Diene-Derived

$N$-(3,4-Dihydro-4-oxoquinazolin-3-yl)aziridines:
Preparation and Reactivity

A thesis submitted to the Faculty of Science in fulfilment
of the requirements for the degree of Doctor of Philosophy in the
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by

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### Chapter 3: Aziridination of Cyclic Dienes with 3-Acetoxyaminoquinazolines

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Statement

The accompanying thesis submitted for the degree of Doctor of Philosophy entitled "Diene-Derived N-(3,4-Dihydro-4-oxoquinazolin-3-yl)aziridines: Preparation and Reactivity" is based on work conducted by the author in the Department of Chemistry of the University of Leicester in the period October 1996 to September 1999.

All the work in this thesis is original unless otherwise acknowledged by references. None of this work has been submitted for any other degree.

Signed

Date

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Abbreviations

Ac : acetyl
Ar : aryl
azir. : aziridine
Bn : benzyl
Bu' : tert-butyl
COSY : correlation spectroscopy
DEF : diethyl fumarate
DHA : 9,10-dihydroanthracene
DMF : N,N-dimethylformamide
DMSO : dimethylsulphoxide
dr : diastereoselectivity
ee : enantiomeric excess
e.g. : exempli gratia (latin “for example”)
eq : equivalents
Et : ethyl
Fig. : figure
h. : hour(s)
Het : heterocycle
HMDS : hexamethyldisilazane
LTA : lead tetra-acetate
mCPBA : meta-chloroperbenzoic acid
Me : methyl
min. : minute(s)
mp : melting point
NAQ : N-aminoquinazolinone
NMR : nuclear magnetic resonance
NOESY : nuclear Overhauser effect spectroscopy
Nuc : nucleophile
P : phthalimido
PFPP : 5,10,15,20-tetrakis(pentafluorophenyl)porphyrin
Ph : phenyl
PMA : polymolybdic acid
Pr' : ispropyl
pyr : pyridine
Q : quinazolinone
R : alkyl
R_f : retardation factor
TBDMS : tert-butyldimethylsilyl
TEA : triethylamine
TFA : trifluoroacetic acid
THF : tetrahydrofuran
TLC : thin layer chromatography
Ts : tosyl
ts' : transition state
Throughout this thesis

= $Q^1$

= $Q^2$

= $Q^3$

= $Q^4$

= $Q^5$

= $Q^6$

= $Q^7$

= $Q^8$
Diene-Derived
*N-(3,4-Dihydro-4-oxoquinazolin-3-yl)aziridines:*
Preparation and Reactivity

Christopher K. Meades

Abstract

The reaction of naphthalene with 3-acetoxyamino-2-alkylquinazolinones (QNHOAc) in the presence of hexamethyldisilazane (HMDS) gave a mixture of mono- and bis-aziridines in a ratio which depends upon the bulk of the (Q)2-substituent. By following the aziridination by NMR spectroscopy it was concluded that the first formed aziridine was the endo-N-invertomer and that bis-aziridination occurred only after N-inversion to the exo-N-invertomer. In the absence of HMDS the corresponding bis-aziridine is the major product.

\[ \text{Q}^6 \text{NHOAc} \]

\[ \text{(Q}^6 = 2(\text{S})-(2,2\text{-dimethyl-1-hydroxypropyl})\text{quinazolin-4(3\text{H})-one}) \]

was found to convert cyclopentadiene, 1,3- and 1,4-cyclohexadiene and cycloheptadiene into the corresponding \(N-(Q^6)\)-aziridines in the presence of titanium(IV) tert-butoxide with complete or high diastereoselectivity. Accompanying these aziridines in the case of 1,3- and 1,4-cyclohexadiene were \(N-(Q^6)\)-substituted dienylamines formed with complete diastereoselectivity by formal insertion into the (bis)allylic carbon hydrogen bonds.

In ring-opening of the 1,3-cyclohexadiene-derived aziridine above (two diastereoisomers) by mild acid, formation of the alcohol product involves participation by the \(Q^6\)-carbonyl oxygen. Cyclisation of each of these alcohols with carbonyl diimidazole and \(N-Q^6\) bond reduction using samarium(II) iodide gave the corresponding oxazolidinones in enantiopurified form.

