiplet (width 18Hz), J-6, 3.8 and 3.8Hz;

irradiation at $\delta$ 4.95 caused the double doublet at $\delta$ 2.5 to collapse to a doublet J-15.5Hz but had no effect on the signal at $\delta$ 2.34.

M/Z (%): 327(M$^+$,60), 284(100), 268(55), 238(5), 226(35), 213(10), 200(20), 189(15), 174(25), 173(40), 157(10), 146(5), 131(45), 130(55), 119(14), 112(7) and 103(23).
Preparation of 7-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-3β-hydroxy-7-aza-
bicyclo-[4.1.0]heptane (178)

The acetate (159) (10 mg) was suspended in a solution of potassium hydroxide (5 mg) in methanol (0.5 ml) and then heated for 1 min. at 60°C during which the solid dissolved. T.l.c. of the solution showed complete conversion of the starting material (Rf = 0.75; ethyl acetate) into a product (Rf = 0.5; ethyl acetate). The solution was neutralised with dilute acetic acid, diluted with water (1.5 ml) and then extracted with ether (2x1 ml). After drying the ether solution and then evaporating, 7-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-3β-hydroxy-7-aza-
bicyclo[4.1.0]heptane (178) was obtained as a colourless oil (Found: M/Z 285.1473. C_{18}H_{19}N_{3}O requires M, 285.1477);

$\delta_H$ (CDCl$_3$, 300 MHz): 8.18 (ddd, J8.1, 1.4 and 0.5Hz, ArH$_9$), 7.69 (ddd, J8.0, 7.6 and 1.4Hz, ArH$_7$), 7.62 (dd, J8.0 and 1.5Hz, ArH$_9$), 7.41 (ddd, J8.1, 7.6 and 1.5Hz, ArH$_6$), 3.96 (m, CH$_2$OH), 2.99 (q, J7.5Hz, CH$_2$CH$_3$), 2.84 (ddd, J8, 6.6 and 1.4Hz, H-1), 2.78 (ddd, J8, 4.5 and ~2Hz, H-6), 2.58 (dd, J14.5 and 4.5Hz, H-2α), 2.29 (m, 2xH), 1.98 (ddd, J14.5, 4.5 and 4.5Hz, H-5α), 1.73 (m, 1xH), 1.52 (m, 1xH) and 1.44 (t, J7.5Hz, CH$_2$CH$_3$);

M/Z (%) : 285(M$^+$,66), 268(18), 242(16), 228(18), 227(11), 226(53), 213(22), 201(23), 200(77), 190(51), 189(60), 187(12), 175(58), 174(95), 173(100), 158(14), 157(13), 146(12), 131(51), 130(57), 119(23), 112(20), 103(23), 90(13) and 84(14).
Epoxidation of cyclohex-3-enyl acetate (177) using m-chloroperbenzoic acid

\[
\text{\text{C}}\text{\text{H}}_{\text{2}}\text{C}_{\text{l}}\text{2} \text{CH}_{\text{2}}\text{OAc}
\]

To an ice-cooled solution of cyclohex-3-enyl acetate (0.31g, 2.2x10^{-3} mol) in CH\text{2}Cl\text{2} (5 ml) was added m-chloroperbenzoic acid (0.42g, 2.43x10^{-3} mol). After the disappearance of the starting material (t.l.c.), the reaction mixture was warmed to room temperature and washed with saturated sodium bicarbonate solution, water, and then dried (MgSO\text{4}). The solvent was removed by evaporation under reduced pressure to give a 1.2:1 mixture of syn- and anti-epoxyacetates from non-superimposed signals at \$ 4.86 and \$ 4.63 in the 300 MHz n.m.r. spectrum of the crude reaction product.

When the signals due to the syn-epoxide (179) (see below), were subtracted from this 300 MHz n.m.r. spectrum, characteristic signals from the anti-epoxide (180) were found;

\$\text{H} (\text{CDCl}_3, 300 \text{ MHz}): \ 4.86 (\text{dddd, J6.4, 4.9, 4.5 and 2.6Hz, CH}_2\text{OAc}), 3.2 (\text{m, epoxide ring H}), 3.14 (\text{m, epoxide ring H}), 2.03 (s, OCOCH}_3\text{) and 2.4-1.4 (m, 6 x aliphatic H}).

Epoxidation of cyclohex-3-ene-1-ol using V\text{O(acac)}\text{2} and tert-butylhydroperoxide

\[
\text{\text{C}}\text{\text{H}}_{\text{2}}\text{C}_{\text{l}}\text{2} \text{OH}
\]

To a solution of cyclohex-3-ene-1-ol (0.753g, 7.67x10^{-3} mol) and
vanadyl acetylacetonate (0.02g) in refluxing 1,2-dichloroethane (8 ml) was added, dropwise, over a period of 20 min. dry (MgSO₄) tert-butylhydroperoxide (1.5 ml of 74% solution). The initially colourless solution of cyclohex-3-ene-1-ol in 1,2-dichloroethane turned bright green upon addition of the vanadium salt, the colour faded as the reflux temperature was approached and then turned deep red as the hydroperoxide was added. The reaction was heated under reflux and monitored by t.l.c. and was complete after 3h as judged by the disappearance of the starting material.

The reaction mixture was then cooled and a solution of acetic anhydride (1.5 ml) in pyridine (3.8 ml) was added. After stirring overnight the resulting solution was poured into water (20 ml) and washed with dilute hydrochloric acid (2M, 10 ml) and sodium bicarbonate, dried over MgSO₄ and the solvent removed by evaporation under reduced pressure.

Chromatography of the crude oxidation product over silica with ethyl acetate-light petroleum (1:3) as eluant, gave the syn-epoxyacetate (179) (Rf = 0.5) as a colourless oil (0.273g, 27%).

δH (CDCl₃, 300 MHz): 4.63 (dddd, J10.9, 10.2, 6.4 and 3.9Hz, CHOAc), 3.12 (m, epoxide ring protons), 2.45-1.45 (m, 6 x aliphatic H) and 2.02 (s, OOCCH₃).
Aziridination of diol (184)

![Diagram of molecule (185)](image)

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.5g, 2.64x10^-3 mol), LTA (1.23g, 2.77x10^-3 mol) and the diol (184) (0.95g, 5.28x10^-3 mol) in dry dichloromethane (5 ml). Chromatography of the crude oxidation product over silica with ethyl acetate as eluant, gave 4α,5α dihydroxy-3-trifluoromethyl-7-(4-oxo-2-ethyl-3(4H) quinazolinonyl)-7-azabicyclo[4.1.0]hept-2-ene (185) (Rf = 0.34) as colourless crystals (0.71g, 74%), m.p. 182-183°C (from ethanol) (Found: C, 55.5; H, 4.4; N, 11.5. C17H16N303F3 requires C, 55.6; H, 4.4; N, 11.45%);

νmax (Nujol): 3400br.s, 1660s, 1635s, 1585s, 1310s, 1280s, 1175s, 1110s, 1085s, 1040m, 995m, 930m, 770s, 700m and 685m cm⁻¹;

δH (CDCl₃, 300 MHz): 8.12 (ddd, J8.1, 1.5 and 0.55Hz, ArH₆), 7.68 (ddd, J8.2, 7.1 and 1.5Hz, ArH₇), 7.58 (ddd, J8.2, 1.4 and 0.55Hz, ArH₈), 7.42 (ddd, J8.1, 7.1 and 1.4Hz, ArH₇), 6.97 (m, J5.1 and 1.6Hz, H-2), 4.42 (ddd, J11.5, 4.7, 2.0 and 1.6Hz, H-4), 4.35 (d, J9.2, OH-5, exch. D₂O), 4.5 (ddd, J9.2, 4.7 and 2.1Hz, H-5), 3.65 (ddd, J7.7, 2.1 and 2.0Hz, H-6), 3.3 (dd, J7.7 and 5.1Hz, H-1), 3.06 (dq, J17 and 7Hz, HCH₃CH₃), 3.0 (d, J11.5Hz, OH-4, exch. D₂O), 2.95 (dq, J17 and 7Hz, HCH₃CH₃) and 1.43 (t, J7Hz, CH₂CH₃);

M/Z (%): 367(M⁺,24), 338(14), 336(34), 333(30), 213(34), 200(39), 190(24), 175(100), 172(42), 162(60), 160(55), 147(75), 132(52), 120(64) and 103(67).
Attempted aziridination of diol (184) in the presence of Ti(OPr̈_3)_4.

Powdered N-aminoquinazolone (77) (0.5g, 2.64x10^{-3} mol) and LTA (1.23g, 2.77x10^{-3} mol) were added alternately and in very small portions over 15 min. to a stirred solution of dry dichloromethane (5 ml), containing titanium tetra-isopropoxide (0.75g, 2.64x10^{-3} mol) and diol (184) (0.95g, 5.28x10^{-3} mol) at room temperature. After stirring for a further 15 min. at room temperature the mixture was poured into water (50 ml) and extracted with dichloromethane (2x25 ml), the extracts combined and washed successively with sodium bicarbonate solution (50 ml) and water (50 ml), dried with magnesium sulphate and the solvent evaporated under reduced pressure.

Examination by 300 MHz n.m.r. of the crude reaction product showed that it contained only the de-aminated quinazolone (79) which was isolated by trituration using ice-cold ether in 85% yield.
Attempted aziridination of ethyl vinyl ether

\[
\begin{array}{c}
\text{HNQ} \\
\text{OAc} \\
\text{OEt}
\end{array}
\]

(187)

The general procedure (2) was followed using the N-aminquinazolone (77) (0.255g, 1.35x10^-3 mol), LTA (0.628g, 1.41x10^-3 mol) and ethyl vinyl ether (0.146g, 2.02x10^-3 mol) in dry dichloromethane (2.5 ml). Chromatography of the crude oxidation product over silica, with ethyl acetate-light petroleum (1:1) as eluant, gave the acetal (187) (Rf = 0.43) as colourless crystals (0.281g, 69%), m.p. 53-54°C (from diethyl ether-light petroleum) (Found: C, 60.3; H, 6.8; N, 12.7. C_{16}H_{21}N_{3}O_{4} requires C, 60.2; H, 6.6; N, 13.1%);

\[\nu_{\text{max}} \text{ (Nujol): } 3290 \text{s}, 1740 \text{s}, 1675 \text{s}, 1595 \text{m}, 1235 \text{s}, 1140 \text{s}, 1050 \text{s}, 1015 \text{g}, 930 \text{s}, 850 \text{m}, 775 \text{s}, 735 \text{w}, 700 \text{s} \text{ and } 645 \text{w cm}^{-1}.\]

\[\delta_{\text{H}} \text{ (CDCl}_3, 300 \text{ MHz): } 8.23 \text{ (ddd, J8.0, 1.5 and 0.6Hz, ArH}_6\), 7.74 \text{ (ddd, J8.1, 7.3 and 1.5Hz, ArH}_7\), 7.67 \text{ (ddd, J8.1, 1.3 and 0.6Hz, ArH}_8\), 7.45 \text{ (ddd, J8.0, 7.3 and 1.3Hz, ArH}_8\), 6.02 \text{ (t, J5Hz, CH}_2\text{CH(OEt)OCOCH}_3\), 5.74 \text{ (t, J7.1Hz, exch. D}_2\text{O N-H)}, 3.82 \text{ (dq, J9 and 7Hz, CH}_3\text{HCHO)}, 3.65 \text{ (dq, J9 and 7Hz, CH}_3\text{HCHO)}, 3.21 \text{ (br.m, NH.HCH)}, 3.17 \text{ (br.m, NH.HCH)}, 3.03 \text{ (br.q, J7Hz, CH}_2\text{CH}_3\), 2.11 \text{ (s, OCOCCH}_3\), 1.38 \text{ (t, J7Hz, CH}_2\text{CH}_3\) and 1.23 \text{ (t, J7Hz, OCH}_2\text{CH}_3\);}

\[M/Z \text{ (%): } 3.19(M+1,1), 260(15), 259(75), 230(7), 203(19), 202(50), 175(80), 174(100), 173(70), 157(15), 131(20) \text{ and } 119(13).\]
Preparation of 3-chloro-1-(trimethylsilyl)propan-2-one (188)

\[
\begin{align*}
\text{Me}_3\text{Si} & \quad \text{O} \\
\text{Cl} & \quad \text{Cl}
\end{align*}
\]

A solution of trimethylsilylmethylmagnesium chloride (6x10^{-3} mol) in diethyl ether (10 ml) was added dropwise to a solution of chloroacetic anhydride (1.0 g, 6x10^{-3} mol) in diethyl ether (10 ml) at -78°C. The solution was stirred at -78°C for 8h and allowed to warm slowly to 0°C. The reaction mixture was re-cooled to -10°C and 10% aqueous ammonium chloride solution (20 ml) was added. The organic layer was separated, washed with aqueous sodium bicarbonate solution, and dried over anhydrous potassium carbonate. The solvent was removed in vacuo (15 mmHg) and the residue purified by vacuum distillation to give a colourless oil (0.69 g, 70%), b.p. 40°C (1 mmHg) which was identified as 3-chloro-1-(trimethylsilyl)propan-2-one (188).^9

\[\nu_{\text{max}} \text{ (Film): } 2960\text{m}, 2900\text{w}, 1710\text{s}, 1405\text{m}, 1300\text{w}, 1250\text{s}, 1190\text{m}, 1100\text{s}, 1065\text{m}, 1040\text{m}, 910\text{w}, 850\text{w}, 810\text{w}, 760\text{w}, 695\text{w}, 670\text{w} \text{ and } 660\text{w} \text{ cm}^{-1};\]

\[\delta_{\text{H (CDCl}_3, 90 \text{ MHz)}: } 3.8 \text{ (s, CH}_2\text{Cl, 2H), 2.3 \text{ (s, } -\text{CH}_2\text{SiMe}_3, 2\text{H) and 0.1 (s, SiMe}_3, 9\text{H).}\]

Isomerisation reaction of 3-chloro-1-(trimethylsilyl)propan-2-one (188)

\[
\begin{align*}
(188) & \quad \text{Me}_3\text{Si} \quad \text{O} \\
& \quad \text{Cl} \quad \text{Cl}
\end{align*}
\]

To 3-chloro-1-(trimethylsilyl)propan-2-one (188) (0.1 g, 6.0x10^{-3} mol) was added [Pd(PPh_3)_4] (0.05 g, 0.04x10^{-3} mol) and the mixture was stirred
for 2h at room temperature. After this stirring, the \textsuperscript{1}H n.m.r. spectrum showed that complete isomerisation to the 3-chloro-2-(trimethylsiloxy)-prop-1-ene (189) had occurred by comparison with the chemical shift values reported in the literature.\textsuperscript{79}

\textbf{Attempted aziridination of 3-chloro-2-(trimethylsiloxy)prop-1-ene (189)}

\[ \begin{array}{c}
\text{QNH} \\
\text{O} \\
\text{Cl} \\
\end{array} \]

\textit{(191)}

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.25g, 1.32x10\textsuperscript{-3} mol), LTA (0.616g, 1.38x10\textsuperscript{-3} mol) and the 3-chloro-2-(trimethylsiloxy)prop-1-ene (189) (0.762g, 4.64x10\textsuperscript{-3} mol) in dry dichloromethane (2.5 ml). The crude oxidation product was triturated with hot light petroleum and the insoluble chloroketone (191) was separated off. Recrystallization afforded the chloroketone (191) as colourless crystals (0.22g, 58%), m.p. 116-119\textdegree C (from ethanol) (Found: C, 55.5; H, 5.07; N, 14.5. C\textsubscript{13}H\textsubscript{14}N\textsubscript{3}O\textsubscript{2}Cl requires C, 55.8; H, 5.04; N, 15.0%);

\( \nu_{\text{max}} \) (Nujol): 3280 br.m, 1710s, 1665s, 1595s, 1490s, 1370m, 1300w, 1250m, 1110m, 1070m, 1045m, 885w, 765s and 695m cm\textsuperscript{-1};

\( \delta_{\text{H}} \) (CDCl\textsubscript{3}, 90 MHz): 8.15 (d, J6Hz, ArH\textsubscript{6}), 7.25-7.8 (m, ArH\textsubscript{7}, ArH\textsubscript{8} and ArH\textsubscript{9}), 5.9 (t, J6Hz, exch. D\textsubscript{2}O, N-H), 4.15 (d, J6Hz, NH.CH\textsubscript{2}CO), 4.15 (s, COCH\textsubscript{2}Cl), 3.0 (q, J7Hz, CH\textsubscript{2}CH\textsubscript{3}) and 1.31 (t, J7Hz, CH\textsubscript{2}CH\textsubscript{3});

M/Z (%): 282(M\textsuperscript{+},\textsuperscript{37}Cl,1), 280(M\textsuperscript{+},\textsuperscript{35}Cl,3), 203(7), 202(47), 201(15), 200(90), 175(39), 174(100), 173(91), 146(47), 145(16), 130(19), 120(21), 119(95), 118(20), 117(10), 103(10), and 102(11).
Evaporation of the filtrate after removal of the chloroketone (191) by filtration afforded the acetal (192). Recrystallization from ethyl acetate-light petroleum gave (192) as colourless crystals (0.005g, 10%), m.p. 49-52°C.

```
\begin{align*}
\text{QNH} \\
&\text{OSiMe}_3 \\
&\text{OAc} \\
&\text{Cl} \\
(192)
\end{align*}
```

ν\text{max} (Nujol): 3300w, 1745s, 1675s, 1595s, 1500m, 1420m, 1300s, 1145s, 1020s, 920s, 850s, 770s, and 700s cm\(^{-1}\);

\(\delta_H\text{ (CDCl}\_3, 300 \text{ MHz}): 8.23\text{ (ddd, J8.1, 1.6 and 0.6Hz, ArH}\_5\text{), 7.73 (ddd, J8.2, 6.9 and 1.6Hz, ArH}\_7\text{), 7.62 (ddd, J8.2, 1.5 and 0.6Hz, ArH}\_6\text{), 7.43 (ddd, J8.1, 6.9 and 1.5Hz, ArH}\_6\text{), 5.77 (t, J7.3Hz, exch. D}_2\text{O, N-H), 4.26 (d, J11.6Hz, HCHCl), 4.1 (d, J11.6Hz, HCHCl), 3.51 (br.m, NHCH}_2\text{), 2.99 (br.m, CH}_2\text{CH}_3\text{), 2.10 (s, COOCH}_3\text{), 1.38 (t, J7.4Hz, -CH}_2\text{CH}_3\text{), and 0.29 (s, -OSiMe}_3\text{);}\)

\(M/Z\ (%): 413(M^+,^{37}\text{Cl,1}), 411(M^+,^{35}\text{Cl,1}), 385(3), 353(52), 351(100), 316(93), 248(28), 246(41), 245(31), 231(39), 203(24), 202(93), 175(98), 174(96), 173(91), 162(32), 119(48),\) and 101(11).

When the crude oxidation product from above was chromatographed over silica, with ethyl acetate-light petroleum (1:2) as eluant, then the major product was the imine (193) obtained as colourless crystals (64%), m.p. 76-78°C (from ethanol) (Found: C, 64.25; H, 5.45; C, 17.20. \(C_{13}H_{13}N_3O_3\) requires C, 64.2; H, 5.48; N, 17.25%).

```
\begin{align*}
\text{Q} &\text{N} \\
&\text{H}_2 \\
&\text{O} \\
(193)
\end{align*}
```
\textit{v}_{\text{max}}\text{ (Nujol): 1695s, 1620s, 1605m, 1580s, 1355m, 1330m, 1260m, 1245m, 1230m, 1210m, 1155m, 1140m, 1080w, 930w, 920w, 775s, 695s, and 650m cm}^{-1};
\begin{align*}
\delta_{\text{H}}\text{ (CDCl}_{3}\text{, 300 MHz): 9.07 (s, N=CHCOCH}_{3}\text{), 8.23 (ddd, J8.1, 1.43 and 0.6Hz, ArH}_{5}\text{), 7.75 (ddd, J8.0, 7.3 and 1.43Hz, ArH}_{7}\text{), 7.66 (ddd, J8.0, 1.5 and 0.6Hz, ArH}_{9}\text{), 7.45 (ddd, J8.1, 7.3 and 1.5Hz, ArH}_{6}\text{), 3.04 (q, J7.5Hz, CH}_{2}\text{CH}_{3}\text{), 2.52 (s, COCH}_{3}\text{), and 1.40 (t, J7.5Hz, CH}_{2}\text{CH}_{3};}
\end{align*}
\begin{align*}
\delta_{\text{C}}\text{ (CDCl}_{3}\text{, 75 MHz): 198.3(s), 159.8(s), 157.7(s), 155.8(d), 145.7(s), 134.8(d), 127.3(d), 127.2(d), 126.8(d), 121.3(s), 28.6(t), 24.7(q), and 11.2(q);}
\end{align*}
M/Z (%): 243(M^{+},1), 202(14), 201(98), 200(100), 175(10), 174(63), 173(89), 146(24), 145(16), 131(19), 130(51), 129(12), 120(19), 119(38), 118(13), 103(26), and 102(20).

Further elution with ethyl acetate-light petroleum (1:2) gave the acetal (192) in 12% yield.

\textbf{Preparation of the methyl trimethylsilylacetal of methyl ketene (216)}

\begin{center}
\begin{tikzpicture}
\begin{scope}
\node (a) at (0,0) {MeO\text{O}};
\node (b) at (1,0) {1. LDA\rightarrow};
\node (c) at (2,0) {CHCH_{3}};
\node (d) at (0,-1) {MeO\text{O}};
\node (e) at (1,-1) {2. Me_{3}\text{SiCl}};
\node (f) at (2,-1) {OSiMe_{3}};
\end{scope}
\end{tikzpicture}
\end{center}

An equimolar amount of n-butyllithium (150 ml) of 0.15M solution in hexane (255x10^{-3} mol) was added dropwise with stirring to a solution of diisopropylamine (22.5g, 225x10^{-3} mol) in dry THF (150 ml) at 0°C under nitrogen. Stirring was continued for 15 min. under the same conditions and the flask was cooled in a dry ice-acetone bath. Methyl propionate (297) (19.8g, 225x10^{-3} mol) was added dropwise and the mixture was stirred for an
additional 30 min. to complete the formation of lithiomethyl propionate. Trimethylsilylchloride (29.2g, 270x10^{-3} mol) was added dropwise with stirring at -78°C over 10 min. and the mixture was stirred for 3h under the same conditions. Methyl iodide (42 ml, 673x10^{-3} mol) and then petroleum ether (b.p. 60-40°C) (100 ml) were added to the mixture which was kept in a fridge overnight and the resultant LiCl and quaternary salt were separated off by filtration. The filtrate was concentrated in vacuo to produce a liquid, which was distilled to give the ketene acetal (216) in 57% yield (b.p. 46-48°C/22 mmHg) (lit. b.p. 46°C/23 mmHg).

$^6$H (CDCl$_3$, 90 MHz): 3.56 (q, 1H, =CH-CH$_3$), 3.45 (s, 3H, OCH$_3$), 1.42 (d, 3H, =CH-CH$_3$), and 0.2 (s, 9H, SiMe$_3$).

Attempted aziridination of the methyl trimethylsilylacetal of methyl ketene (216)

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.25g, 1.32x10^{-3} mol), LTA (0.616g, 1.38x10^{-3} mol) and the foregoing ketene acetal (216) (0.317g, 1.98x10^{-3} mol) in dry dichloromethane (2.5 ml). After work-up the crude product was chromatographed over silica with ethyl acetate-light petroleum (1:2) as eluant, and gave the benzoxazinone (222) as colourless crystals (0.025g, 11%), m.p. 77-79°C (from light petroleum).

$\nu_{\text{max}}$ (Nujol): 1755s, 1650s, 1600m, 1320m, 1255m, 1165m, 1140m, 1105w, 1085m, 1035m, 1020s, 935w, 800w, 780s, 740w, and 690m cm$^{-1}$;
\( \delta_{H} (CDCl_3, 300 \text{ MHz}): 8.2 \) (ddd, J 8.0, 1.57 and 0.5 Hz, ArH\(_{5}\)), 7.8 (ddd, J 8.8, 7.0 and 1.57 Hz, ArH\(_{7}\)), 7.57 (ddd, J 8.8, 1.2 and 0.6 Hz, ArH\(_{5}\)), 7.5 (ddd, J 8.0, 7.0 and 1.2 Hz, ArH\(_{6}\)), 2.73 (q, 7.5 Hz, CH\(_2\)CH\(_3\)), and 1.37 (t, J 7.5 Hz, CH\(_2\)CH\(_3\));

M/Z (%): 175(M\(^+\), 80), 146(100), 120(10), 119(20), and 90(30).

Further elution with the same solvent system afforded the amino ester (219) as colourless crystals (0.079g, 22%), m.p. 64–67°C (from light petroleum) (Found: C, 61.15; H, 6.3; N, 15.25. C\(_{14}\)H\(_{17}\)N\(_3\)O\(_3\) requires C, 61.05; H, 6.2; N, 15.25%);

\( \nu_{max} \) (Nujol): 3280m, 1740s, 1675s, 1595s, 1470s, 1370m, 1335m, 1225s, 1205s, 1180s, 1150m, 880m, 775s, 700s, and 645m cm\(^{-1}\);

\( \delta_{H} (CDCl_3, 300 \text{ MHz}): 8.21 \) (ddd, J 8.1, 1.5 and 0.6 Hz, ArH\(_{5}\)), 7.73 (ddd, J 8.1, 7.2 and 1.5 Hz, ArH\(_{7}\)), 7.66 (ddd, J 8.1, 1.4 and 0.6 Hz, ArH\(_{5}\)), 7.43 (ddd, J 8.1, 7.2 and 1.4 Hz, ArH\(_{6}\)), 5.79 (br.d, J 4.1 Hz, exch. D\(_2\)O, N-H), 3.97 (dq, J 6.9 and 4.1 Hz, NHCHCH\(_3\)), 3.73 (s, CO\(_2\)CH\(_3\)), 3.1 (dq, J 17 and 7.4 Hz, HCHCH\(_3\)), 3.01 (dq, J 17 and 7.4 Hz, HCHCH\(_3\)), 1.4 (d, J 6.9 Hz, NHC(CH\(_3\))H), and 1.35 (t, J 7.4 Hz, CH\(_2\)CH\(_3\));

M/Z (%): 275(M\(^+\),1), 217(30), 175(20), 174(100) and 173(45).

When 3.5 mole equivalents of the ketene acetal (216) were used in this reaction then the aminoester (219) was isolated in ~80% yield by chromatography with no evidence for formation of the benzoxazinone (222).

Attempted aziridination of the methyl trimethylsilyl acetal of methyl ketene (216) in the presence of 2, 6 di-t-butyl-4-methyl pyridine

The same procedure (2) was followed as described in the previous experiment but after the LTA was added, the solution was stirred for 15
min. at low temperature and then 2 mole equivalents of 2,6 di-t-butyl-4-methyl pyridine (223) (0.54g, 2.64x10^-3 mol) added. Stirring was continued for an additional 15 min. and then the acetal (216) was added and the solution allowed to warm to room temperature and worked-up in the manner previously described. Chromatography of the crude oxidation product over silica, with ethyl acetate-light petroleum (1:2) as eluant, isolated the amino ester in 63% yield with no evidence for the benzoazinone (222).

**Preparation of the methyltrimethylsilylacetal of phenyl ketene (217)**

\[
\begin{align*}
\text{MeO} & \quad \text{CH}_2\text{Ph} \quad 1.\text{LDA} \\
\text{MeO} & \quad \text{CHPh} \quad 2.\text{Me}_3\text{SiCl}
\end{align*}
\]

(298) \quad (217)

To a solution of LDA (0.04 mol) was added methyl phenylacetate (298) (6g, 0.04 mol) over a 5 min. period and the stirred solution was maintained at 0°C for 30 min. An excess of trimethylsilylchloride (10.86g, 0.1 mol) was added during a 5 min. period and the mixture was allowed to warm to room temperature. After stirring for 30 min., the mixture was filtered and the solution was concentrated under reduced pressure. The residue was washed with dry ether and filtration was repeated. After removal of the ether, an oil remained that was distilled under reduced pressure (b.p. 92-95°C, 0.5 mmHg). The product (217) was obtained in yields of 80-90% and spectral data were consistent with quoted literature values. 100
Attempted aziridination of the methyl trimethylsilylacetal of phenyl ketene (217)

\[
\begin{align*}
\text{Ph} & \quad \text{NH} \\
\text{H}^- & \quad \text{CO}_2\text{Me} \\
(220)
\end{align*}
\]

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.305g, 1.62x10^{-3} mol), LTA (0.717g, 1.62x10^{-3} mol) and the foregoing acetal (217) (1.257g, 5.65x10^{-3} mol) in dry dichloromethane (5 ml). After work-up the crude oxidation product was chromatographed over silica with ethyl acetate-light petroleum (1:2) as eluant, and gave the ester (220) as colourless crystals (0.42g, 76%), m.p. 86-88°C (from ethanol) (Found: C, 67.6; H, 5.8; N, 12.4. \( \text{C}_{19}\text{H}_{19}\text{N}_3\text{O}_3 \) requires C, 67.6; H, 5.7; N, 12.5%);

\[\nu_{\text{max}} \text{ (Nujol): 3290m, 1745s, 1670s, 1600s, 1435m, 1335s, 1205s, 1180s, 1070m, 1050m, 905m, 775m, 735s, 700s, and 650m cm}^{-1};\]

\[\delta_{\text{H}} \text{ (CDCl}_3, 300 \text{ MHz): 8.24 (ddd, J=8.1, 1.5 and 0.6Hz, ArH}_5), 7.73 (ddd, J=8.1, 7.4 and 1.5Hz, ArH)_7, 7.63 (ddd, J=8.1, 1.3 and 0.6Hz, ArH}_6, 7.45 (ddd, J=8.1, 7.4 and 1.3Hz, ArH)_6, 7.45-7.3 (m, 5xPhH), 6.08 (br.s, exch. D}_2\text{O, N-H), 4.94 (d, J=2Hz, PhCHCO}_2\text{Me), 3.72 (s, CO}_2\text{CH}_3), 2.77 (br.m, CH}_2\text{CH}_3)}, \text{ and 1.17 (t, J=7Hz, CH}_2\text{CH}_3);\]

\[\text{M/Z (%): 338(M+1,1), 279(6), 278(25), 175(40), 174(100), 173(32), 164(10), 146(5), 130(10), 119(13), and 104(40).}\]

The 300 MHz n.m.r. spectrum of (220) at room temperature shows a broad signal for the methylene protons of the quinazolone ethyl group.

When a solution of (220) in dideuterodichloromethane is cooled to -90°C signals assigned to individual rotamers around the N-N bond are identifiable whose ratio from integration is 3:1.

\[\delta_{\text{H}} \text{ (CD}_2\text{Cl}_2, 400 \text{ MHz, 183K, major rotamer): 8.17 (ddd, J=8.1, 1.5 and 0.6Hz, ArH}_5), 7.76 (ddd, J=8.1, 7.4 and 1.5Hz, ArH}_7, 7.63-7.2 (m, 5xPhH, ArH}_6 and} \]

-220-
ArH₆, 6.41 (d, J2Hz, N-H), 4.79 (d, J2Hz, PhCH₂CO₂Me), 3.7 (s, CO₂Me), 2.7 (dq, J17 and 7.5Hz, HCH₂), 1.96 (dq, J17 and 7.5Hz, HCH₂), and 0.98 (t, J7.5Hz, CH₂CH₃);

$^1$H (CD₂Cl₂, 400 MHz, 183K, minor rotamer): 8.1 (dd, J8 and 1.5Hz, ArH₆), 7.76-7.2 (m, 5xPhH, ArH₂, ArH₆ and ArH₆), 5.6 (s, N-H or PhCH₂CO₂Me; in the minor rotamer either the N-H proton or the PhCH₂CO₂Me proton is obscured), 3.62 (dq, J17 and 7.5Hz, HCH₂), 3.48 (s, CO₂Me), 3.33 (dq, J17 and 7.5Hz, HCH₂), and 1.28 (t, J7.5Hz, CH₂CH₃).

Preparation of 1-methoxy-2-methyl-1-trimethylsiloxypropene (218)

To a solution of LDA (0.081 mol) was added methyl isobutyrate (299) (8g, 0.078 mol) over a 5 min. period and the solution was magnetically stirred under nitrogen at 0°C for approximately 1h. An excess of trimethylsilylchloride (21.27g, 0.195 mol) was added over a 15 min. period and the reaction mixture was allowed to warm to room temperature. After stirring for a further 30 min., the mixture was filtered and the solution was concentrated under reduced pressure. The residue was washed with dry ether and filtration was repeated. After removal of the ether, an oil remained that was distilled under reduced pressure (b.p. 30-35°C, 15 mmHg). The product (218) obtained in yields >80% had spectral data consistent with quoted literature values.¹⁰⁰

$^1$H (CDCl₃, 90 MHz): 3.45 (s, OMe), 1.58 (s, CH₃), 1.5 (s, CH₃), and 0.2 (s, OSiMe₃).
Attempted aziridination of 1-methoxy-2-methyl-1-trimethylsiloxyp propane (218)

\[
\begin{array}{c}
\text{Q} \\
\text{NH} \\
\text{CO}_2\text{CH}_3
\end{array}
\]

(221)

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.3g, 1.58x10^{-3} mol), LTA (0.739g, 1.66x10^{-3} mol) and the foregoing ketene acetal (218) (0.968g, 5.56x10^{-3} mol) in dry dichloromethane (3 ml). Chromatography of the crude oxidation product over silica with ethyl acetate-light petroleum (1:2) as eluant, gave the amino ester (221) as colourless crystals (0.4g, 88%), m.p. 87-89°C (from light petroleum) (Found: C, 62.5; H, 6.55; N, 14.55. C\textsubscript{15}H\textsubscript{19}H\textsubscript{3}O\textsubscript{3} requires C, 62.25; H, 6.6; N, 14.5%);

\(\nu_{\text{max}}\) (Nujol): 3300m, 1740s, 1680s, 1600s, 1330m, 1295m, 1275m, 1245m, 1220m, 1185s, 1150s, 1140s, 1000m, 865m, 825w, 795m, 775s, 760m, 695s, and 645m cm\(^{-1}\);

\(\delta_{\text{H}}\) (CDCl\textsubscript{3}, 300 MHz): 8.19 (ddd, J8.0, 1.5 and 0.6Hz, Ar\textsubscript{b}), 7.72 (ddd, J8.1, 7.4 and 1.5Hz, Ar\textsubscript{b}), 7.65 (ddd, J8.1, 1.3 and 0.6Hz, Ar\textsubscript{a}), 7.41 (ddd, J8, 7.4 and 1.3Hz, Ar\textsubscript{a}), 5.87 (br.s, exch. D\textsubscript{2}O, N-H), 3.81 (s, CO\textsubscript{2}Me), 3.01 (br.m, CH\textsubscript{2}CH\textsubscript{3}), 1.35 (t, J7.5Hz, CH\textsubscript{2}CH\textsubscript{3}), and 1.32 (br.s, (CH\textsubscript{3})\textsubscript{2}C);

M/Z (%): 289(M\textsuperscript{+},5), 231(15), 230(100), 176(10), 175(9), and 174(7).
Preparation of 1-methoxy-1-trimethylsiloxy-3-methyl-1,3-butadiene (224)

To a solution of LDA (0.0552 mol) at -78°C in THF (30 ml) was added the ester (300) (6g, 0.0525 mol) over a 5 min. period and the stirred solution was maintained at -78°C by means of a dry ice-acetone bath. An excess of trimethylsilylchloride (6.85g, 0.063 mol) was added at -78°C over a 10 min. period and the mixture was allowed to warm to room temperature. After stirring at room temperature for 30 min. the mixture was filtered and the solvent was concentrated by evaporation under reduced pressure. The residue was washed with dry ether and filtration was repeated. The ether was then evaporated under reduced pressure to give the acetal (224). The product was distilled (b.p. 45-49°C, 0.5 mmHg) (lit.101 b.p. not quoted) and was obtained in 90% yield.

$\delta_H$ (CDCl$_3$, 90 MHz): 4.9 (m, C=CHH), 4.6 (m, C=CHH), 4.4 (s, CH), 3.6 (s, OMe), 2.05 (s, CH$_3$), and 0.3 (s, OSiMe$_3$).

Attempted aziridination of 1-methoxy, 1-trimethylsiloxy-3-methyl-1,3-butadiene (224)

The general procedure (2) was followed using the N-aminoquinazolone
(77) (0.5g, 2.64x10^{-3} mol), LTA (1.23g, 2.77x10^{-3} mol) and the foregoing butadiene (224) (1.72g, 9.25x10^{-3} mol) in dry dichloromethane (5 ml). After work-up, the crude oxidation product was chromatographed over silica with ethyl acetate-light petroleum (1:2) as eluant, to give the ester (225) as colourless crystals (0.34g, 43%), m.p. 59-61°C (from light petroleum) (Found: C, 64.0; H, 6.5; N, 13.6. C_{16}H_{19}N_{3}O_{3} requires C, 63.8; H, 6.4; N, 13.9%);

\[ \nu_{\text{max}} \text{ (Nujol): } 3280\text{m}, 1745\text{s}, 1680\text{s}, 1595\text{s}, 1335\text{s}, 1220\text{s}, 1180\text{s}, 1100\text{m}, 1050\text{m}, 1020\text{m}, 940\text{m}, 910\text{m}, 770\text{s}, 735\text{m}, 700\text{s}, \text{and } 645\text{m }\text{cm}^{-1}; \]

\[ \delta_{\text{H}} \text{ (CDCl}_{3}, 300 \text{ MHz): } 8.22 \text{ (ddd, J8.0, 1.62 and 0.6Hz, ArH}_{5}), 7.74 \text{ (ddd, J8.1, 7.3 and 1.6Hz, ArH}_{2}), 7.66 \text{ (ddd, J8.1, 1.5 and 0.6Hz, ArH}_{3}), 7.44 \text{ (ddd, J8.0, 7.3 and 1.5Hz, ArH}_{6}), 6.00 \text{ (d, J3Hz, exch. D}_{2}O, N-H), 5.03 \text{ (m, HCH=C(CH}_{3})_{2}), 4.94 \text{ (m, HCH=C(CH}_{3})_{2}), 4.27 \text{ (d, J3Hz, NHCH}_{3}), 3.81 \text{ (s, CO}_{2}CH}_{3}), 3.1 \text{ (dq, J16 and 7.5Hz, } HCHCH_{3}), 2.89 \text{ (dq, J16 and 7.5Hz, HCHCH}_{3}), 1.86 \text{ (m, CH}_{2}=C(CH}_{3})_{2}), \text{and } 1.34 \text{ (t, J7.5Hz, CH}_{2}CH}_{3}); \]

\[ M/Z \text{ (%): } 301(M^+1), 242(25), 175(29), 174(100), 173(50), 146(10), 130(8), \text{and } 119(12). \]

Further elution with ethyl acetate-light petroleum (1:2) afforded the ester (226) (0.33g, 42%) as two double bond stereoisomers in a 1:1 ratio. Fractional crystallization from ethanol gave a single stereoisomer of the ester (226), m.p. 104-107°C (Found: C, 63.8; H, 6.35; N, 13.95. C_{16}H_{19}N_{3}O_{3} requires C, 63.75; H, 6.35; N, 13.95%);

\[ \nu_{\text{max}} \text{ (Nujol): } 3260\text{s}, 1710\text{s}, 1595\text{s}, 1530\text{s}, 1230\text{s}, 1180\text{s}, 1160\text{s}, 1105\text{m}, 1050\text{m}, 915\text{m}, 880\text{m}, 840\text{m}, 775\text{s}, 700\text{m}, \text{and } 650\text{m }\text{cm}^{-1}; \]

\[ \delta_{\text{H}} \text{ (CDCl}_{3}, 300 \text{ MHz, single stereoisomer): } 8.24 \text{ (ddd, J8.1, 1.5 and 0.6Hz, ArH}_{5}), 7.75 \text{ (ddd, J8.1, 7.2 and 1.5Hz, ArH}_{2}), 7.67 \text{ (ddd, J8.1, 1.4 and 0.6Hz, ArH}_{3}), 7.45 \text{ (ddd, J8.1, 7.2 and 1.4Hz, ArH}_{6}), 6.04 \text{ (m, } =CH.CO_{2}Me), 5.59 \text{ (t, J7Hz, exch. D}_{2}O, N-H), 4.10 \text{ (br.m, NHCH}_{2}), 3.72 \text{ (s, CO}_{2}CH}_{3}, 3.00 \]
(br. q, \(-\text{CH}_2\text{CH}_3\)), 2.27 (d, J14Hz, vinylic Me), and 1.39 (t, J7.3Hz, \(\text{CH}_2\text{CH}_3\));

M/Z (%): 302(M+1,1), 270(5), 175(70), 174(100), 173(90), 146(15), 130(22), 128(25), and 119(17).