The electron-withdrawing effect of the quinazolinone ring activates \(N-(Q)\)-aziridines towards attack by nucleophiles including thiolate and selenolate in the absence of acid. Several factors were found to influence regioselectivity in ring-opening of \(N-(Q)\)-aziridine-2-carboxylic esters at C2 including co-ordination of the aziridine to samarium(III) ion and overlap of the C-N \(\sigma^*\) anti-bonding orbital with the carbonyl \(\pi^*\) anti-bonding orbital. \(Q^2\)-Trifluoromethyl-substituted aziridines undergo ring-opening at a faster rate due to increased stabilisation of the nitrogen anion intermediate.
1.1 Introduction

Aziridines are saturated three-membered heterocycles containing one nitrogen atom (Fig 1.1).

![Fig 1.1](image)

Like other 3-membered ring systems, such as cyclopropanes and epoxides, aziridines are highly strained rendering them susceptible to ring-opening reactions which dominate their chemistry.

![Scheme 1.1](image)

Aziridines are therefore useful synthetic intermediates in organic chemistry. They were first unwittingly synthesised by Gabriel in 1888, who treated 2-bromoethylamine with base and isolated a product which he believed to be vinylamine (Scheme 1.1); the correct aziridine structure 1 was later assigned by Markwald.

1.2 Bonding of aziridines

![Fig 1.2](image)

Fig 1.2; C-X bond energy in three-membered rings
The bond energy in aziridines is similar to that measured in epoxide and cyclopropane rings (Fig 1.2). To accommodate the small angles of the ring, the hybridisation of the ring atoms results in high p-orbital character in the orbitals overlapping to form the ring bonds. Electron density maps have shown that overlap of these orbitals is outside the axes joining the nuclei and result in the formation of so-called "banana" bonds (Fig 1.3).

![Fig 1.3](image)

As a corollary, the bonds exocyclic to the ring have high s-orbital character and the angle between the two geminal exocyclic bonds at C2 or C3 is widened to an angle (~119°) significantly greater than the value for a normal tetrahedral species (~109°). This has the effect of facilitating ring-opening reactions as ingress of the nucleophile is eased considerably. Aziridines are also less basic (pKa=8.04) than secondary amines (pKa=11) as the lone pair-containing orbital on nitrogen has high s-character.

### 1.3 N-inversion in aziridines and amines

The inversion frequency at the nitrogen atom in amines bearing three different substituents is rapid at ambient temperature (ca. $2 \times 10^{11} \text{ s}^{-1}$), interconverting a pair of enantiomers via a planar transition state 2 where the nitrogen is sp$^3$-hybridised. Alkylation of the nitrogen lone pair in such an amine prevents N-inversion and allows separation of enantiomeric quaternary salts such as 3 (Scheme 1.2).
The barrier to $N$-inversion in aziridines is abnormally high and changes in $N$-substituent have a dramatic effect on the rate of $N$-inversion. The higher barrier in aziridines arises from the increase in energy required to attain the planar ts' in which the C-N-C bond angle is (formally) $60^\circ$ as in the pyramidal ground state (4 in Scheme 1.3) compared with corresponding angles of $109^\circ$ and $120^\circ$ for an acyclic amine. Alternatively one can say that in the ts' for $N$-inversion, the lone pair of electrons must occupy a p-orbital (of 4); rehybridisation to achieve this will be more difficult for an aziridine where, in the pyramidal ground state the lone pair is in an orbital having higher $s$-character than in the case of an acyclic amine.

The $N$-inversion barrier in aziridines is greatly reduced when the nitrogen substituent is alkoxycarbonyl; conjugation of the nitrogen lone pair (in a p-orbital) with the carbonyl $\pi$-bond leads to the transition state being stabilised by resonance thus lowering the inversion barrier. Electron-withdrawing substituents such as
chlorine greatly increase the \( N \)-inversion barrier. The ring-nitrogen responds to the electron-withdrawing demand of chlorine by supplying more p-character to the orbital involved in the \( \sigma \)-bond with chlorine.\(^9\) The result is to further increase the energy required to achieve the planar \( ts' \) with its p-orbital-containing lone pair (see above).