The other stereoisomer of the ester (226) could not be obtained in a pure form free from the other double bond isomer but was identified in the 1:1 mixture of (226) by characteristic signals at; 8.3-7.4 (m, 4xArH), 3.59 (s, \(\text{CO}_2\text{CH}_3\)), 2.12 (d, J1.4Hz, vinylic Me), and 1.38 (t, J7.3Hz, \(\text{CH}_2\text{CH}_3\)).

**Attempted aziridination of the methyl trimethylsilylacetal of phenyl ketene (217) using (116)**

![Diagram](image)

The general procedure (2) was followed using the N-aminoquinazolone (116) (0.45g, 1.60x10^-3 mol), LTA (0.746g, 1.68x10^-3 mol) and the ketene acetal (217) (1.245g, 5.6x10^-3 mol) in dry dichloromethane (4.5 ml). Chromatography of the crude oxidation product over silica, with ethyl acetate-light petroleum (1:1) as eluant, afforded the amino ester (229) (\(R_f = 0.5\)) as a colourless oil (0.39g, 56%).

The high resolution accurate mass scan showed no molecular ion at 429 however, an (M+H^+) ion was present at 430, Found: M+H/Z 430.1763. 

C_{25}H_{24}N_3O_4 requires M, 430.1766;

\(\nu_{\text{max}}\) (Film): 3280br.m, 1735s, 1675s, 1600s, 1490s, 1465s, 1430s, 1370s,
890m, 775s, 735s, and 700 cm\(^{-1}\);

\(\delta_H (\text{CDCl}_3, 300 \text{ MHz})\): 8.19 (ddd, J7.9, 1.3 and 0.6Hz, ArH\(_6\)), 7.72 (ddd, J8, 7.3 and 1.3Hz, ArH\(_7\)), 7.62 (ddd, J8, 1.2 and 0.6Hz, ArH\(_8\)), 7.5-7.1 (m, 10 x ArH\(_6\) and ArH\(_8\)), 6.92 (d, J2Hz, exch. D\(_2\)O, N-H), 5.05 (d, J2Hz, CHCO\(_2\)Me), 4.8 (d, J15Hz, HCH-quinaz.), 4.57 (s, PhCH\(_2\)), 4.4 (d, J15Hz, HCH-quinaz.), and 3.67 (s, CO\(_2\)CH\(_3\));

M/Z (%): 430(M+H,2), 371(3), 370(13), 267(15), 237(15), 236(6), 235(7), 175(7), 164(9), 161(27), 160(100), 121(5), 119(5), 104(14), 91(78), 85(5), 83(9), and 77(10).

**Attempted aziridination of the methyl trimethylsilylacetal of phenyl ketene (217) using (230)**

\[
\begin{align*}
\text{Ph} & \quad \text{CO}_2\text{Me} \\
\text{N} & \quad \text{NH} \\
\text{Bu} & \quad \text{N}
\end{align*}
\]

(232)

The general procedure (2) was followed using the N-aminoquinazolone (230) (0.3g, 1.449x10\(^{-3}\) mol) and the ketene acetal (217) (1.074g, 4.83x10\(^{-3}\) mol) in dry dichloromethane (3 ml). Chromatography of the crude oxidation product over silica with ethyl acetate-light petroleum (1:4) as eluant, gave the amino ester (232) as colourless crystals (0.176g, 35%), m.p. 187-189\(^{\circ}\)C (from acetonitrile) (Found: C, 68.90; H, 6.45; N, 11.75. C\(_{21}\)H\(_{23}\)N\(_3\)O\(_3\) requires C, 69.0; H, 6.35; N, 11.5%);

\(\nu_{\max} (\text{Nujol})\): 3260s, 1740s, 1665s, 1580m, 1565m, 1260m, 1175m, 1150m, 900m,
780m, 725m, and 700m cm⁻¹;

\( \delta_H (\text{CDCl}_3, 300 \text{ MHz}) \): 8.2 (dd, J8.1, 1.38 and 0.55Hz, ArH₅), 7.72 (dd, J8.2, 7.29 and 1.38Hz, ArH₇), 7.64 (dd, J8.2, 1.52 and 0.55Hz, ArH₇), 7.42 (dd, J8.1, 7.29 and 1.52Hz, ArH₆), 7.38-7.27 (m, 5xArH), 6.14 (d, J5.37, exch. D₂O, N-H), 4.55 (d, J5.37Hz, CHCO₂CH₃), 3.77 (s, CO₂CH₃), and 1.33 (s, C(CH₃)₃).
EXPERIMENTAL
Chapter 5
Attempted aziridination of 3-trimethylsilyl-3-buten-2-one (233)

\[
\begin{array}{c}
\text{N} \\
\text{C} \quad \text{O} \\
\text{C} \quad \text{H}_3
\end{array}
\]

(234)

The general procedure (2) was followed using the N- aminoquinazolone (77) (0.2 g, 1.05 x 10^{-3} mol), LTA (0.493 g, 1.11 x 10^{-3} mol) and (233) (0.45 g, 3.17 x 10^{-3} mol), in dry dichloromethane (2 ml). Chromatography of the crude oxidation product over silica with ethyl acetate-light petroleum (1:2) as eluant, gave aziridine (234) (0.029 g, 11%), m.p. 70-72°C (from ethanol) [see following experiment].

Aziridination of methyl vinylketone

The general procedure (2) was followed using the N- aminoquinazolone (77) (0.2 g, 1.05 x 10^{-3} mol), LTA (0.493 g, 1.11 x 10^{-3} mol) and methyl vinylketone (0.22 g, 3.17 x 10^{-3} mol) in dry dichloromethane (2 ml). Chromatography of the crude oxidation product over silica with ethyl acetate-light petroleum (1:2) as eluant, gave methyl-1-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-aziridine-2-vl ketone (234) as colourless crystals (0.167 g, 61%), m.p. 70-72°C (from ethanol) (Found: C, 65.25; H, 5.97; N, 16.09. \( C_{14}H_{15}N_3O_2 \) requires C, 65.35; H, 5.85; N, 16.35%);

\( \nu_{\text{max}} \) (Nujol): 1700s, 1665s, 1600s, 1470s, 1285s, 1240s, 1225s, 1135m, 915m, 815m, 775s, 700s, and 690m cm^{-1};

\( \delta_H \) (CDCl₃, 300 MHz): 8.14 (ddd, J8, 1.4 and 0.65Hz, ArH₅), 7.69 (ddd, J8.1, 7.6 and 1.4Hz, ArH₇), 7.62 (ddd, J8.1, 1.3 and 0.65Hz, ArH₅), 7.42 (ddd, J8, 7.6 and 1.35Hz, ArH₆), 3.57 (dd, J8.1 and 5.2Hz, HCOCH₃), 3.03 (m,
CH₂CH₃), 3.00 (d, J8.1Hz, azir. H-3 trans to COCH₃), 2.93 (dd, J5.2 and 1.32Hz, azir. H-3 cis to COCH₃), 2.35 (s, COCH₃), and 1.42 (t, J7.4Hz, CH₂CH₃);

M/Z (%): 257(M⁺,72), 200(17), 185(11), 175(22), 174(62), 173(65), 146(10), 132(14), 131(100), 130(66), 119(20), and 109(25).

Preparation of benzenesulphonylhydrazine (301)

\[
\text{PhSO}_2\text{Cl} + 2\text{N}_2\text{H}_4 \rightarrow \text{PhSO}_2\text{NHNH}_2 + \text{N}_2\text{H}_4\cdot\text{HCl}
\]

(302) (301)

Into a 500 ml round-bottomed three-necked flask fitted with a thermometer, a mechanical stirrer, and a dropping funnel was placed benzenesulphonylchloride (302) (50g, 0.283 mol) and THF (80 ml). The stirred mixture was then cooled in an acetone-ice bath to 10°C, then a solution of hydrazine in water (96%, 32.47g, 0.648 mol) was added at such a rate that the temperature was maintained between 10°C and 15°C. Stirring was continued for 15 min. after the addition was complete. The reaction mixture was then transferred to a separating funnel. The lower layer was drawn off, and the upper THF solution was washed with saturated, aqueous sodium chloride (2x60 ml). The THF layer was dried over anhydrous magnesium sulphate then filtered through anhydrous magnesium sulphate. The filter cake was then washed with dry THF (35 ml) to remove the absorbed hydrazine. The clear combined filtrates were transferred to a 500 ml conical flask and diluted with petroleum ether (100 ml) whilst being vigorously agitated.

The benzenesulphonylhydrazine (301) separated as colourless platelets.
The hydrazide (301), after cooling in a fridge overnight to complete crystallization was then filtered, recrystallization from petroleum ether gave benzenesulphonylhydrazide (301) in 90% yield as colourless crystals, m.p. 101-103°C (lit.\textsuperscript{147} m.p. 101-103°C).

$\nu_{\text{max}}$ (Nujol): 3380s, 3220s, 1440m, 1300s, 1155s, 1115s, 1085s, 815s, 750s, 730s, and 680s cm$^{-1}$;

$\delta_{\text{H}}$ (CDCl\textsubscript{3}, 90 MHz): 8.0-7.35 (m, 5 x PhH and N-H), and 3.15 (br.s, NH$_2$).

Preparation of the benzenesulphonylhydrazone of acetophenone (237)

\[
\begin{align*}
\text{PhSO}_2\text{NNHNH}_2 & \rightarrow \text{PhSO}_2\text{NNH} & \text{Ph} \\
(301) & & (237)
\end{align*}
\]

Acetophenone (13.97g, 0.116 mol) was added to a solution of the benzenesulphonylhydrazine (301) (10g, 0.058 mol) in ethanol (100 ml). The reaction mixture was then stirred overnight at room temperature. After such time the ethanol was removed under reduced pressure to leave a white solid. The solid was recrystallized from ethanol to yield acetophenone-benzenesulphonylhydrazone (237) (14g, 89%), m.p. 128-130°C (lit.\textsuperscript{156} m.p. not quoted).

$\nu_{\text{max}}$ (Nujol): 3160s, 1325s, 1295s, 1155s, 1080m, 1040m, 1020m, 915m, 745s, 730s, and 685s cm$^{-1}$;

$\delta_{\text{H}}$ (CDCl\textsubscript{3}, 90 MHz): 8.2-7.1 (m, 10xPhH and N-H), and 2.15 (s, CH$_3$).
Preparation of α-trimethylsilylstyrene (235)

\[
\begin{align*}
\text{PhSO}_2\text{NNHN} & \quad \text{Ph} \\
\text{CH}_3 & \quad 1 \text{n-BuLi} \\
& \quad 2 \text{Me}_3\text{SiCl} \\
\rightarrow & \quad \text{Ph} \quad \text{SiMe}_3
\end{align*}
\]

(237) (235)

A solution of the benzenesulphonylhydrazone of acetophenone (237) (7g, 0.025 mol) in dry and distilled THF (40 ml) was stirred and cooled to -78°C. To the mixture, a solution of n-butyllithium (40.87 ml, 0.102 mol) was added dropwise. After 1.5h, the reaction mixture was allowed to warm to room temperature. After 40 min. the reaction mixture was cooled back to -78°C. Trimethylsilylchloride (11.1g, 0.102 mol) was added dropwise and the mixture was allowed to warm to room temperature overnight. The reaction mixture was extracted with ether, the ether solution washed with 3% hydrochloric acid, then with saturated salt solution. The ether solution was then dried (MgSO\textsubscript{4}), evaporated under reduced pressure and the residue distilled to give α-trimethylsilylstyrene (70%); b.p. 73-78°C at 5 mmHg (lit.\textsuperscript{110} b.p. 73-78°C at 8 mmHg).

\[\delta_H (\text{CDCl}_3, 90 \text{ MHz}): 7.5-7.1 (\text{m, 5xPhH}), 5.88 (\text{d, J2Hz, C=CHH}), 5.65 (\text{d, J2Hz, C=CHH}), \text{and } 0.25 (\text{s, SiMe}_3)\].

Aziridination of α-trimethylsilylstyrene

\[
\begin{align*}
\text{Q} & \quad \text{SiMe}_3 \\
\text{N} & \quad \text{Ph}
\end{align*}
\]

(238)

The general procedure (2) was followed using the N-aminooquinazolone
(77) (0.25g, 1.32x10^{-3} mol), LTA (0.616g, 1.38x10^{-3} mol) and α-trimethylsilylstyrene (235) (0.349g, 1.98x10^{-3} mol) in dry dichloromethane (2.5 ml). Chromatography of the crude oxidation product over silica with ethyl acetate-light petroleum (1:2) as eluant, afforded 1-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-2-trimethylsilyl-2-phenylaziridine (238) as colourless crystals (0.12g, 25%), m.p. 108-110°C (from light petroleum) (Found: C, 69.55; H, 7.05; N, 11.5. C_{21}H_{25}N_{3}OSi requires C, 69.4; H, 6.95; N, 11.55%);

ν_{max} (Nujol): 1660s, 1585s, 1360m, 1330m, 1280m, 1240s, 1220m, 905m, 835s, 760s, 730s, and 700s cm^{-1};

ν_{H} (CDCl_{3}, 300 MHz, major inver TOMER, quinaz. and SiMe_{3} cis): 8.26 (ddd, J7.9, 1.4 and 0.6Hz, ArH_{5}), 7.72 (ddd, J8, 7.4 and 1.4Hz, ArH_{7}), 7.65 (ddd, J8, 1.25 and 0.6Hz, ArH_{6}), 7.45 (ddd, J8, 7.4 and 1.25Hz, ArH_{8}), 7.72-7.27 (m, 5xPhH), 3.17 (dq, J16 and 7.5Hz, HCHCH_{3}), 3.06 (d, J1.2Hz, azir. ring H-3 cis to quinaz.), 3.04 (dq, J16 and 7.5Hz, HCHCH_{3}), 2.65 (d, J1.2Hz, azir. ring H-3 trans to quinaz.), 1.42 (t, J7.5Hz, CH_{2}CH_{3}), and -0.1 (s, SiMe_{3}).

Aziridine (238) exists in solution at room temperature as a 13:1 ratio of inver TOMERS at nitrogen. The presence of the minor inver TOMER (quinaz. and SiMe_{3} trans) was recognised by its distinguishable signals at: 7.89 (dd, J7.9 and 1.4Hz, ArH_{5}), 7.57 (ddd, J8, 7.4 and 1.4Hz, ArH_{7}), and 0.19 (s, SiMe_{3});

M/Z (%): 363 (M^{+},8), 348(5), 334(52), 246(14), 245(26), 231(22), 200(37), 176(16), 175(17), 174(26), 173(13), 157(16), 147(11), 135(12), 131(12), 130(21), 117(25), 103(13), and 73(100).
Preparation of the benzenesulphonylhydrazone of propiophenone (239)

$$\text{PhSO}_2\text{NHN}\text{H}_2 \rightarrow \text{PhSO}_2\text{NHN} \equiv \text{Ph}$$

(301) (239)

Propiophenone (15.6g, 0.116 mol) was added to a solution of the benzenesulphonylhydrazine (10g, 0.058 mol) in ethanol (100 ml). The reaction mixture was then stirred overnight at room temperature. After such time the ethanol was removed under reduced pressure to leave a white solid. The solid was crystallized from ethanol to yield the benzene-sulphonylhydrazone (239) (14.2g, 85%), m.p. 136-138°C (lit.\textsuperscript{156} m.p. not quoted).

$\nu_{\text{max}}$ (Nujol): 3220s, 1383s, 1345s, 1180s, 1170s, 1090m, 1045m, 840s, 762s, 755s, 740s, 720s, 685s, and 625s cm\(^{-1}\);

$\delta_H$ (CDCl\(_3\), 90 MHz): 8.3-7.3 (m, 10xPhH and N-H), 2.56 (q, J7.5Hz, CH\(_2\)CH\(_3\)), and 1.2 (t, J7.5Hz, CH\(_2\)CH\(_3\));

M/Z (%): 288(M\(^+\),11), 148(12), 147(100), 146(14), 119(51), 118(37), and 117(25).

Preparation of \(\beta\)-methyl-\(\alpha\)-trimethylsilylstyrene (236)

$$\text{PhSO}_2\text{NHN} \equiv \text{Ph} \xrightarrow{1.\text{n-BuLi}, 2.\text{Me}_3\text{SiCl}} \text{Ph} \equiv \text{SiMe}_3$$

(239) (236)

Using the same procedure as for the preparation of (235), the hydrazone (239) (7g, 0.024 mol) and n-butyllithium (38.88 ml, 0.097 mol) in THF (40
ml) were reacted together at -78°C for 1.5h and the reaction mixture was quenched with trimethylsilylchloride (10.56 ml, 0.097 mol). After work-up and distillation (b.p. 68-72°C, 1 mmHg) β-methyl-α-trimethylsilylstyrene (236) was obtained as a colourless liquid (3.1g, 67%) (lit.157 b.p. 73-75°C, 4 mmHg) as a 3:1 ratio of double bond isomers.

$\delta_H$ (CDCl$_3$, 90 MHz): 7.6-6.9 (m, 10xPhH), 6.2 (q, J7Hz, C=CH, major), 6.1 (q, J7Hz, C=CH, minor), 1.9 (d, J7Hz, CHCH$_3$, major), 1.55 (d, J7Hz, CHCH$_3$, minor), 1.5 (s, SiMe$_3$, major), and 0.5 (s, SiMe$_3$, minor).

Aziridination of β-methyl-α-trimethylsilylstyrene (236)

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.5g, 2.64x10$^{-3}$ mol), LTA (1.23g, 2.77x10$^{-3}$ mol) and β-methyl-α-trimethylsilylstyrene (236) (1.5g, 7.93x10$^{-3}$ mol) in dry dichloromethane (5 ml). Chromatography of the crude oxidation product over silica with ethyl acetate-light petroleum (1:3) as eluant, afforded 1-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-2-methyl-3-trimethylsilyl-3-phenylaziridine (240) (R$_f$ = 0.46) as colourless crystals (0.075g, 11%), m.p. 111-114°C (from light petroleum) (Found: M/Z 377.1915. C$_{22}$H$_{27}$N$_3$O$_2$Si requires M, 377.1923);

$\nu_{max}$ (Nujol): 1665s, 1595s, 1470m, 1440m, 1220m, 1050m, 900m, 840s, 740s, 705m, and 690m cm$^{-1}$;

$\delta_H$ (CDCl$_3$, 300 MHz, major invertomer, Ph and quinaz. cis): 7.88 (d, J8Hz,
Further elution with ethyl acetate-light petroleum (1:3) gave the aziridine (91) (0.44g, 55%) which was identical in all respects to that isolated previously (see experimental relating to Chapter 2).

The aziridine (240) exists in solution as a 5:1 ratio of invertomers. In the major invertomer the quinazolone was cis to the phenyl group: the minor invertomer (quinazolone trans to the phenyl group) was identified by its characteristic signals at: 8.22 (d, J8Hz, ArH₅), 1.45 (d, J6.5Hz, CHCH₃), 1.36 (t, J7Hz, CH₂CH₃), and 0.01 (s, SiMe₃);

M/Z (%) : 377(M⁺,2), 348(13), 274(12), 245(15), 231(14), 214(20), 204(86), 176(100), 162(19), 157(21), 147(25), 137(23), 130(51), 119(36), and 105(74).

Preparation of α-tributylstannylstyrrene (245)

Following the same procedure given for the preparation of (235), α-tributylstannylstyrrene was prepared using the hydrazone (237) (7g, 0.025 mol), n-butyllithium (40 ml) in dry THF (40 ml) and tributylstannylchloride (33.26g, 0.1 mol). After work-up and distillation, α-tributylstannyl-
styrene (245) (b.p. 120-125°C, 1 mmHg) was obtained as a colourless liquid (5.72 g, 57%) (lit. b.p. 135°C, 1 mmHg).

$\delta_H$ (CDCl$_3$, 90 MHz): 7.15 (m, 5 x PhH), 6.0 (d, J=2 Hz, C=CH$_2$), 5.3 (d, J=2 Hz, C=CH$_2$), and 1.6-0.6 (m, 3 x (CH$_2$)$_3$CH$_3$).

**Preparation of $\beta$-methyl-\(\alpha\)-tributylstannylstyrene (241)**

\[
\begin{align*}
\text{PhSO$_2$NHN=Ph} & \xrightarrow{1. n-BuLi} \text{PhSnBu$_3$} \\
\text{PhSO$_2$NHN=Ph} & \xrightarrow{2. Bu$_3$SnCl} \text{PhSnBu$_3$} \\
(239) & \quad (241)
\end{align*}
\]

Using the same procedure as for the preparation of (235), $\beta$-methyl-\(\alpha\)-tributylstannylstyrene (241) was prepared using the hydrazone (239) (7 g, 0.024 mol), n-butyllithium (40 ml) in THF (40 ml) and tributylstannylchloride (26.37 ml, 0.1 mol). After work-up and flash chromatography over silica with petroleum ether as eluant, $\beta$-methyl-\(\alpha\)-tributylstannylstyrene was obtained as a colourless liquid (5.85 g, 60%) and a 3:1 ratio of double bond isomers.

$R_f$ = 0.7 (light petroleum);

$\delta_H$ (CDCl$_3$, 90 MHz): 7.5-6.8 (m, 10 x PhH), 6.25 (q, J=6 Hz, C=CH, major stereoisomer), 5.8 (q, J=6 Hz, C=CH, minor stereoisomer), and 1.9-0.6 (m, 3 x (CH$_2$)$_3$CH$_3$, obscuring CH$_3$'s).
Preparation of $\beta$-methyl-$\alpha$-trimethylstannylstyrene (242)

\[
\begin{align*}
\text{PhSO}_2\text{NNH} & \rightarrow \text{Ph}^\prime \text{SnMe}_3 \\
\text{(239)} & \rightarrow \text{(242)}
\end{align*}
\]

Using the same procedure as for the preparation of (235), the hydrazone (239) (7g, 0.024 mol) and n-butyllithium (38.88 ml, 0.096 mol) in THF were reacted together at $-78^\circ$C for 1.5h. After raising the solution temperature to ambient and re-lowering, the crude reaction mixture was quenched with trimethylstannylicloride (7.26g, 0.036 mol) in THF (5 ml). After work-up and distillation (b.p. 75-80°C, 1 mmHg) $\beta$-methyl-$\alpha$-trimethylstannylstyrene was obtained as a colourless liquid (3.61g, 53%) and as a 3:1 ratio of double bond isomers.

$\delta_H$ (CDCl$_3$, 90 MHz): 7.6-6.9 (m, Ph), 6.54 (q, J7Hz, C=CH, major stereoisomer), 5.95 (q, J7Hz, C=CH, minor stereoisomer), 1.95 (d, J7Hz, CHCH$_3$, major stereoisomer), 1.7 (d, J7Hz, CHCH$_3$, minor stereoisomer), 0.45 (s, SnMe$_3$, major stereoisomer), and 0.3 (s, SnMe$_3$, minor stereoisomer).

Preparation of the 2',4',6'-triisopropylbenzenesulphonyldrazone of propan-2-one (247)

\[
\begin{align*}
\text{SO}_2\text{NNHNH}_2 & \rightarrow \text{SO}_2\text{NNHNH} \\
\text{(303)} & \rightarrow \text{(247)}
\end{align*}
\]

Acetone (40 ml, 0.87 mol) was added to 2,4,6-triisopropylbenzenesulphonyldrazine (303) (5g, 16.8x10$^{-3}$ mol$^{159}$ under nitrogen at 0°C.
When the hydrazine had been dissolved, the excess acetone was removed under reduced pressure to leave a white solid. The solid was recrystallized from light petroleum (80-100°C) to yield the 2',4',6'-triisopropylbenzenesulphonylhydrazone (247) (4.74g, 84%), m.p. 135-137°C (lit.160 m.p. 130-132°C).

\[ R_f = 0.48 \text{ (dichloromethane);} \]

\[ ^{1}{\text{H}} (\text{CDCl}_3, 90 \text{ MHz}): 7.09 \text{ (s, 2xArH), 4.2 (quintet, J7.5Hz, 2 x ortho CH(CH}_3)_2), 2.85 \text{ (quintet, J7.5Hz, 1 x para -CH(CH}_3)_2), 1.85 \text{ (s, CH}_3), 1.75 \text{ (s, CH}_3), \text{ and } 1.25 \text{ (d, J7.5Hz, 3 x CH(CH}_3)_2). \]

**Preparation of 2-triphenylstannylpropene (246)**

\[
\begin{align*}
\text{(247)} & \xrightarrow{\text{n-ButLi, } 2\text{Ph}_3\text{SnCl}} \text{(246)} \\
\text{n-Butyllithium} (8.28 \text{ ml, 0.0207 mol}) & \text{ was added to a stirred solution of the foregoing 2',4',6'-triisopropylbenzenesulphonylhydrazone (247) (3.5g, 0.0103 mol) at } -78^\circ\text{C, in DME (5 ml), under nitrogen. The yellow solution was warmed to 0^\circ\text{C for 15 min. during which time bubbles of nitrogen were evolved. The mixture was re-cooled to } -78^\circ\text{C and triphenylstannylchloride (5.98g, 0.015 mol) was added in DME (3 ml) and after 10 min. at } -78^\circ\text{C the solution was allowed to warm slowly to room temperature, then poured into water and extracted with ether. The ether solution was washed with 3% hydrochloric acid, then with saturated salt solution. The ether solution was dried (MgSO}_4) \text{ and evaporated under reduced pressure to give 2-tri-}
\end{align*}
\]
phenylstannylpropene (246) as colourless crystals (3.05g, 76%) from ethanol, m.p. 69-72°C (lit. m.p. 77-79°C).

\( \nu_{\text{max}} \) (Nujol): 1420s, 1070s, 1015m, 990m, 925m, 725s, and 695s cm\(^{-1}\);

\( \delta_H \) (CDCl\(_3\), 90 MHz): 8.0-7.3 (m, 3 x Ph), 6.1 (br.s, C=CHH), 5.5 (br.s, C=CHH), and 2.25 (m, CH\(_3\)).

**Aziridination of \( \alpha \)-tributylstannylstylene (245)**

![Structure](image)

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.6g, 3.17x10\(^{-3}\) mol), LTA (1.47g, 3.33x10\(^{-3}\) mol) and \( \alpha \)-tributylstannylstylene (245) (2.49g, 6.34x10\(^{-3}\) mol) in dry dichloromethane (6 ml). Chromatography of the crude oxidation product over silica with ethyl acetate-light petroleum (1:5) as eluant, afforded 1-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-2-tributylstannyl-2-phenylaziridine (248) \((R_f = 0.34)\) as a colourless oil (0.68g, 37%); (Found: M/Z 582.2503. \( C_{30}H_{44}N_3O\)Sn requires M. 582.2506). The required mass was calculated using the \( ^{120} \text{Sn} \) isotope, atomic mass = 119.902199.

\( \nu_{\text{max}} \) (Film): 1665s, 1595s, 1445m, 1215m, 1050m, and 690s cm\(^{-1}\);

\( \delta_H \) (CDCl\(_3\), 300 MHz): 8.22 (ddd, J7.9, 1.4 and 0.55Hz, ArH\(_5\)), 7.69 (ddd, J8, 7.25 and 0.55Hz, ArH\(_7\)), 7.66-7.15 (m, 5xPhH and ArH\(_9\)), 7.43 (ddd, J7.9, 7.25 and 1.3Hz, ArH\(_8\)), 3.16 (dq, J17 and 7.5Hz, HCHCH\(_3\)), 3.04 (dq, J17 and 7.5Hz, HCHCH\(_3\)), 3.02 (s, azir. H-3 cis to quinaz.), 2.63 (s, azir. H-3 trans to quinaz.), 1.40 (t, J7.5Hz, CH\(_2\)CH\(_3\)), and 1.5-0.5 (m, 3 x Sn (CH\(_2\))\(_3\)CH\(_3\));
Aziridination of β-methyl-α-tributylstannylstylene (241)

\[
\begin{align*}
Q & \quad \text{SnBu}_3 \\
\text{Me} & \quad \text{Ph}
\end{align*}
\]

(249)

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.4g, 2.11x10^-3 mol), LTA (0.986g, 2.22x10^-3 mol) and β-methyl-α-tri- butylstannylstylene (241) (2.58g, 6.34x10^-3 mol) in dry dichloromethane (4 ml). Chromatography of the crude oxidation product over silica with ethyl acetate-light petroleum as eluant, gave 1-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-Z-2-tributylstannyl-3-methyl-2-phenylaziridine (249) (R_f = 0.47) as colourless crystals (0.401g, 32%), m.p. 53-56°C (from ethanol) (Found: C, 62.7; H, 7.65; N, 7.1. C_{31}H_{49}N_2OSn requires C, 62.65; H, 7.65; N, 7.05%); v_{max} (Nujol): 1665s, 1597s, 1460s, 1375m, 1275m, 1210m, 1070w, 925w, 770s, 745m, and 695s cm^{-1};

\[\delta_H\] (CDCl_3, 300 MHz, -40°C, major invertomer, phenyl trans to quinaz.): 8.21 (ddd, J8, 1.3 and 0.6Hz, ArH_6), 7.77 (ddd, J8, 7.3 and 1.3Hz, ArH_7), 7.67 (ddd, J8, 1.4 and 0.6Hz, ArH_6), 7.65-7.10 (m, 5xPhH), 7.4 (ddd, J8, 7.3 and 1.4Hz, ArH_6), 3.21 (dq, J16.5 and 7.5Hz, HCHCH_3), 3.02 (q, J6Hz azir. ring H-3 trans to quinaz. ), 2.94 (dq, J16.5 and 7.5Hz, HCHCH_3), 1.38 (t, J7.5Hz, CH_2CH_3), 1.36 (d, J6Hz, CHCH_3), and 1.3-0.5 (m, 3xSn(CH_2)_3CH_3).

The \[\delta_H\] n.m.r. spectrum of aziridine (249) was recorded after a crystalline sample was dissolved in CDCl_3 at -40°C when only one invertomer

M/Z (%): 582(M^-,1), 523(10), 464(5), 407(100), 405(80), 404(45), 336(10), 294(45), 293(42), 234(10), 175(20), 157(45), 118(52), and 103(10).
at nitrogen was observed. When this sample was allowed to warm to room
temperature then the appearance of the minor invertomer (phenyl cis to
quinaz.) was observed by new signals at: 7.98 (dd, J8.0 and 1.4Hz, ArH₅),
7.7-7.0 (m, 4xArH and 5xPhH), 4.47 (q, J6Hz, azir. ring H-3 cis to quinaz.)
and 1.68 (d, J6Hz, CH₃). The multiplet at 7.65-7.10 in the major
invertomer also increased in complexity due to the presence of signals from
the minor invertomer. In solution at room temperature the aziridine (249)
exists as a 4:1 ratio of invertomers.

Further elution with ethyl acetate-light petroleum (1:4) afforded the
benzoxazinone (222) (0.035g, 9%) which was identical in all respects to
that isolated previously (see experimental relating to Chapter 4).

Aziridination of β-methyl-α-trimethylstannylstyrene (242)

![Structure](250)

The general procedure (2) was followed using the N-aminoquinazolone
(77) (0.5g, 2.64x10⁻³ mol), LTA (1.23g, 2.77x10⁻³ mol) and β-methyl-α-tri-
methylestannylstyrnene (242) (3.72g, 7.92x10⁻³ mol) in dry dichloromethane (5
ml). Chromatography of the crude oxidation product over silica with ethyl
acetate-light petroleum (1:4) as eluant, gave 1-(4-oxo-2-ethyl-3(4H)-quin-
azoliny1)-Z-2-trimethylstannyl-3-methyl-2-phenylaziridine (250) (Rf = 0.41)
as colourless crystals (0.79g, 64%), m.p. 115-118°C (from light petroleum)
(Found: C, 56.55; H, 5.8; N, 8.95. C₂₂H₂₇N₃OSn requires C, 56.45; H, 5.8;
N, 8.95%);
$\nu_{\text{max}}$ (Nujol): 1655s, 1595s, 1565s, 1445m, 1310m, 1220m, 1050m, 1020m, 925w, 770s, 745m, 695s, 690m, and 660m cm$^{-1}$;

$\delta_{H}$ (CDCl$_3$, 300 MHz, -40°C, major invertomer, phenyl and quinaz. trans):
8.18 (ddd, J = 8, 1.4 and 0.5Hz, Ar$H_g$), 7.75 (ddd, J = 8, 7.3 and 1.4Hz, Ar$H_g$),
7.65 (ddd, J = 8, 1.3 and 0.5Hz, Ar$H_g$), 7.6-7.1 (m, 5xPhH), 7.45 (ddd, J = 8, 7.3
and 1.3Hz, Ar$H_g$), 3.19 (dq, J13.5 and 6Hz, HCHCH$_3$), 3.02 (q, J6Hz, azir.
H-3 trans to quinaz.), 2.9 (dq, J13.5 and 6Hz, HCHCH$_3$), 1.38 (d, J6Hz,
CHCH$_3$), 1.35 (t, J6Hz, CH$_2$CH$_3$), and -0.07 (s, SnMe$_3$);

When the crystalline aziridine (250) was dissolved at -40°C the $^1$H
n.m.r. spectrum showed it to exist as a 16:1 ratio of invertomers. In the
major invertomer the quinazolone was found to be trans to the phenyl group;
the minor invertomer (phenyl group cis to the quinazolone) was character­
ised by signals at 7.9 (dd, J7.8 and 1.4Hz, Ar$H_g$), 4.55 (br.s, azir. H-3
 cis to quinaz.), 1.65 (d, J6Hz, CHCH$_3$), 1.82 (t, J6Hz, CH$_2$CH$_3$), and 0.53
(s, SnMe$_3$).

When the temperature of the $^1$H n.m.r. solution was raised to ambient a
change from 16:1 to 8:1 was observed in the invertomer equilibrium re­
measured at -40°C.

N.O.e. experiments were carried out at 233°K and 294°K in order to
assign the stereochemistry in the aziridine ring and the results obtained
were consistent with those predicted for (250a), the major invertomer.

(i) At 233°K (16:1 ratio of invertomers):
1.38 (CHCH$_3$) shows an n.o.e. with 3.02 (azir. H-3, 2.4%) and -0.07 (SnMe$_3$,
1.6%); -0.07 (SnMe$_3$) shows an n.o.e. with 1.38 (CHCH$_3$, 1%); 7.53 (PhH)
shows an n.o.e. with 3.02 (azir. H-3, 2.2%) and -0.07 (SnMe$_3$, 2.5%).

(ii) At 294°K (8:1 ratio of invertomers):
1.65 (CHCH$_3$, minor invertomer) shows an n.o.e. with 4.55 (azir. H-3, 2.5%)
and 0.53 (SnMe$_3$, minor invertomer, 1%).
A further product in this reaction was the aziridine (91) (0.089g, 11%), which was identical in all respects to that isolated previously (see experimental relating to Chapter 2).

Aziridination of 2-triphenylstannylpropene (246)

\[
\begin{array}{c}
\text{Q} \\
\text{N} \\
\text{SnPh}_3 \\
\text{Me}
\end{array}
\]

(251)

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.4g, 2.11x10^{-3} mol), LTA (0.986g, 2.22x10^{-3} mol) and 2-triphenyl-stannylpropene (246) (1.65g, 4.23x10^{-3} mol) in dry dichloromethane (4 ml). Chromatography of the crude oxidation product over silica with ethyl acetate-light petroleum (1:4) as eluant, gave 1-(4-oxo-2-ethyl-3(4H)-quinazoliny1)-2-methyl-2-triphenylstannylaziridine (251) as colourless crystals (0.38g, 31%), m.p. 157-159°C (from light petroleum) (Found: C, 64.35; H, 5.25; N, 7.25. C_{31}H_{29}N_{3}O_{2}Sn requires C, 64.5; H, 4.9; N, 7.25%);

\[\nu_{\max} \text{ (Nujol): } 1645s, 1595s, 1480m, 1425m, 1280m, 1235m, 1220m, 1075m, 770s, 740s, 730s, \text{ and } 700s \text{ cm}^{-1};\]

\[\delta_{H} \text{ (CDCl}_3, \text{ 300 MHz)}: 7.79 \text{ (ddd, J}_8, 1.4 \text{ and } 0.6 \text{Hz, ArH}_5), 7.7-7.1 \text{ (m, ArH}_6, \text{ ArH}_7, \text{ ArH}_8 \text{ and } 15 \text{PhH}), 3.04 \text{ (dq, J}_7 \text{ and } 1.5 \text{Hz, CH}_2\text{CH}_3), 2.95 \text{ (d, J1.5Hz, azir. H-3 cis to quinaz.), 2.78 (d, J1.5Hz, azir. H-3 trans to quinaz.), 1.77 (s, CH}_3\text{), and 1.31 (t, J7Hz, CH}_2\text{CH}_3).\]
Preparation of trans-β-trimethylsilylstyrene (252)

n-Butyllithium (50 ml, 0.124 mol) was added under nitrogen at room temperature to a solution of N,N,N',N'-tetramethylethylenediamine (15 ml) and bis(trimethylsilyl)methane (10 g, 0.0623 mol) in light petroleum (b.p. 60-80°C). The mixture was heated under reflux for 10 h, cooled, and treated with benzaldehyde (6.61 g, 0.062 mol) at 0°C with stirring until the deep red colour had been discharged. The crude reaction product was then poured into water and separated. The organic layer was then washed with saturated sodium metabisulphite solution and dried with MgSO₄ and the solvent was removed by evaporation under reduced pressure. Distillation of the residue gave trans-β-trimethylsilylstyrene (252) (7.5 g, 69%), b.p. 32-37°C, 0.05 mmHg (lit. b.p. 32-34°C, 0.05 mmHg).

ν_max (Film): 1635s, 1600s, 1505s, and 1255s cm⁻¹;  
δ_H (CDCl₃, 90 MHz): 7.5-7.1 (m, 5xPhH), 6.9 (d, J₁₈Hz, HC=CH), 6.35 (d, J₁₈Hz, HC=CH), and 0.02 (s, SiMe₃).

Aziridination of trans-β-trimethylsilylstyrene

The general procedure (2) was followed using the N-aminoquinazolone (77) (0.5 g, 2.64x10⁻³ mol), LTA (1.23 g, 2.77x10⁻³ mol) and trans-β-trimethylsilylstyrene (252) (1.93 g, 7.93x10⁻³ mol) in dry dichloromethane (5 ml). Chromatography of the crude oxidation product over silica with ethyl
acetate-light petroleum (1:6) as eluant, gave 1-(4-oxo-2-ethyl-3(4H)-quinazoliny1)-E-2-trimethylsilyl-3-phenylaziridine (253) as a colourless oil ($R_f = 0.49$) (0.81g, 86%) (Found: M/Z 363.1779. $C_{21}H_{28}N_3OSi$ requires M, 363.1767);

$\nu_{\text{max}}$ (Film): 3040m, 2940m, 1655s, 1585s, 1460m, 1360m, 1330m, 1245m, 1215m, 1020m, 965w, 840s, 770s, 750s, 690s, and 635w cm$^{-1}$;

$\delta_H$ (CDCl$_3$, 300 MHz, major inveromer SiMe$_3$ and quinaz. cis): 8.28 (ddd, $J_{8.1}$, 1.4 and 0.6Hz, ArH$_5$), 7.8-7.0 (m, 5xPhH, ArH$_6$, ArH$_7$, and ArH$_8$), 4.33 (d, J7.5Hz, azir. H-3 cis to quinaz.), 3.27 (dq, J18 and 7Hz, HCHCH$_3$), 3.06 (dq, J18 and 7Hz, HCHCH$_3$), 2.27 (d, J7.5Hz, azir. H-2 trans to quinaz.), 1.47 (t, J7Hz, CH$_2$CH$_3$), and 0.08 (s, SiMe$_3$);

$\delta_H$ (CDCl$_3$, 300 MHz, minor inveromer phenyl and quinaz. cis): 8.34 (d, J8Hz, ArH$_5$), 3.58 (d, J7.5Hz, azir. H-3), 3.37 (d, J7.5Hz, azir. H-2), 2.49 (m, CH$_2$CH$_3$), 1.22 (t, J7Hz, CH$_2$CH$_3$), and 0.38 (s, SiMe$_3$).