Optically active aziridines can be obtained as a result of a sufficiently high inversion barrier. Chlorination of aziridine 5 at low temperature with an enantiopure chlorinating agent gives aziridine 6 which is optically active as the nitrogen is a chiral centre.\(^{10}\) Racemisation of 6 occurs over four days at 0°C (Scheme 1.3).

### 1.4 Epoxidation vs. Aziridination

- **Scheme 1.4**

An invaluable route to chiral alcohols as single diastereoisomers uses epoxides as synthetic relay intermediates (Scheme 1.4a).\(^{11-13}\) Methods for stereospecific epoxidation and epoxide ring-opening are available which make the \( E \) or \( Z \)-alkene \( \rightarrow \) epoxide \( \rightarrow \) ring-opened alcohol product sequence widely applicable to the organic
Analogous alcohols of high enantiopurity have been made available by the catalytic enantioselective epoxidation methods employed by Sharpless\textsuperscript{14-16} (Scheme 1.4b) and Jacobsen\textsuperscript{12,17-18} (Scheme 1.4c) among others.

In contrast there are a very few general methods for direct and stereoselective aziridination of alkenes – aziridination. This is a major reason for the lesser use made of aziridines in synthesis in spite of access to a wide range of \(\alpha\)- and \(\beta\)-amino acids, 1,2-diamines, 1,2-amino alcohols and other useful products that the sequence alkene \(\rightarrow\) aziridine \(\rightarrow\) ring-opened (amine) product potentially affords.

Two versatile methods for stereospecific (inherently diastereoselective)\textsuperscript{19} epoxidation of double bonds use peroxyacids (HOOCOR) – in particular \(m\)-chloroperoxybenzoic acid – or tert-butylhydroperoxide (Bu'OOH) in the presence of a metal catalyst [\([\text{Ti(IV)}, \text{V(V)} \text{ or Mo(IV)}]\)]. However, their nitrogen analogues, the corresponding \(O\)-acylhydroxylamines (RNHOCOR') and \(O\)-tert-butylhydroxylamines (Bu'ONHR) are not aziridinating agents (see, however, below).\textsuperscript{14}

Dioxirane 7 can be used as an epoxidising agent (Scheme 1.5),\textsuperscript{20} but di\textsuperscript{21} (and tri)\textsuperscript{22} aziridines 8 and 9 which have been prepared are not used as aziridinating agents. Interestingly oxaziridine 10 functions as a highly enantioselective epoxidising agent rather than effecting aziridination.\textsuperscript{23}
If the hydroperoxide anion is used to epoxidise an electron deficient alkene such as an \( \alpha,\beta \)-unsaturated ester, then stereospecificity in the 2-step reaction is lost due to rotation around the C-C bond in the intermediate 11 resulting in isolation of a mixture of diastereoisomers 12 (Scheme 1.6).

1.5 Synthesis of aziridines from amino alcohols

A conceptually obvious route to aziridines uses 1,2-amino alcohol precursors since the hydroxyl group is readily converted into a good leaving group\(^{24}\) and an aziridine ring results from intramolecular nucleophilic displacement by amide anion or amine lone pair (Scheme 1.7). Synthesis of enantiopure aziridines is possible from enantiopure amino alcohols.\(^{25}\)

Some enantiopure 1,2-amino alcohols used in aziridine synthesis are commercially available, others are obtained by reduction of enantiopure \( \alpha \)-amino acids.\(^{26-29}\) The conversion of ethanolamine to ethylene imine by Wenker\(^{30}\) is an alternative early example of the amino-alcohol \( \rightarrow \) aziridine transformation via an intermediate cyclic sulphamidate, in addition to aziridine synthesis from 2-haloamines 'demonstrated by Gabriel.\(^{31}\)
More recent methods for conversion of the hydroxy group in amino alcohols to good leaving groups used triphenylphosphine plus bromine,\textsuperscript{32} carbon tetrachloride\textsuperscript{33-34} or diethylazodicarboxylate (DEAD),\textsuperscript{35} the latter proceeding via a Mitsunobu type ring-closure reaction (Scheme 1.8).\textsuperscript{36}