The aziridine (253) in a solution of CDCl$_3$ at room temperature exists as a 1:1.8 ratio of inveromers at nitrogen.

M/Z (%): 363(M$^+$,11), 335(56), 334(100), 272(11), 247(13), 246(22), 245(45), 231(22), 200(50), 189(16), 175(13), 174(55), 173(43), 157(16), 146(11), 130(10), 120(22), 119(25), 118(11), 117(29), 116(11), and 105(44).

If the aziridine (253) is exposed to the air for prolonged periods (ca. 2 weeks) then decomposition occurs: a crystalline material isolated from the decomposition products is under further investigation.
Desilylation of aziridine (238)

\[
\begin{align*}
\text{N} & \quad \text{SiMe}_3 \\
\text{Q} & \quad \text{Ph} \\
\text{CsF} & \quad \text{DMF} \\
\text{ca. 5h, R.T.} & \quad \rightarrow \\
\text{N} & \quad \text{Ph}
\end{align*}
\]

(238) \quad (256)

To a solution of CsF (0.040 g, 2.68 \times 10^{-3} \text{ mol}) in dry DMF (2 ml) was added the aziridine (256) (0.065 g, 1.79 \times 10^{-3} \text{ mol}) as a solution in dry DMF (2 ml). The reaction was stirred under nitrogen at room temperature whilst the disappearance of the starting material was monitored by t.l.c. After approximately 5 h, when t.l.c. showed no starting material to be present, the crude reaction mixture was poured into water (25 ml) and extracted with ether (2 \times 25 ml). The organic extracts were combined and dried (MgSO\textsubscript{4}) and the solvent was removed by evaporation under reduced pressure.

Chromatography of the crude reaction product over silica with ethyl acetate-light petroleum (1:4) as eluant, gave a colourless oil (0.019 g, 91%) which was identified as 3-phenyl-2H-azirine (256).\textsuperscript{162}

\[\nu_{\text{max}}\text{ (Film): 3040m, 2980m, 1740m, 1445m, 1320m, 990m, 760s, 690s, and 670m cm}^{-1};\]

lit.\textsuperscript{162} \[\nu_{\text{max}}\text{ (Film): 1740 cm}^{-1};\]

\[\delta_{\text{H}}\text{ (CDCl}_3, 90 \text{ MHz): 8.0-7.5 (m, 5xPhH), and 1.9 (s, CH}_2);\]

lit.\textsuperscript{162} \[\delta_{\text{H}}\text{ (CCl}_4): 8.0-7.8 (m, 5xPhH), and 1.73 (s, CH}_2);\]

M/Z (%): 117(M\textsuperscript{+}, 100), 116(17), 90(35), 89(34), and 77(60).

Further elution using ethyl acetate-light petroleum (1:1) as eluant yielded the de-aminated quinazolone (79) (0.026 g, 84%). No other products were isolated.
Desilylation of aziridine (240)

To a solution of dry CsF (0.074g, 4.88x10^-4 mol) in dry DMF (2 ml) was added the aziridine (240) (0.123g, 3.25x10^-4 mol) as a solution in DMF (2 ml). The reaction was stirred under nitrogen at room temperature and the disappearance of the starting material (240) was monitored by t.l.c. After approximately 5h, when t.l.c. showed no starting material to be present, the crude reaction mixture was poured into water (50 ml) and extracted with ether (2x50 ml). The organic extracts were combined and dried (MgSO_4) and the solvent was removed by evaporation under reduced pressure.

Chromatography of the crude reaction product over silica with ethyl acetate-light petroleum (1:10) as eluant, gave a colourless oil (0.026g, 61%) (R_f = 0.61) which was identified as 2-methyl-3-phenyl-2H-azirine (257).^{125}

\[
\nu_{\text{max}} \text{ (Film): } 1730 \text{ cm}^{-1};
\]

lit.^{125} \nu_{\text{max}} \text{ (Film): } 1730 \text{ cm}^{-1};

\delta_H (CDCl_3, 90 \text{ MHz}): 8.4-8.0 \text{ (m, 5 x PhH)}, 2.26 \text{ (q, J5Hz, CH)}, \text{ and } 1.32 \text{ (d, J5Hz, CH}_3); \\
\text{lit.}^{125} \delta_H (CDCl_3): 8.36-8.0 \text{ (m, 5 x PhH)}, 2.26 \text{ (q, J5Hz, CH)}, \text{ and } 1.32 \text{ (d, J5Hz, CH}_3);

Further elution using ethyl acetate-light petroleum (1:1) yielded the de-aminated quinazolone (79) (0.041g, 73%). No other products were isolated.
Desilylation of aziridine (253)

\[
\begin{align*}
\text{Q} & \overset{\text{CsF}}{\underset{\text{DMF}}{\rightarrow}} \\
\text{SiMe}_3 & \\
\text{Ph} & \quad \text{HN} & \quad \text{Ph} \\
(253) & \quad (259) & \quad (86)
\end{align*}
\]

To a stirred solution of CsF (0.215g, 1.4x10^{-3} mol) in DMF (5 ml) was added the aziridine (253) (0.49g, 1.34x10^{-3} mol). The solution was stirred at room temperature under nitrogen and the disappearance of the starting material (253) was monitored by t.l.c. After 4h, t.l.c. showed no starting material and so the mixture was poured into water (25 ml). The organic extracts were combined and dried (MgSO\(_4\)) and the solvent was removed by evaporation under reduced pressure.

Chromatography of the crude reaction product over silica with ethyl acetate-light petroleum (1:2) as eluant, gave the aziridine (253) (R\(_f\) = 0.49) (0.009g, 23%) which was found to be identical in all respects to that isolated previously (see experimental relating to Chapter 2). Further elution using the same solvent system afforded E-2-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-3-phenylaziridine (259) (R\(_f\) = 0.81) as colourless crystals (0.23g, 58%), m.p. 112-115\(^\circ\)C (from dichloromethane-ether) (Found: C, 73.9; H, 6.0; N, 14.3. C\(_{16}\)H\(_{17}\)N\(_3\)O requires C, 74.2; H, 5.9; N, 14.4%);

\(\nu_{\text{max}}\) (Nujol): 3260s, 1650s, 1590s, 1320m, 1285m, 1250m, 1190m, 1020m, 875m, 775m, 750m, and 690 cm\(^{-1}\);

\(\delta\)\(_H\) (CDCl\(_3\), 300 MHz, room temperature): 8.22 (ddd, J\(_8\), 1.4 and 0.6Hz, ArH\(_5\)), 7.71 (ddd, J8.1, 7.35 and 1.4Hz, ArH\(_7\)), 7.64 (ddd, J8.1, 1.3 and 0.6Hz, ArH\(_8\)), 7.5-7.2 (m, 5xPhH and ArH\(_6\)), 3.99 (br.s, azir. H-3), 3.4 (br.s, azir. H-2), 3.25-2.9 (br.m, CH\(_2\)CH\(_3\)), 1.91 (br.s, exch. D\(_2\)O, N-H), 1.41 (t, J7.5Hz, CH\(_2\)CH\(_3\)).
In the 300 MHz $^1$H n.m.r. spectrum of aziridine (259) some of the signals were broadened at room temperature due to slow inversion at nitrogen. The low temperature spectra (-55°C) was recorded in which both invertomers of aziridine (259) are observed.

At -55°C the ratio of the quinaz. N-H anti aziridine (259a) to the quinaz. N-H syn-aziridine (259b) is 4:1 respectively.

![Diagram of aziridine invertomers]

$^6$H (CD$_2$Cl$_2$, 400 MHz, 233 K) (major invertomer (259a)): 8.17 (ddd, J8, 1.4 and 0.55Hz, ArH$_g$), 7.75 (ddd, J7.9, 7.3, and 1.4Hz, ArH$_r$), 7.61 (d, J7.9, ArH$_b$), 7.47-7.32 (m, 5 x PhH and ArH$_g$), 4.02 (dd, J7.7 and 2.1Hz, azir. H-3), 3.28 (dd, J9.4 and 2.1Hz, azir. H-2), 3.26 (dq, J17 and 7Hz, HCHCH$_3$), 2.91 (dq, J17 and 7Hz, HCHCH$_3$), 2.03 (dd, J9.4 and 7.7Hz, exch. D$_2$O, N-H), 1.36 (t, J7Hz, CH$_2$-Q).

$^6$H (CD$_2$Cl$_2$, 400 MHz, 233 K) (minor invertomer): 8.11 (dd, J7.95 and 1.35Hz, ArH$_g$), 7.75 (ArH$_r$, obscured by signal from major invertomer), 7.60 (d, J8Hz, ArH$_b$), 7.47-7.32 (m, 5 x PhH and ArH$_g$), 3.67 (dd, J6.7 and 1.7Hz, azir. H-3), 3.32 (dd, J10.1 and 1.7Hz, azir. H-2), 3.97 (dq, J17 and 7Hz, HCHCH$_3$), 2.79 (dq, J17 and 7Hz, HCHCH$_3$), 2.25 (dd, J10.1 and 6.7Hz, exch. D$_2$O, N-H), and 1.30 (t, J7Hz, HCHCH$_3$).

N.O.e. experiments were also carried out at 233°K and the following results were obtained:

major invertomer (259a): 4.02 (H-3) shows a n.o.e. with 3.28 (H-2, 2.7%), 2.9 (HCHCH$_3$, 3.5%) and 2.03 (N-H, 5.5%); 2.03 (N-H) shows a n.o.e. with 4.02 (H-3, 8.4%), 3.28 (H-2, 3.9%) and 7.4 (PhH, 7.8%);
minor invertomer (259b): 2.25 (N-H) shows a n.O.e. with 3.32 (H-3, 9.7%) and 3.67 (H-2, 1.7%).

M/Z (%): 291(M^-,5), 289(13), 288(28), 273(13), 272(17), 176(12), 175(17), 174(55), 173(66), 159(20), 157(100), 155(10), 146(10), 130(18), 129(34), 119(31), 118(15), 117(17), 105(13), 103(11), and 102(30).

Desilylation of aziridine (253) in the presence of benzaldehyde

To a stirred solution of CsF (0.248g, 1.63x10^-3 mol) in dry DMF (2 ml) and benzaldehyde (0.47g, 4.46x10^-3 mol) was added the aziridine (253) (0.54g, 1.49x10^-3 mol) as a solution in DMF (5 ml). The solution was stirred at room temperature under nitrogen and the disappearance of the starting material was monitored by t.l.c. After 5h, no starting material remained so the mixture was poured into water and extracted with ether (2x50 ml). The organic extracts were combined and washed with saturated sodium metabisulphite solution and then dried (MgSO_4) and the solvent was removed by evaporation under reduced pressure to give the crude product in 85% yield.

Examination of the ^1H n.m.r. spectrum of the crude reaction product showed an increase in number of aromatic ring protons, indicating that benzaldehyde had been incorporated into the reaction product. This product decomposed on attempted purification by chromatography on silica.

The mass spectrum of the crude product showed a molecular ion at 397 which was consistent with incorporation of benzaldehyde into the reaction products.
Desilylation of aziridine (253) in the presence of benzaldehyde and subsequent oxidation using activated manganese dioxide

\[ \text{CsF, DMF, PhCHO} \rightarrow \text{MnO,} \]

(253)  
(267)

To a stirred solution of CsF (0.345g, 2.27x10⁻³ mol) in dry DMF (3 ml) and benzaldehyde (0.65g, 6.19x10⁻³ mol) was added the aziridine (253) (0.75g, 2.06x10⁻³ mol) as a solution in dry DMF (7 ml). The solution was stirred at room temperature under nitrogen and the disappearance of the starting material was monitored by t.l.c. After approximately 5h, t.l.c. showed no starting material and so the mixture was poured into water (50 ml) and extracted with ether (2x50 ml). The organic extracts were combined and washed with saturated sodium metabisulphite solution, then dried (MgSO₄) and the solvent was removed by evaporation under reduced pressure. The crude reaction product (0.73g, 1.83x10⁻³ mol) was then diluted with CH₂Cl₂ (40 ml) and oxidised using freshly prepared activated manganese dioxide (3.19g, 0.036 mol). The heterogeneous reaction mixture was stirred overnight, then the solution was filtered and the solvent removed by evaporation under reduced pressure to yield E(2,3)-phenyl-1-(4-oxo-2-ethyl-3(4H)-quinazolinyl)-2-phenylaziridine-3-yl ketone (267) as colourless crystals (0.693g, 85% yield from aziridine (253)), m.p. 163-165°C (from ethyl acetate) (Found: C, 75.7; H, 5.5; N, 10.55. C₂₅H₂₁N₃O₂ requires C, 75.95; H, 5.35; N, 10.6%);

\( \nu_{\text{max}} (\text{Nujol}): 1655s, 1590m, 1320w, 1280w, 1215m, 935w, 770m, 740m, 710m, \) and 695s \( \text{cm}^{-1}; \)

\( \delta_H (\text{CDCl}_3, 300 \text{ MHz}, \text{major inverterm benzoyl and quinaz. cis}): 8.05 (dd, J8 and 1.3Hz, ArH₆), 8.0-7.0 (m, 10xPhH, ArH₇, ArH₈ and ArH₇), 4.65 (d, J5Hz,
azir. H-2 cis to quinaz.), 4.31 (d, J5Hz, azir. H-3 trans to quinaz.), 2.92 (dq, J16.5 and 7.3Hz, HCH\textsubscript{3}), 2.8 (dq, J16.5 and 7.3Hz, HCH\textsubscript{3}), 1.29 (t, J7.3Hz, CH\textsubscript{2}CH\textsubscript{3}).

The ratio of invertomers in aziridine (267) was 12:1 at room temperature. The minor invertomer was recognized by the presence of signals at; 5.68 (d, J5Hz, azir. H-2 trans to quinaz.), 4.16 (d, J5Hz, azir. H-3 cis to quinaz.), 3.11 (dq, J16.5 and 7.3Hz, H\textsubscript{CHCH\textsubscript{3}}), 2.46 (dq, J16.5 and 7.3Hz, HCH\textsubscript{3}), and 1.29 (t, J7.3Hz, CH\textsubscript{2}CH\textsubscript{3}).

All other signals due to the minor invertomer of aziridine (267) were either obscured or not observed.

$^1$H-NMR (CDCl\textsubscript{3}, 75 MHz): 188.4(s), 159.2(s), 155.6(s), 145.9(s), 136.8(s), 134.8(s), 133.4(d), 133.1(d), 128.8(d), 128.7(d), 128.5(d), 126.8(d), 126.4(d), 126.05(d), 126.0(d), 120.9(s), 55.4(d), 52.2(d), 27.8(t), and 10.6(q);

M/Z (%): 395(M\textsuperscript{+},1), 290(43), 221(90), 207(14), 193(13), 174(100), 173(95), 166(31), 165(38), 146(17), 131(19), 130(16), 119(48), 118(12), 117(10), 116(24), 106(14), 105(98), and 103(15).

**Aziridination of benzylidene acetophenone**

![Aziridination of benzylidene acetophenone](attachment:image)

(267)

The general procedure (3) was followed using the N-aminoquinazolone (77) (0.5g, 2.64x10\textsuperscript{-3} mol), LTA (1.23g, 2.77x10\textsuperscript{-3} mol) and benzylidene acetophenone (1.65g, 7.93x10\textsuperscript{-3} mol) in dry dichloromethane (5 ml).
Chromatography of the crude oxidation product over silica with ethyl acetate-light petroleum (1:3) as eluant, gave the aziridine (267) ($R_f = 0.32$) as colourless crystals (0.81g, 77%) (from ethyl acetate).

The aziridine (267) produced in this experiment was identical in all respects to that isolated from the previous experiment.
EXPERIMENTAL
Chapter 6
Genercil procedure (4) for the aziridination of alkenes using oxidative (LTA) addition of N-aminoquinazolones in the presence of trifluoroacetic acid

Powdered N-aminoquinazolone (1 mol equiv.) and acetic acid-free lead tetra-acetate (LTA) (1.05-1.1 mol equiv.) were added alternately and continuously in very small portions over 15 min. to a vigorously stirred solution of dry dichloromethane (1 ml/100 mg of N-aminoquinazolone), the alkene(s) (1.5-3.5 mol equiv.) and trifluoroacetic acid (TFA) (1-6 mol equiv.) at room temperature. The mixture was then stirred for 30 min. at room temperature (lead salts remaining in solution) and then washed successively with sodium bicarbonate solution and water, dried with magnesium sulphate and the solvent removed by evaporation under reduced pressure.

Aziridination of hex-1-ene using (77) and procedure (4)

The general procedure (4) was followed using the N-aminoquinazolone (77) (0.5g, 2.64x10^{-3} mol), LTA (1.23g, 2.77x10^{-3} mol), hex-1-ene (0.33g, 3.96x10^{-3} mol) and TFA (1.80g, 1.58x10^{-2} mol) in dry dichloromethane (5 ml). Chromatography of the crude oxidation product over silica, with ethyl acetate-light petroleum (1:3) as eluant, gave the ring-opened aziridine (273) (R_f = 0.5) as an unstable pale yellow oil (0.36g, 35%).

ν_{max} (Film): 3280w, 1785s, 1675s, 1600s, 1470m, 1335m, 1220s, 1170s, 775s, 730w and 700m cm^{-1};
$\delta_H (\text{CDCl}_3, 90\text{ MHz})$: 8.15 (d, J8Hz, ArH$_5$), 7.7-7.2 (m, ArH$_6$, ArH$_7$, and ArH$_8$), 5.5 (br.m, NH and CHOCOCF$_3$), 2.6-3.0 (m, CH$_2$), 2.9 (q, J7Hz, CH$_2$CH$_3$), 1.3 (t, J7Hz, CH$_2$CH$_3$), and 1.8-0.8 (m, 9 x aliphatic H);

M/Z (%): 385(M+,1), 290(9), 289(13), 258(85), 244(73), 216(90), 203(91), 202(98), 200(25), 198(14), 190(33), 189(15), 176(50), 175(100), 174(97), 173(92), 172(89), 160(30), 145(32), 132(45), 131(40), 120(46), 103(47) and 102(37).

Further elution with ethyl acetate-light petroleum (1:3) gave the aziridine (85) ($R_f = 0.36$) (35%) which was identical in all respects to the product isolated previously from aziridination of hex-1-ene in the absence of TFA. When the above experiment was repeated with the addition of smaller amounts of TFA the following observations were made:

(i) the use of TFA (3 mol equiv.) resulted in isolation of the aziridine (85) (64%) together with the ring-opened product (273) (11%) after chromatography,

(ii) the use of TFA (1.8 mol equiv.) gave the aziridine (85) (37%), the de-aminated quinazolone (79) (27%) and the ring-opened aziridine (273) in 5% yield after chromatography,

(iii) in the absence of TFA, the aziridine (85) (11%) and the de-aminated quinazolone (79) (68%), were isolated after chromatography.

Aziridination of allyl chloride in the presence of TFA

\[ \text{N} \quad \text{Q} \quad \text{Q} \]

(274)

The general procedure (4) was followed using the N-aminoquinazolone
(77) (0.5g, 2.64x10⁻³ mol), LTA (1.23g, 2.77x10⁻³ mol), allyl chloride (0.303g, 3.96x10⁻³ mol) and TFA (1.80g, 1.58x10⁻² mol) in dry dichloromethane (5 ml) and after work-up afforded 2-chloromethyl-1-(4-oxo-2-ethyl-3(4H)-quinazolinyl)aziridine (274) as colourless crystals (0.634g, 91%), m.p. 75-77°C (from ethanol) (Found: C, 58.95; H, 5.15; N, 15.45. C₁₃H₁₄N₃OCl requires C, 59.2; H, 5.35; N, 15.9%);

νₘₐₓ (Nujol): 1665s, 1598s, 1340m, 1290m, 1265m, 1240m, 1180w, 1060w, 990w, 995w, 900w, 770s, 740m and 695m cm⁻¹;

Sₜ (CDCl₃, 300 MHz): 8.15 (ddd, J8.1, 1.5 and 0.6Hz, ArH₅), 7.69 (ddd, J8.0, 7.4 and 1.5Hz, ArH₇), 7.62 (ddd, J8.0, 1.4 and 0.6Hz, ArH₈), 7.42 (ddd, J8.1, 7.4 and 1.4Hz, ArH₅), 4.14 (dd, J11.5 and 4.8Hz, HCHCl), 3.61 (dd, J11.5 and 6.8Hz, HCHCl), 3.46 (dddd, J7.6, 6.8, 5.3 and 4.8Hz, CH₂Cl), 3.08 (dq, J17 and 7.3Hz, HCH₃), 3.05 (dq, J17 and 7.3Hz, HCH₃), 2.72 (dd, J7.6 and 1.6Hz, azir. ring H-3 trans to CH₂Cl), 2.58 (dd, J5.3 and 1.6Hz, azir. ring H-3 cis to CH₂Cl) and 1.42 (t, J7.3Hz, CH₂CH₃);

M/Z (%): 265(M⁺,16,³⁷Cl), 263(M⁺,45,³⁵Cl), 228(56), 200(26), 175(24), 174(64), 173(48), 132(14), 131(100), 130(64), 119(14) and 103(24).

Repetition of the above experiment with the addition of smaller amounts of TFA gave the following results:

(i) with the use of TFA (3 mol equiv.) the aziridine (274) was obtained in 85% yield,

(ii) in the absence of TFA no aziridine corresponding to (274) was isolated; the major product was the de-aminated quinazolone (79) isolated in 77% yield after crystallisation from ethanol.
Preparation of allyl acetate

Allyl acetate was prepared from allyl alcohol using pyridine (6 mol equiv.) and acetic anhydride (2 mol equiv.) in the usual way (see p.191) and was distilled prior to use (b.p. 100-103°C) (lit.147 103-104°C).

Aziridination of allyl acetate in the presence of TFA

The general procedure (4) was followed using the N-aminooquinazolone (77) (0.5g, 2.64×10⁻³ mol), LTA (1.23g, 2.77×10⁻³ mol), allyl acetate (0.397g, 3.96×10⁻³ mol) and TFA (0.9g, 7.93×10⁻³ mol) in dry dichloromethane (5 ml). After work-up 2-acetoxyethyl-1-(4-oxo-2-ethyl-3(4H)-quinazolinyl)aziridine (276) was obtained as colourless crystals (0.62g, 82%), m.p. 96-97°C (from ethanol) (Found: C, 62.6; H, 5.6; N, 14.45. C₁₅H₁₇N₃O₃ requires C, 62.7; H, 5.9; N, 14.6%);

ν_max (Nujol): 1745s, 1685s, 1600s, 1460s, 1335m, 1235s, 1035s, 980m, 905m, 895m, 880w, 845m, 800w, 770s, 700m, 695m and 635m cm⁻¹;

δ_H (CDCl₃, 300 MHz): 8.17 (ddd, J₈, 1.4 and 0.6Hz, ArH₆), 7.7 (ddd, J₈.1, 7.4 and 1.4Hz, ArH₇), 7.62 (ddd, J₈.1, 1.3 and 0.6Hz, ArH₈), 7.42 (ddd, J₈, 7.4 and 1.3Hz, ArH₈), 4.45 (dd, J₁₂.1 and 4.8Hz, HCHOOCCH₃), 4.38 (dd, J₁₂.1 and 5.7Hz, HCHOOCCH₃), 3.28 (ddddd, J₈.4, 5.7, 5.7 and 4.8Hz, azir. ring H-2), 3.09 (2xdq, J₁₈ and 7.1Hz, CH₂CH₃), 2.66 (dd, J₈.4 and 1.8Hz, azir. ring H-3 trans to CH₂OAc), 2.58 (dd, J₅.7 and 1.8Hz, azir. ring H-3 cis to CH₂OAc), 2.15 (s, OOCCH₃) and 1.44 (t, J₇.1Hz, CH₂CH₃);
M/Z (%): 287(M+,74), 228(13), 214(14), 200(21), 189(10), 175(33), 174(100),
173(82), 146(12), 131(43), 130(46), 119(24) and 103(17).

Preparation of 3-chloro-2-diethylphosphoryloxy-1-propene (277)

This was prepared\textsuperscript{163} by the treatment of 1,3-dichloroacetone with triethylphosphite. Distillation of the residue gave 3-chloro-2-diethylphosphoryloxy-1-propene (277) (80%), b.p. 86-91°C at 1 mmHg (lit.\textsuperscript{163} 76-89°C at 1 mmHg) as a colourless liquid.

Attempted aziridination of (277) in the presence of TFA

\begin{center}
\begin{tikzpicture}
\node (Q) at (0,0) {$Q$};
\node (NH) at (0,-1) {$\text{NH}$};
\node (O) at (0,-2) {$\text{O}$};
\node (Cl) at (0,-3) {$\text{Cl}$};
\draw (Q) -- (NH);
\draw (NH) -- (O);
\draw (O) -- (Cl);
\end{tikzpicture}
\end{center}

The general procedure (4) was followed using the N-aminooquinazolone (77) (0.5g, 2.64x10\textsuperscript{-3} mol), LTA (1.23g, 2.77x10\textsuperscript{-3} mol), 3-chloro-2-diethylphosphoryloxy-1-propene (277) (1.2g, 5.28x10\textsuperscript{-3} mol) and TFA (1.8g, 1.58x10\textsuperscript{-2} mol) in dry dichloromethane (5 ml). Trituration of the crude oxidation product with cold light petroleum yielded the chloroketone (191) (71%) (from ethanol) which was identical in all respects to that isolated from attempted aziridination of 3-chloro-2-(trimethylsiloxy)prop-1-ene (see experimental relating to Chapter 4).

When the attempted aziridination was repeated in the absence of TFA the
major product was the de-aminated quinazolone (79) (68%): the presence of the chloroketone (191) was not detected.

Amination of toluene using oxidative (LTA) addition of NAQ (77) in the presence of TFA

The general procedure (4) was followed using the N-aminoquinazolone (77) (0.5g, 2.64x10^{-3} mol), LTA (1.23g, 2.77x10^{-3} mol), toluene (0.365g, 3.96x10^{-3} mol) and TFA (0.9g, 7.93x10^{-3} mol) in dry dichloromethane (5 ml). Chromatography of the crude oxidation product over silica with ethyl acetate-light petroleum (1:2) as eluant afforded (280) as colourless crystals (0.25g, 34%), m.p. 124-126°C (from light petroleum) (Found: M/Z 279.1385. C_{17}H_{17}N_{3}O requires M, 279.1371);

ν_{max} (Nujol): 3280m, 1675s, 1600s, 1515m, 1335m, 1300m, 1250m, 1050w, 930w, 810m, 775m, 735w and 700m cm^{-1};

δ_{H} (CDCl_{3}, 300 MHz): 8.18 (ddd, J_{8}, 1.3 and 0.6Hz, ArH_{6}), 7.71 (m, ArH_{7} and ArH_{8}), 7.40 (m, ArH_{6}), 6.99 (d, J_{8}Hz, 2xArH), 6.58 (d, J_{8}Hz, 2xArH), 3.07 (br.dq, J_{16} and 7Hz, HCHCH_{3}), 2.82 (br.dq, J_{16} and 7Hz, HCHCH_{3}), 2.23 (s, CH_{3}) and 1.35 (t, J_{7}Hz, CH_{2}CH_{3});

M/Z (%): 279 (M^{+}, 89), 264(12), 250(10), 175(20), 174(31), 173(48), 160(14), 130(10), 119(14), 107(37), 106(100), 105(32), and 104(15).
Competitive aziridination of methyl methacrylate and α-methylene-γ-butyrolactone using procedure (3)

![Chemical structures](image)

Powdered N-aminoquinazolone (77) (0.2g, 1.05x10^-3 mol) and acetic acid-free lead tetra-acetate (0.493g, 1.11x10^-3 mol) were added alternately and continuously in very small portions over 15 min. to a vigorously stirred solution of dry dichloromethane (2 ml), containing equimolar amounts of methyl methacrylate (0.211g, 2.11x10^-3 mol) and α-methylene-γ-butyrolactone (0.207g, 2.11x10^-3 mol) at room temperature. Work-up was carried out as outlined in the general procedure (3). The 300 MHz ¹H n.m.r. spectrum of the crude reaction product revealed that the aziridines (92) and (93) were formed in a 2:1 ratio respectively from comparison of the integration values of the signals at δ 4.55 and δ 3.56.

Competitive aziridination of methyl methacrylate and α-methylene-γ-butyrolactone in the presence of TFA

This aziridination was carried out under identical conditions to those given in the previous experiment but in the presence of TFA (3 mol equiv.). Work-up was carried out as outlined in the general procedure (4), and the ¹H n.m.r. spectrum of the crude product revealed only the aziridine (93) to be present.
Preparation of methyl-N-(2,2-dimethylpropanoyl)anthranilate (304)

This was obtained by the general procedure for the synthesis of methyl N-substituted anthranilates (see experimental relating to Chapter 2) from trimethylacetyl chloride and methyl anthranilate and the product (304) obtained as colourless crystals (13.45g, 73%), m.p. 34-36°C (from light petroleum);

\[ \nu_{\text{max}} \text{(Nujol)}: 3260s, 1690s, 1675s, 1605s, 1595s, 1535s, 1470s, 1435s, 1295s, 1250s, 1155s, 1140s, 1085s, 970m, 920m, 750s, \text{and 700s cm}^{-1}; \]

\[ \delta_{\text{H}} \text{(CDCl}_3, 90 \text{ MHz)}: 11.2 \text{ (br.s, exch. D}_2\text{O, N-H), 8.72 (dd, J}_8 \text{ and 1Hz, } \text{ArH}_3), 7.97 \text{ (dd, J}_7 \text{ and 2Hz, ArH}_6), 7.48 \text{ (ddd, J}_8, 8 \text{ and 2Hz, ArH}_4), 7.0 \text{ (ddd, J}_8, 7 \text{ and 1Hz, ArH}_5), 3.87 \text{ (s, CO}_2\text{CH}_3 \text{) and 1.3 (s, t-Bu);} \]

\[ \text{M/Z (%): 235(M}^+\text{,67), 178(75), 151(67), 146(100), 120(51), \text{and 119(91).} \]

Preparation of 3-amino-2-(t-butyl)quinazolin-4(3H)-one (230)

This was prepared by a modification of the general procedure\textsuperscript{39} using the foregoing anthranilate (304) (4.76g, 0.02 mol) and hydrazine hydrate (95%, 5.06g, 0.101 mol) with ethanol (40 ml) as solvent in a Carius tube.
After approximately 3 freeze-thaw cycles to eliminate oxygen, the mixture was sealed, in vacuo, and heated overnight at 145-155°C. The bulk of the ethanol was removed under reduced pressure and the crude reaction mixture was diluted with dichloromethane (100 ml) washed with water (2x100 ml), dried over magnesium sulphate and the solvent removed by evaporation under reduced pressure. Chromatography of the crude reaction mixture over silica with ethyl acetate-light petroleum (1:2) as eluant gave 2-t-butylquinazolin-4(3H)-one (282) as colourless crystals (1.3g, 32%), m.p. 180-183°C (from ethanol) (the spectroscopic data for this compound are given later.

Further elution using the same solvent system afforded 3-amino-2-t-butylquinazolin-4(3H)-one (230) as colourless crystals (1.84g, 42%), m.p. 94-95°C (from ethanol) (Found: C, 66.20; H, 7.0; N, 19.15. C_{12}H_{15}N_{3}O requires C, 66.35; H, 6.95; N, 19.35%);

ν_{max}(Nujol): 3300s, 3220s, 1635s, 1580s, 1175m, 970m, 910m, 760s, and 690s cm^{-1};

S_{H}(CDCl_{3}, 90 MHz): 8.19 (dd, J=8 and 1Hz, ArH_{5}), 7.7-7.15 (m, ArH_{6}, ArH_{7} and ArH_{8}), 4.72 (br.s, exch. D_{2}O, NH_{2}), and 1.5 (s, t-Bu);

M/Z (%): 217(M^{+},25), 202(35), 201(13), 187(27), 175(100), 160(23), 146(15), 144(13) and 132(66).
Attempted aziridination of i) methyl acrylate and ii) α-methylene-γ-butyrolactone

![Chemical structures](image)

i) Using methyl acrylate:
The general procedure (3) was followed using the N-aminoquinazolone (230) (0.27g, 1.24x10^{-3} mol), LTA (0.579g, 1.3x10^{-3} mol) and methyl acrylate (0.32g, 3.72x10^{-3} mol) in dry dichloromethane (2.7 ml). Chromatography of the crude oxidation product over silica, with ethyl acetate-light petroleum (1:3) as eluant, afforded the benzoxazinone (231) (0.03g, 12%) as a colourless unstable oil;

ν_{max} (Film): 2985m, 1760s, 1635s, 1605m, 1475m, 1465m, 1310m, 1220m, 1155m, 1110s, 1040m, 1005m, 945m, 935m, 775m, and 690m cm^{-1};

δ_{H} (CDCl₃, 300 MHz): 8.18 (ddd, J7.8, 1.6 and 0.6Hz, ArH_g), 7.77 (ddd, J8.5, 7.3 and 1.6Hz, ArH_p), 7.68 (ddd, J8.5, 1.2 and 0.6Hz, ArH_g), 7.47 (ddd, J7.8, 7.3 and 1.2Hz, ArH_p), and 1.4 (s, t-Bu);

M/Z (%): 203(M^+,40), 189(12), 188(100), 161(13), 160(10), 149(17), 148(11), 146(90), 132(11), 119(23), 94(19), and 90(32).

Further elution with the same solvent system afforded the de-aminated quinazolone (282) as colourless crystals (0.095g, 38%), m.p. 180-183°C (from ethanol);

ν_{max} (Nujol): 3130m, 3180m, 1665s, 1605s, 1340m, 1260m, 1250m, 1165s, 1100w, 970m, 880m, 810w, 780m, 770s, 685m, and 630s cm^{-1};

δ_{H} (CDCl₃, 90 MHz): 11.15 (br.s, exch. D₂O, N-H), 8.22 (dd, J8 and 1Hz, ArH_g), 7.7-7.2 (m, ArH_e, ArH_p, and ArH_g), 1.5 (s, t-Bu);

M/Z (%): 202(M^+,37), 201(27), 188(14), 187(100), 160(36), 146(10), and
ii) Using α-methylene-γ-butyrolactone:

Repetition of the experiment above using α-methylene-γ-butyrolactone gave the corresponding benzoxazinone (281) (14%) and the de-aminated quinazolone (282) (39%) after chromatography: no aziridine containing products were isolated.

**Preparation of N-acetoxyamino-2-t-butylquinazolone (231) at -20°C**

![Diagram of the reaction](image)

The general procedure (1) was followed using the N-aminoquinazolone (230) (0.1g, 4.6x10^-4 mol) and LTA (0.214g, 4.83x10^-4 mol) and dry deutero-chloroform (1 ml). Examination of the low temperature ¹H n.m.r. spectrum (-40°C) revealed the only product to be the N-acetoxyamino-2-t-butylquinazolone (231);

$\delta_H$ (CDCl₃, -40°C, 300 MHz): 10.96 (s, N-H), 8.23 (ddd, J₈, 1.4 and 0.6Hz, ArH₅), 7.81 (ddd, J₈.1, 7.4 and 1.4Hz, ArH₇), 7.72 (ddd, J₈.1, 1.5 and 0.6Hz, ArH₅), 7.5 (ddd, J₈, 7.4 and 1.5Hz, ArH₅), 2.18 (s, OCOCH₃), and 1.55 (s, t-Bu).
Aziridination of styrene using (230)

![Diagram](image)

(283)

The general procedure (3) was followed using the N-aminoquinazolone (230) (0.25g, 1.15x10^{-3} mol), LTA (0.537g, 1.2x10^{-3} mol) and styrene (0.359g, 3.45x10^{-3} mol) in dry dichloromethane (2.5 ml). Chromatography of the crude oxidation product over silica, with ethyl acetate-light petroleum (1:9) as eluant, afforded 1-(4-oxo-2-t-butyl-3(4H)-quinazoliny1)-2-phenyl-aziridine (283) (Rf = 0.5) as a colourless oil (0.029g, 8%) (Found: M/Z 319.1674. C_{20}H_{21}N_{3}O requires M, 319.1684);

ν^{max} (Film): 2970s, 2920s, 1670s, 1585s, 1570s, 1470s, 1310s, 1290m, 1185s, 1120s, 770s, 750s, 740m, 690s, 760m, 640m, and 615m cm^{-1};

δ_{H} (CDCl_{3}, 300 MHz): 8.14 (dd, J8.1 and 1.5Hz, ArHg), 7.69 (ddd, J8, 7.2 and 1.5Hz, ArH), 7.62 (ddd, J8 and 1.3Hz, ArHg), 7.41 (ddd, J8.1, 7.2 and 1.3Hz, ArHg), 7.36-7.22 (m, 5xPhH), 5.28 (dd, J7.1 and 4.2Hz, azir. ring H-2), 4.28 (d, J7.1Hz, azir. ring H-3 trans to Ph), 2.36 (d, J4.2Hz, azir. ring H-3 cis to Ph), and 1.5 (s, t-Bu);

M/Z (%): 319(M^{+},10), 262(8), 228(52), 203(41), 202(17), 201(13), 189(13), 188(96), 187(34), 172(24), 161(15), 160(20), 147(12), 146(100), 120(10), 119(36), 118(19), 117(25), 104(16), and 103(24).
Aziridination of hexene using (230) and procedure (4) (with TFA)

The general procedure (4) was followed using the N-aminoquinazolone (230) (0.21g, 9.67x10^{-4} mol), LTA (0.451g, 1.01x10^{-3} mol), hex-1-ene (0.122g, 1.45x10^{-3} mol) and TFA (0.33g, 2.9x10^{-3} mol) in dry dichloromethane (2.1 ml). Chromatography of the crude oxidation product over silica, with ethyl acetate-light petroleum (1:9) as eluant, afforded 1-(4-oxo-2-t-butyl-3(4H)-quinazolinyl)-2-n-butylaziridine (284) (R_f = 0.53) as a colourless oil (0.115g, 40%) (Found: M/Z 299.2005. C_{16}H_{26}N_{9}O requires M, 299.1997);

\[ \text{v}_{\text{max}} \text{ (Film): 2930m, 1675s, 1610m, 1585m, 1570s, 1475m, 1390w, 1310w, 1290w, 1190m, 1125m, 770m, 725w, and 690m cm}^{-1}; \]

\[ \delta_{H} \text{ (CDCl}_3, 300 \text{ MHz): 8.07 (ddd, J8.1, 1.5 and 0.6Hz, ArH}_5), 7.64 (ddd, J8.1, 6.5 and 1.5Hz, ArH}_7), 7.59 (ddd, J8.1, 1.7 and 0.6Hz, ArH}_6), 7.35 (ddd, J8.1, 6.5 and 1.7Hz, ArH}_6), 4.25 (m, azir. ring H-2), 3.73 (d, J7Hz, azir. ring H-3 trans to (CH}_2)_3CH}_3), 1.76 (d, J4Hz, azir. ring H-3 cis to (CH}_2)_3CH}_3), 1.81-1.2 (m, (CH}_2)_3, 6 x aliphatic H), 1.58 (s, t-Bu), and 0.9 (t, J7.5Hz, (CH}_2)_3CH}_3); \]

M/Z (%): 299(M^+,14), 228(20), 203(9), 202(7), 201(11), 187(85), 172(14), 160(35), 159(58), 158(12), 146(10), 145(12), 146(36), 130(22), 119(10), 117(10), 104(54), 103(100), and 102(23).

Further elution with ethyl acetate-light petroleum (1:3) afforded the
ring-opened aziridine (285) (R₁ = 0.34) as a colourless oil (0.086g, 28.2%) (Found: M/Z 317.2093. C₁₈H₂₇N₃O₂ requires M, 317.2103);

νₛ макс (Film): 3440br.m, 3280m, 1665s, 1610s, 1580s, 1470s, 1390m, 1320m, 1295m, 1210m, 1170s, 1140m, 910s, 775s, 735s, and 700s cm⁻¹;

$^1$H (CDCl₃, 300 MHz): 8.17 (ddd, J7.9, 1.3 and 0.6Hz, ArH₃), 7.7 (ddd, J8.2, 7.3 and 1.3Hz, ArH₇), 7.65 (ddd, J8.2, 1.2 and 0.6Hz, ArH₈), 7.4 (ddd, J7.9, 7.3 and 1.2Hz, ArH₆), 5.78 (br.m, exch. D₂O, N-H), 4.0-2.6 (br.m, 4 x aliphatic H), 1.5 (s, t-Bu), 1.7-1.2 (m, 4 x aliphatic H), and 0.89 (t, J=7Hz, (CH₃)₃CH₃).

The 300 MHz $^1$H n.m.r. spectrum of this ring-opened aziridine (285) showed some signals broadened at room temperature which was attributed to slow N-N bond rotation on the n.m.r. time-scale. When the sample was cooled to 243°C in CD₂Cl₂ structured signals were obtained from the individual rotamers which were present in a 2.3:1 ratio from comparison of the integration values of the signals at δ 2.72 and δ 2.82;

M/Z (%): 317(M⁺,7), 299(15), 231(16), 230(86), 203(25), 202(62), 201(20), 188(15), 187(100), 175(11), 174(12), 160(40), 146(24), and 119(13).

Aziridination of E-but-2-ene using (230) and procedure (4) (with TFA)

The general procedure (4) was carried out at 0°C using the N-aminoquin-
azolone (230) (0.5g, 2.3×10⁻⁳ mol), LTA (1.07g, 2.41×10⁻³ mol), E-but-2-ene (0.19g, 3.45×10⁻³ mol) and TFA (0.788g, 6.9×10⁻³ mol) in dry dichloromethane (4 ml). Chromatography of the crude reaction product over silica, with ethyl acetate-light petroleum (1:8) as eluant gave 1-(4-oxo-2-t-butyl-3(4H)-quinazolinyl)-E-2,3-dimethylaziridine (286) (Rf = 0.5) as a colourless oil (0.149g, 24%) (Found: M/Z 271.1671. C₁₈H₂₁N₂O requires M, 271.1684);

νₚ (Film): 2960s, 1670s, 1570s, 1470s, 1460s, 1390m, 1380m, 1300m, 1290m, 1190s, 1135s, 1040s, 1020s, 920w, 880w, 770s, 695s, 670m, and 615m cm⁻¹;
Sₜ (CDCl₃, 300 MHz): 8.2 (ddd, J₈, 1.4 and 0.5Hz, ArH₅), 7.73 (ddd, J₈.1, 7.4 and 1.4Hz, ArH₇), 7.62 (ddd, J₈.1, 1.3 and 0.5Hz, ArH₉), 7.42 (ddd, J₈, 7.4 and 1.3Hz, ArH₆), 4.05 (quintet, J₅.8Hz, azir. ring H-2 cis to quinz.), 2.3 (quintet, J₅.8Hz, azir. ring H-3 trans to quinz.), 1.6 (s, t-Bu), 1.45 (d, J₅.8Hz, CH₃), and 1.1 (d, J₅.8Hz, CH₃);

M/Z (%): 271(M⁺,42), 256(22), 242(15), 202(11), 201(11), 188(21), 187(100), 186(14), 172(13), 160(18), 159(68), 158(13), 145(15), 144(33), 130(11), 119(11), 104(53), 103(83), and 102(15).

Further elution with ethyl acetate-light petroleum (1:8) afforded the ring-opened aziridine (287) (Rf = 0.4) as a colourless oil (0.15g, 17%) (Found: M/Z 385.1620. C₁₈H₂₂N₃O₃F₃ requires M, 385.1613);

νₚ (Film): 3260m, 2975s, 1780s, 1665s, 1610s, 1570s, 1465s, 1380s, 1330s, 1290m, 1220s, 1165s, 1090m, 860m, 770s, 730m, 715m, 695m, and 650w cm⁻¹;
Sₜ (CDCl₃, 300 MHz): 8.15 (ddd, J₈, 1.4 and 0.6Hz, ArH₅), 7.74 (ddd, J₈, 7.4 and 1.4Hz, ArH₇), 7.65 (ddd, J₈, 1.4 and 0.6Hz, ArH₉), 7.45 (ddd, J₈, 7.4 and 1.4Hz, ArH₆), 5.39 (d, J₆Hz, N-H), 5.25 (dq, J₆.25 and 3Hz, CHOOCOF₃), 3.87 (m, CHNH), 1.51 (s, t-Bu), 1.4 (d, J₆.25Hz, CH₃), and 1.02 (d, J₆.25Hz, CH₃);

M/Z (%): 385(M⁺,33), 271(34), 245(48), 244(100), 242(16), 203(46), 202(86),
Aziridination of Z-but-2-ene using (230) and procedure (4) (with TFA)

The general procedure (4) was followed at 0°C using the N-aminoquinazolone (230) (0.47g, 2.16x10^{-3} mol), LTA (1.009g, 2.27x10^{-3} mol), Z-but-2-ene (0.36g, 6.49x10^{-3} mol) and TFA (0.74g, 6.49x10^{-3} mol) in dry dichloromethane (4 ml). Chromatography of the crude oxidation product over silica, with ethyl acetate-light petroleum (1:4) as eluant, afforded 1-(4-oxo-2-t-butyl-3(4H)-quinazolinyl)-Z-2,3-dimethylaziridine (288) (R_f = 0.66) as colourless crystals (0.27g, 46%), m.p. 79-80°C (from ethanol) (Found: C, 70.55; H, 7.9; N, 15.22. C_{16}H_{21}N_{3}O requires C, 70.8; H, 7.8; N, 15.5%); 

ν_{max} (Nujol): 1675s, 1610s, 1585s, 1565s, 1470m, 1455m, 1375m, 1310m, 1290m, 1235m, 1190m, 1145m, 1130m, 1070m, 945m, 770s, and 695s cm^{-1};

δ_H (CDCl_3, 90 MHz): 8.10 (dd, J8 and 1Hz, ArH_g), 7.7-7.2 (m, ArH_6, ArH_7, and ArH_8), 4.35-4.05 (m, azir. ring H-2 and H-3), 1.6 (s, t-Bu), and 1.25 (d, J6.0Hz, CH_3);

M/Z (%): 271(M^+,30), 256(19), 242(15), 202(12), 201(11), 186(12), 187(100), 186(13), 172(13), 160(19), 159(56), 158(10), 144(29), 130(11), 104(52), 103(76), and 102(14).

Further elution with ethyl acetate-light petroleum (1:4) afforded the
ring-opened aziridine (289) \( (R_f = 0.28) \) as a colourless oil \( (0.063g, 10\%) \) [Found: M+H/Z 290.1874. \( C_{16}H_{24}N_3O_3 \) requires M=H, 290.1868 (under ionization conditions used a M+H ion was obtained)];

\[ \nu_{\text{max}} \] (Film): 3460br.m, 3280m, 1660s, 1610s, 1580s, 1565s, 1470s, 1290s, 1250m, 1165s, 1015m, 935m, 895m, 770s, 735m, and 695m cm\(^{-1}\);

\( \delta_H \) (CDCl\(_3\), 300 MHz): 8.19 (dd, J8.2 and 1.3Hz, ArH\(_5\)), 7.4 (ddd, J8.2, 6.6 and 1.3Hz, ArH\(_7\)), 7.69 (d, J8.2Hz, ArH\(_9\)), 7.45 (ddd, J8.2, 6.6 and 1.5Hz, ArH\(_8\)), 5.55 (d, J10.5Hz, exch. D\(_2\)O, N-H), 4.07 (br.s, exch. D\(_2\)O, OH), 3.61 (br.m, CH\(_3\)CH), 2.93 (br.m, CH\(_3\)CH), 1.52 (s, t-Bu), 1.12 (d, J7.5Hz, CH\(_3\)CH), and 1.06 (d, J7.5Hz, CH\(_3\)CH);

M/Z (%): 289(M\(^+\),1), 272(2), 244(100), 202(98), 188(53), 187(95), 186(14), 185(10), 175(31), 160(92), 147(31), 146(39), 145(27), 144(18), 132(28), 130(23), 129(24), 120(19), 119(37), 118(19), 117(12), and 104(35).

**Aziridination of 3-methylcyclohex-1-ene using (230) and procedure (4) (with TFA)**

\[ \text{Het} = \]

\( \text{Het} = \)

(290)

The general procedure (4) was followed using the N-aminoquinazolone (230) \( (0.23g, 1.05\times10^{-3} \text{ mol}) \), LTA \( (0.494g, 1.11\times10^{-3} \text{ mol}) \), 3-methylcyclohex-1-ene \( (0.152g, 1.58\times10^{-3} \text{ mol}) \) and TFA \( (0.362g, 3.18\times10^{-3} \text{ mol}) \) in dry dichloromethane \( (2.3 \text{ ml}) \). Chromatography of the crude oxidation product over silica, with ethyl acetate-light petroleum \( (1:9) \) as eluant afforded 7-(4-oxo-2-t-butyl-3(4H)-quinazolinyl)-28-methyl-7-azabicyclo[4.1.0]heptane
(290) \((R_f = 0.58)\) as a colourless oil \((0.138g, 42\%)\) (Found: M/Z 311.2005. \(C_{19}H_{25}N_2O\) requires M, 311.1997);

\(\nu_{\text{max}}\) (Film): 2920s, 1660s, 1565s, 1450s, 1340m, 1300m, 1295m, 1230m, 1200m, 1180s, 1150s, 770s, 735s, and 690m cm\(^{-1}\);

\(\delta_H\) (CDCl\(_3\), 300 MHz): 8.07 (ddd, 7.9, 1.4 and 0.6Hz, ArH\(_5\)), 7.64 (ddd, J8.0, 7.4 and 1.4Hz, ArH\(_7\)), 7.58 (ddd, J8.0, 1.3 and 0.6Hz, ArH\(_6\)), 7.35 (ddd, J7.9, 7.4 and 1.3Hz, ArH\(_8\)), 4.29 (ddd, J6.8, 4.1 and 1.1Hz, azir. ring H-6), 4.15 (dd, J6.8 and 1.1Hz, azir. ring H-1), 2.2-0.75 (m, 7 x aliphatic H), 1.61 (s, t-Bu), and 1.09 (d, J7.2Hz, CH\(_3\)).

The above \(^1\)H n.m.r. spectrum of aziridine (290) showed that it contained 10\% of an impurity (probably the C-2 epimer) which showed signals at \(\delta 8.19\) (d, J8.0Hz, ArH\(_5\)), 4.45 (ddd, J7.5, 3.8 and 0.8Hz, azir. ring H-6), 4.24 (m, azir. ring H-1), 1.64 (s, t-Bu), and 1.1 (d, J7.2Hz, CH\(_3\));

M/Z (%): 311(M\(^+\),21), 296(18), 269(15), 268(26), 255(11), 254(41), 229(15), 228(100), 203(24), 202(13), 201(24), 187(55), 172(21), 160(18), 159(16), 110(64), 104(16), 103(34) and 102(6).

Aziridination of allyl chloride using pre-formed N-acetoxvaminouzolone (78)

A solution of (77) in dichloromethane (6 ml) was obtained at -20°C by oxidation of \(N\)-aminoquinazolone (0.4g, 2.11x10\(^{-3}\) mol) with LTA (1.03g, 2.32x10\(^{-3}\) mol). This solution held at -20°C (containing suspended lead di-acetate) was added dropwise with stirring to a solution of allyl chloride (0.486g, 6.35x10\(^{-3}\) mol) and TFA (1.45g, 12.7x10\(^{-3}\) mol) in dichloromethane (2 ml) held at 0°C. After allowing to warm to room temperature, a saturated solution of sodium hydrogen carbonate was added and the insoluble solids separated. The dichloromethane layer was
separated, washed with water, dried and evaporated to give the aziridine (274) as a crystalline solid (0.513g, 92%). Examination of this solid by n.m.r. at 300 MHz showed that it contained ca. 8% of the de-aminated quinazolone (79).

**Preparation of N-acetoxyaminoquinazolone (78) followed by addition of allyl chloride and TFA**

The N-acetoxyaminoquinazolone (78) was prepared in solution at -20°C by the general procedure (2) using the N-aminoquinazolone (77) (0.2g, 1.05x10^-3 mol) and LTA (0.493g, 1.11x10^-3 mol). Subsequently, allyl chloride (0.242g, 3.17x10^-3 mol) was added followed by TFA (0.36g, 3.17x10^-3 mol) dissolved in dichloromethane (2 ml) and the solution allowed to warm to ambient temperature. After work-up and chromatography as described previously the aziridine (274) was obtained in 43% yield.

**N.m.r. spectrum of N-acetoxyaminoquinazolone (78) in the presence of TFA**

A solution of (78) in CDCl₃ solution was prepared by oxidation of (77) at -20°C as described previously and freed from lead-diacetate by filtration through a cotton wool plug. The solution was cooled to -40°C and TFA added (3 mol equiv.). The n.m.r. of this solution was measured at -40°C without any intermediate warming and had δ(CDCl₃) 11.00 (s, N-H), 8.37 (d, J₈Hz, ArH₅), 8.08 (t, J₈Hz, ArH₅), 7.84 (d, J₈Hz, ArH₆), 7.83 (t, J₈Hz, ArH₆), 3.44 (m, [10 lines], CH₂CH₃), 2.18, 2.19 (2xs, OOCOCH₃ and HOOCOCH₃), and 1.57 (t, J₆Hz, CH₂CH₃).

For comparison of (78) in the absence of TFA see experimental relating to Chapter 2.
Aziridination of allyl chloride using (77) and (bis[trifluoroacetoxy]iodo)benzene

Powdered N-aminoquinazolone (77) (0.2g, 1.05x10^{-3} mol) and (bis[trifluoroacetoxy]iodo)benzene (0.477g, 1.11x10^{-3} mol) were added alternately and portionwise over a period of 20 min. to a stirred solution of allyl chloride (0.12g, 1.58x10^{-3} mol) in dry dichloromethane (2 ml) at room temperature. The mixture was stirred for a further 20 min. then worked-up by the method outlined in general procedure (4). Chromatography of the crude oxidation product over silica, with ethyl acetate-light petroleum (1:1) as eluant, gave the aziridine (274) (R_f = 0.33) as colourless crystals (0.033g, 12%).

The effect of added TFA on the aziridination of allyl chloride using oxidative [PhI(OOCF_3)_2] addition of (77)

(i) Using 1 mole equivalent of TFA:
Powdered N-aminoquinazolone (77) (0.3g, 1.58x10^{-3} mol) and (bis[trifluoroacetoxy]iodo)benzene (0.716g, 1.66x10^{-3} mol) were added to a stirred solution of allyl chloride (0.182g, 2.37x10^{-3} mol) and TFA (0.18g, 1.58x10^{-3} mol) in dry dichloromethane (3 ml). Crystallisation of the crude product gave the aziridine (274) as a colourless solid (0.326g, 78%) (from ethanol).

(ii) Using 2 mole equivalents of TFA:
Repetition of the above reaction using TFA (2 mol equiv.) gave the aziridine (274) in 94% yield.
Oxidation of N-aminophthalimide (15) with lead tetra-acetate and trifluoroacetic acid at room temperature in the presence of i) hex-1-ene and ii) allyl chloride

i) Using hex-1-ene:
The general oxidation procedure (4) was followed but using N-aminophthalimide (15) instead of N-aminoquinazolone. N-aminophthalimide (15) (0.2g, 1.23x10^-3 mol) was oxidised using LTA (0.575g, 1.29x10^-3 mol) in the presence of hex-1-ene (0.155g, 1.85x10^-3 mol), TFA (0.422g, 3.7x10^-3 mol) and dry dichloromethane (2 ml). An n.m.r. spectrum of the crude oxidation product showed only phthalimide to be present and there was no evidence in this n.m.r. spectrum for the presence of the corresponding N-phthalimidoaziridine. Phthalimide was subsequently isolated in 53% yield by trituration using ice-cold ethanol.

ii) Using allyl chloride:
When the above experiment was repeated under identical conditions using allyl chloride instead of hex-1-ene, no aziridine was isolated or detected in the crude reaction product: phthalimide was isolated in 57% yield by trituration using ice-cold ethanol.

Oxidation of N-aminophthalimide (15) with (bis[trifluoroacetoxy]iodo)benzene in the presence of allyl chloride

The general oxidation procedure (3) was followed using N-aminophthalimide (15) (0.2g, 1.23x10^-3 mol) (instead of N-aminoquinazolone and (bis[trifluoroacetoxy]iodo)benzene (0.55g, 1.29x10^-3 mol) (instead of LTA) in dichloromethane (2 ml) containing allyl chloride (0.283g, 3.7x10^-3 mol).

Examination of the 1H n.m.r. spectrum of the crude product showed only phthalimide to be present in greater than 50% yield.
Aziridination of allyl chloride using (111) and procedure (4)

![Diagram](image_url)

The general procedure (4) was followed using the N-aminoquinazolone (111) (0.2g, 8.16x10⁻⁴ mol), LTA (0.38g, 8.57x10⁻⁴ mol), allyl chloride (0.093g, 1.22x10⁻³ mol) and TFA (0.279g, 2.44x10⁻³ mol) in dry dichloromethane (2 ml). A \(^1\)H n.m.r. spectrum of the crude oxidation product showed the presence of two aziridine stereoisomers (291a) and (291b) present in a ratio of 4:1 respectively from integration of peaks at \(\delta 1.04\) and \(\delta 0.98\).

Chromatography of the total crude reaction product over silica, with ethyl acetate-light petroleum (1:3) as eluant gave (291a) \((R_f = 0.53)\) the major stereoisomer of 2-chloromethyl-1-(4-oxo-2-(1,2,2-trimethylpropyl)-3(4H)-quinazolinyl)aziridine (291) as a colourless oil (0.12g, 46%) (Found: M/Z 319.1450. \(\text{C}_{17}\text{H}_{22}\text{N}_3\text{OCl}\) requires M, 319.1451; 

\(\nu_{\text{max}}\) (Film): 1670s, 1610m, 1590s, 1470m, 1360m, 1225m, 1120m, 910m, 880w, 775s, 735s, and 695s cm\(^{-1}\);

\(\delta_H\) (CDCl\(_3\), 300 MHz, major stereoisomer (291a)): 8.13 (ddd, J8.0, 1.5 and 0.6Hz, Ar\(_H\)), 7.66 (ddd, J8.2, 6.9 and 1.5Hz, Ar\(_H\)), 7.59 (ddd, J8.2, 1.4 and 0.6Hz, Ar\(_H\)), 7.37 (ddd, J8.0, 6.9 and 1.4Hz, Ar\(_H\)), 3.87 (dd, J12 and 6Hz, \(\text{HCHCl}\)), 3.72 (q, J6.8Hz, \(\text{CH}_t\)-Bu), 3.63 (dd, J12 and 6Hz, \(\text{HCHCl}\)), 3.26 (dddd, J7.5, 6, 6 and 5.3Hz, \(\text{CHCH}_2\text{Cl}\)), 3.02 (dd, J7.5 and 2.3Hz, azir. ring H-3 trans to \(\text{CH}_2\text{Cl}\)), 2.56 (dd, J5.3 and 2.3Hz, azir. ring H-3 cis to \(\text{CH}_2\text{Cl}\)), 1.36 (d, J6.8Hz, \(\text{CHCH}_3\)-t-Bu) and 1.04 (s, t-Bu);

M/Z (%): 319(M\(^+\),1), 264(11), 263(59), 228(23), 200(12), 176(12), 175(100),
Further elution with ethyl acetate-light petroleum (1:3) afforded the minor aziridine stereoisomer (291b) ($R_f = 0.42$) as a colourless oil (0.039g, 15%); 

$^6$H (CDCl$_3$, 300 MHz, minor stereoisomer (291b)): 8.16 (dd, J8.1 and 1.5Hz, ArH$_5$), 7.67 (ddd, J8.2, 6.9 and 1.5Hz, ArH$_7$), 7.62 (dd, J8.2 and 1.4Hz, ArH$_8$), 7.4 (ddd, J8.1, 6.9 and 1.4Hz, ArH$_9$), 4.39 (dd, J10.5 and 4.5Hz, HCHCl), 3.52 (q, J7.5Hz, CHt-Bu), 3.50 (dd, J10.5 and 7Hz, HCHCl), 3.24 (dddd, J7.5, 7, 5.3 and 4.5Hz, CHCH$_2$Cl), 2.65 (dd, J5.3 and 1.5Hz, azir. ring H-3 cis to CH$_2$Cl), 2.43 (dd, J7.5 and 1.5Hz, azir. ring H-3 trans to CH$_2$Cl), 1.4 (d, J7.5Hz, CHCH$_3$t-Bu) and 0.98 (s, t-Bu).

Aziridination using oxidative (LTA) addition of (111) in allyl chloride as solvent

Powdered N-aminoquinazolone (111) (0.2g, 8.16×10$^{-4}$ mol) and acetic acid-free lead tetra-acetate (0.398g, 8.97×10$^{-4}$ mol) were added alternately and continuously in very small portions over 20 min. to vigorously stirred allyl chloride (2 ml) at room temperature. The mixture was then stirred for 30 min., the insoluble lead di-acetate separated and washed with dichloromethane and the total filtrate washed successively with sodium bicarbonate solution and water, dried with magnesium sulphate and the solvent removed by evaporation under reduced pressure. A $^1$H n.m.r. spectrum of the crude oxidation product showed the presence of aziridine stereoisomers (291a) and (291b) in a ratio of 1:1.4. The major stereoisomer from this experiment corresponds to the minor stereoisomer (291b) obtained in the foregoing aziridination in the presence of TFA.
Aziridination of cyclohexene at -35°C using N-acetoxyaminoquinazolone (78) in the presence of TFA

\[
\begin{align*}
\text{N-acetoxyaminoquinazolone (78) was prepared in solution by alternate and continuous addition of very small portions of N-ama}& \\
\text{ninoquinazolone (77) (0.255 g, 1.34 \times 10^{-3} \text{ mol}) and LTA (0.628 g, 1.41 \times 10^{-3} \text{ mol}) over 20 min. to a deuterochloroform solution (2.5 ml) maintained at -30°C. The solution was stirred for a further 20 min. at this temperature and then precipitated lead di-acetate was separated off. To the filtrate was added firstly cyclohexene (0.331 g, 4.04 \times 10^{-3} \text{ mol}) and then TFA (0.461 g, 4.04 \times 10^{-3} \text{ mol}) without allowing the temperature to rise above -35°C throughout. The solution was then stirred for a further 5 min. at -35°C and a portion of the reaction mixture transferred to a pre-cooled (-40°C) n.m.r. tube. Examination of the 300 MHz spectrum of this solution at -40°C showed only the anti(exo)-aziridine (95) to be present. When the temperature was raised from -40°C to room temperature over ca. 5 min. the n.m.r. spectrum of the solution indicated that partial decomposition of aziridine (95) had occurred: after 30 min. signals from the aziridine were no longer observed in the \(^1\text{H}\) n.m.r. spectrum.}
\end{align*}
\]
The effect of TFA on the inversion barrier of aziridine (94)

\[
\begin{array}{c}
\text{N} \\
\text{CO}_2\text{CH}_3 \\
\text{CH}_3
\end{array}
\]

The crystallised aziridine (94) was dissolved at -40°C in CDCl₃ and the ratio of invertomers was measured at -40°C by ¹H n.m.r.

At -40°C only one invertomer was observed with the CO₂CH₃ group syn to quinazolone. When TFA (3 mol equiv.) was then added at -40°C no change in the invertomer ratio was observed. Thus, addition of TFA does not significantly lower the inversion barrier in aziridine (94). When the n.m.r. sample was removed from the probe, maintained at ambient temperature for 10 min. and then the spectrum re-recorded at -40°C an invertomer ratio of 10:1 (CO₂Me and quinaz. syn:anti) was observed. A crystalline sample of this aziridine dissolved in CDCl₃ at room temperature in the absence of TFA showed a 4:1 ratio of the corresponding invertomers when the n.m.r. spectrum of the solution was measured at -40°C.
APPENDIX 1

Kinetics of Decomposition of N-acetoxyaminoquinazolone (78)

The decomposition of the N-acetoxyaminoquinazolone (78) (prepared at -20°C by the method given in the Experimental) was followed at 10°C by $^1$H n.m.r. spectroscopy (300 MHz) by monitoring the decrease in integral value of the N-H singlet at $\delta$ 10.98 with respect to time.

Let the integral value of this NH singlet = $A$ then, initially at time $t=0$ the NH integral value is $[A]_0$, and at a later time $t$ is $[A]_t$,

we write $\ln \left[ \frac{[A]_t}{[A]_0} \right] = -kt$ ...

Eqn. (1) shows that if $\ln \left[ \frac{[A]_t}{[A]_0} \right]$ is plotted against $t$, then a first order reaction will give a straight line and the value of $k$ may be obtained from the slope (the slope is $-k$). The following results were obtained.

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>NH integral value (mm)</th>
<th>$\ln \left[ \frac{[A]_t}{[A]_0} \right]$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>220 = $[A]_0$</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>193</td>
<td>-0.1309</td>
</tr>
<tr>
<td>20</td>
<td>174</td>
<td>-0.2345</td>
</tr>
<tr>
<td>30</td>
<td>151</td>
<td>-0.3763</td>
</tr>
<tr>
<td>40</td>
<td>125</td>
<td>-0.5653</td>
</tr>
<tr>
<td>50</td>
<td>99</td>
<td>-0.7985</td>
</tr>
<tr>
<td>60</td>
<td>88</td>
<td>-0.9162</td>
</tr>
<tr>
<td>70</td>
<td>64</td>
<td>-1.2347</td>
</tr>
<tr>
<td>80</td>
<td>50</td>
<td>-1.4816</td>
</tr>
<tr>
<td>90</td>
<td>40</td>
<td>-1.7047</td>
</tr>
<tr>
<td>100</td>
<td>32</td>
<td>-1.9278</td>
</tr>
<tr>
<td>110</td>
<td>25</td>
<td>-2.1747</td>
</tr>
<tr>
<td>120</td>
<td>22</td>
<td>-2.3025</td>
</tr>
<tr>
<td>130</td>
<td>14</td>
<td>-2.7545</td>
</tr>
<tr>
<td>140</td>
<td>13</td>
<td>-2.8268</td>
</tr>
<tr>
<td>150</td>
<td>11</td>
<td>-2.995</td>
</tr>
<tr>
<td>160</td>
<td>8</td>
<td>-3.314</td>
</tr>
</tbody>
</table>

A plot of $t$ (time) against $\ln \left[ \frac{[A]_t}{[A]_0} \right]$ gave a first order rate constant of $k_{10°C} = 3.68 \times 10^{-4}$ s$^{-1}$ (see plot 1).
PLOT 1
Decomposition of N-acetoxyaminoquinazolone (78) at 10°C

\[ k_{10^\circ C} = 3.68 \times 10^{-4} \text{ s}^{-1} \]
APPENDIX 2

Decomposition of N-acetoxyaminoquinazolone (78) at -10°C in the presence of styrene

(i) Using 1.5 mole equivalents of styrene the following results were obtained:

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>NH integral value (mm)</th>
<th>ln ([A]_t/[A]_0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>112 = [A]_0</td>
<td>0</td>
</tr>
<tr>
<td>5.5</td>
<td>73</td>
<td>-0.4280</td>
</tr>
<tr>
<td>10</td>
<td>46</td>
<td>-0.8894</td>
</tr>
<tr>
<td>15</td>
<td>32</td>
<td>-1.2527</td>
</tr>
<tr>
<td>20</td>
<td>22</td>
<td>-1.6274</td>
</tr>
<tr>
<td>25</td>
<td>13</td>
<td>-2.1535</td>
</tr>
<tr>
<td>30</td>
<td>9</td>
<td>-2.5217</td>
</tr>
</tbody>
</table>

A plot of time against ln ([A]_t/[A]_0) gave a (pseudo) first order rate constant of k_{-10°C} = 1.4 \times 10^{-3} \text{ s}^{-1}, see plot 2.

(ii) Using 4 mole equivalents of styrene the following results were obtained:

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>NH integral value (mm)</th>
<th>ln ([A]_t/[A]_0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>152</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>92</td>
<td>-0.5020</td>
</tr>
<tr>
<td>6</td>
<td>56</td>
<td>-0.9985</td>
</tr>
<tr>
<td>9</td>
<td>37</td>
<td>-1.4129</td>
</tr>
<tr>
<td>11.75</td>
<td>20</td>
<td>-2.0281</td>
</tr>
<tr>
<td>13.5</td>
<td>11</td>
<td>-2.6259</td>
</tr>
</tbody>
</table>

A plot of time against ln ([A]_t/[A]_0) gave a (pseudo) first order rate constant of k_{-10°C} = 2.9 \times 10^{-3} \text{ s}^{-1}, see plot 3.
The rate of decomposition of the N-acetoxyaminoquinazolone (78) at -10°C in the presence of 1.5 mole equivalents of styrene (Plot 2), and 4 mole equivalents of styrene (Plot 3)

\[ \text{PLOT 2, } k = 1.4 \times 10^{-3} \text{s}^{-1} \]

\[ \text{PLOT 3, } k = 2.9 \times 10^{-3} \text{s}^{-1} \]
(1) **The kinetics of decomposition of aziridine (33) by thermolysis at 80°C in the absence of any alkene**

The aziridine (33) (0.05g, 1.56x10^{-4} mol) was dissolved in dry d_6-benzene (0.75 ml), the solution was placed in an n.m.r. tube and the decomposition of (33) was monitored at 80°C by ^1H n.m.r. The disappearance of the aziridine ring proton singlet in the major invertoner was used to measure the rate of decay at intervals of 30 min. and the following results were obtained:

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Azir. ring H singlet integral value (mm)(A)</th>
<th>ln ([A]_t/[A]_0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>31 = [A]_0</td>
<td>0</td>
</tr>
<tr>
<td>30</td>
<td>26</td>
<td>-0.1758</td>
</tr>
<tr>
<td>60</td>
<td>19</td>
<td>-0.4895</td>
</tr>
<tr>
<td>90</td>
<td>16</td>
<td>-0.6613</td>
</tr>
<tr>
<td>120</td>
<td>11</td>
<td>-1.036</td>
</tr>
<tr>
<td>150</td>
<td>8</td>
<td>-1.1345</td>
</tr>
</tbody>
</table>

where A = the integral value of the azir. ring H which at a later time (t) is [A]_t.

A plot of time against ln ([A]_t/[A]_0) gave a first order rate constant of \( k_{80°C} = 1.5 \times 10^{-4} \text{ s}^{-1} \), see plot 4.

(2) **The kinetics of decomposition of aziridine (33) by thermolysis at 80°C in the presence of alkenes**

The disappearance of aziridine (33) was monitored using the same procedure and identical conditions to those described in the foregoing experiment except for the addition of an alkene and the following results were obtained.
(i) Using 1.5 mole equivalents of styrene

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Azir. ring H singlet integral value (mm)(A)</th>
<th>ln [[A]t/[A]o]</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>36</td>
<td>0</td>
</tr>
<tr>
<td>18</td>
<td>30</td>
<td>-0.1823</td>
</tr>
<tr>
<td>45</td>
<td>15</td>
<td>-0.875</td>
</tr>
<tr>
<td>65</td>
<td>13</td>
<td>-1.0185</td>
</tr>
<tr>
<td>85</td>
<td>11</td>
<td>-1.1856</td>
</tr>
<tr>
<td>105</td>
<td>9</td>
<td>-1.3862</td>
</tr>
<tr>
<td>125</td>
<td>7</td>
<td>-1.637</td>
</tr>
</tbody>
</table>

A plot of time against ln [[A]t/[A]o] gave a (pseudo) first order rate constant of $k_{0°C} = 2.2 \times 10^{-4}$ s$^{-1}$, see plot 5.

(ii) Using 1.5 mole equivalents of methylacrylate

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Azir. ring H singlet integral value (mm)(A)</th>
<th>ln [[A]t/[A]o]</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>30</td>
<td>0</td>
</tr>
<tr>
<td>30</td>
<td>18</td>
<td>-0.5108</td>
</tr>
<tr>
<td>60</td>
<td>10</td>
<td>-1.0985</td>
</tr>
<tr>
<td>90</td>
<td>6.5</td>
<td>-1.5293</td>
</tr>
<tr>
<td>120</td>
<td>5</td>
<td>-1.7917</td>
</tr>
<tr>
<td>150</td>
<td>3.5</td>
<td>-2.148</td>
</tr>
</tbody>
</table>

A plot of time against ln [[A]t/[A]o] gave a (pseudo) first order rate constant of $k_{0°C} = 3.05 \times 10^{-4}$ s$^{-1}$, see plot 6.

(iii) Using 4 mole equivalents of methylacrylate

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Azir. ring H singlet height (mm)(A)</th>
<th>ln [[A]t/[A]o]</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>42</td>
<td>0</td>
</tr>
<tr>
<td>20</td>
<td>17</td>
<td>-0.9044</td>
</tr>
<tr>
<td>40</td>
<td>16</td>
<td>-0.0650</td>
</tr>
<tr>
<td>65</td>
<td>10</td>
<td>-1.4350</td>
</tr>
<tr>
<td>95</td>
<td>5</td>
<td>-2.128</td>
</tr>
</tbody>
</table>

A plot of time against ln [[A]t/[A]o] gave a (pseudo) first order rate constant of $k_{0°C} = 4.02 \times 10^{-4}$ s$^{-1}$, see plot 7.
The thermolysis of aziridine (33) in (1) the absence of any alkene (Plot 4), (2) 1.5 mole equivalents of styrene (Plot 5), (3) 1.5 mole equivalents of methylacrylate (Plot 6), and (4) 4 mole equivalents of methyl acrylate (Plot 7).
APPENDIX 4

Measurement of the rate constant for the disappearance of aziridine (124) in the presence of 2-acetylbenzofuran at different concentrations

The deuterium labelled aziridine (124) (0.025g, 7.73x10^{-5} mol) and 2-acetylbenzofuran (123) (0.0123g, 7.73x10^{-5} mol) were heated at 80°C in d₆-benzene at different concentrations and the rate of disappearance of the methyl group of 2-acetylbenzofuran was measured by ^1H n.m.r. with respect to time.

\[ \text{N-Phthal}^\text{COCD₃} \text{COCH₃} \]

Using kinetics it is possible to determine whether the aziridine (33) is the product of a direct exchange between (124) and (123) or one mediated a pre-equilibrium step, e.g. by reversible formation of an N-nitrene (32).

1. A direct exchange

\[
\text{i.e. } \text{A}_\text{P}B + A \xrightleftharpoons[k_{-1}]{k_1} AB + \text{A}_D
\]

where, \( \text{A}_\text{P}B = (124) \); \( A = (123) \); \( AB = (33) \) and \( \text{A}_D = (125) \) throughout.

From (1),
\[
\frac{d[AB]}{dt} = k_1[A_PB][A] - k_{-1}[AB][A_D]
\]

However, initially the concentrations of [AB] and [A_D] are small making the back reaction in (1) negligible, therefore,

\[
\frac{d[AB]}{dt} = k_1[A_PB][A] \quad \text{(second order)}
\]

If in (1), \([A_PB] = [A]\) initially then, substituting \(A_PB\) and \(A\) for \(a-x\), and \(A_B\) and \(A_D\) for \(x\), (2) reduces to:

\[
\frac{d[AB]}{dt} = k_1(a-x)^2 - k_{-1} x^2
\]
\[ = k_1(a^2 - 2ax + x^2) - k_{-1}x^2 \]

assuming \( k_1 \approx k_{-1} \) then,

\[ \frac{d[AB]}{dt} = k_1a(a-2x) \quad \text{where} \quad a = A \]

Hence, if \( k \) (i.e. \( k \) observed) above changes with increase or decrease in the concentration of \([A]\) then a second order direct exchange is occurring as shown in (1).

(2) An exchange mediated by a pre-equilibrium step, e.g. reversible formation of an N-nitrene

\[ \begin{align*}
\text{i.e.} & \quad A_2B \xrightleftharpoons[k_1]{k_{-1}} A_2 + B \\
\text{B + A} & \xrightleftharpoons[k_1]{k_{-1}} AB
\end{align*} \]  

From (3),

\[ \frac{d[B]}{dt} = k_1[A_2B] - k_{-1}[A_2][B] - k_1[B][A] + k_{-1}[AB] \]

assuming \( \frac{d[B]}{dt} = 0 \), (the steady state approximation for \( B \)) then:

\[ [B] = \frac{k_1[A_2B] + [AB]}{k_{-1}([A_2] + [A])} \]

the rate of formation of \( AB \) is given by:

\[ \frac{d[AB]}{dt} = k_1[B][A] - k_{-1}[AB] \]

substituting (5) into (6) gives:

\[ \frac{d[AB]}{dt} = k_1 \left\{ \frac{[A][A_2B] - [A_2][AB]}{[A_2] + [A]} \right\} \]

Initially, \([AB]\) and \([A_2]\) are small and (7) simplifies to

\[ \frac{d[AB]}{dt} = k_1[A_2B] \quad (1st. \text{order}) \]

However, if \( k_1 \neq k_{-1} \), and \([A_2B] = [A]\) initially then, substituting \( A_2B \) and

-287-
A for a-x and A_D, B, and AB for x, (7) reduces to:

$$\frac{d[AB]}{dt} = k_1 \left( \frac{(a-x)^2 - x^2}{x + (a-x)} \right) = k_1(a-2x)$$

Hence if $k_1$ ($k_{obs}$) remains constant with varying concentration of [A] then the possibility of reaction of (124) with (123) via a pre-equilibrium, e.g. N-nitrene formation cannot be excluded.

(i) Using 1.2 ml of d_6-benzene

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>I (mm)</th>
<th>ln (I)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>137</td>
<td>4.919</td>
</tr>
<tr>
<td>15</td>
<td>116</td>
<td>4.753</td>
</tr>
<tr>
<td>30</td>
<td>93</td>
<td>4.532</td>
</tr>
<tr>
<td>45</td>
<td>90</td>
<td>4.499</td>
</tr>
</tbody>
</table>

where I represents the integral value for the methyl signal in (123) in mm. A plot of time against ln (I) gave an initial first order rate constant of $k = 2.15 \times 10^{-4}$ s$^{-1}$, see plot 8.

(ii) Using 0.6 ml of d_6-benzene

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>I (mm)</th>
<th>ln (I)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>142</td>
<td>4.955</td>
</tr>
<tr>
<td>15</td>
<td>119</td>
<td>4.779</td>
</tr>
<tr>
<td>30</td>
<td>102</td>
<td>4.624</td>
</tr>
<tr>
<td>45</td>
<td>92</td>
<td>4.521</td>
</tr>
</tbody>
</table>

A plot of time against ln (I) gave an initial first order rate constant of $k = 1.83 \times 10^{-4}$ s$^{-1}$, see plot 9.

(iii) Using 0.3 ml of d_6-benzene

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>I (mm)</th>
<th>ln (I)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>84</td>
<td>4.430</td>
</tr>
<tr>
<td>15</td>
<td>68</td>
<td>4.219</td>
</tr>
<tr>
<td>30</td>
<td>56</td>
<td>4.025</td>
</tr>
<tr>
<td>45</td>
<td>50</td>
<td>3.970</td>
</tr>
</tbody>
</table>

A plot of time against ln (I) gave an initial first order rate constant of
$k = 2.25 \times 10^{-4} \text{ s}^{-1}$, see plot 10.

From the initial slopes of plots 8, 9 and 10 the rate constants observed were approximately the same and this indicates that the process for formation of aziridine (33) cannot proceed via the direct exchange mechanism (1) but that a mechanism involving an N-nitrene is not excluded.
Measurement of the rate constant for the disappearance of aziridine (124) in the presence of 2-acetylbenzofuran at different concentrations.
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