1.6 Synthesis of aziridines from hydroxy acids

![Scheme 1.9](image)

Tartaric acid, one of the most familiar and historically important hydroxy acids,\textsuperscript{37} allows access to a wide range of enantiomerically pure building blocks in organic synthesis. Both enantiomers are readily available and can be converted into pairs of enantiomerically pure aziridines 13, 14 and 15, 16 as shown above (Scheme 1.9).\textsuperscript{38-39}
1.7 Synthesis of aziridines using epoxides

Ring-opening of epoxides by nitrogen nucleophiles such as azide followed by subsequent ring-closure of the resulting 1,2-amino alcohol derivative is an attractive route for synthesis of aziridines. Reaction of the azide moiety of an azide alcohol with triphenylphosphine via the Staudinger reaction gives an imino phosphorane/oxaphospholine intermediate which is thermally cyclised to yield aziridine (Scheme 1.10). The overall epoxide → aziridine transformation is stereospecific since inversion takes place at both carbon atoms.

The Sharpless asymmetric epoxidation (AE), mediated by titanium(IV) alkoxide and tert-butyl hydroperoxide in the presence of a tartrate ester, provides a plethora of enantiomerically pure epoxides from allylic alcohols; all possible stereoisomers of the hydroxyalkyl aziridine in Scheme 1.11 can be routinely
prepared. This methodology has also been applied to the synthesis of 1H-aziridine-2-carboxylic acids and aziridine-2,3-dicarboxylic acids.

### 1.8 Synthesis of aziridines from alkenes

![Scheme 1.12](image1.png)

Sharpless et al have recently devised a method for bromine-catalysed aziridination using Chloramine-T (TsNClNa) and PTAB (phenyltrimethylammonium tribromide) as a source of “Br⁺”. This catalyst provides good yields of aziridine products across a range of simple alkenes and allylic alcohols (Scheme 1.12).

![Scheme 1.13](image2.png)

Addition of bromine to alkenes gives 1,2-dibromoalkanes which, on treatment with amines yield racemic aziridines. Treatment of enantiomerically-pure 2-bromoacrylamides with primary amines via a diastereoselective Gabriel-Cromwell reaction gives N-alkylaziridines; best results were obtained using a camphorsultam chiral auxiliary (Scheme 1.13).

The only enantioselective route under this heading of any generality is the catalytic enantioselective aziridination of alkenes devised independently by Evans.
Jacobsen\textsuperscript{49} and by Katsuki.\textsuperscript{50} In this reaction [N-(p-toluenesulphonyl)imino] phenyliodinane (PhI=NTs) in the presence of catalytic quantities of low valent metal complexes (Cu or Mn) with a variety of chiral ligands 18-20 provided an exciting development in aziridine synthesis in the early 1990s (Scheme 1.14).

However, this reaction is not invariably stereospecific and aziridines derived from \textit{cis} alkenes may yield \textit{trans}-disposed substituents on the aziridine ring; application of the method is therefore favoured for synthesis of mono-substituted, 2,2-disubstituted or 2,3 \textit{trans}-substituted aziridines. This methodology has also been applied to the aziridination of dienes including butadiene, cyclopentadiene, 1,3-cyclohexadiene and cycloheptadiene in good yield.\textsuperscript{51}

Recently, Komatsu \textit{et al} have reported enantioselective and stereospecific aziridination of styrene derivatives using chiral nitrodomanganese complexes and similar ligands to 20 with up to 94\% \textit{ee}.\textsuperscript{52}

\textit{via Nitrene addition}

The development of mild conditions for nitrene generation has allowed electron-rich alkenes and cyclic alkenes to be aziridinated by oxidation of \textit{N}-2,4-dinitrobenzenesulphenamide with \textit{N}-bromosuccinimide.\textsuperscript{53} \textit{N}-(2,4-dinitrobenzenesulphenyl)-substituted aziridines are potentially useful since \textit{N}-deprotection has been achieved, at least in one case, without aziridine ring-opening.\textsuperscript{54}
Treatment of 1,4-dihydro-1,4-iminonaphthalene with 2,4-dinitrophenylsulphenyl chloride gave sulphenamide 21 which acts as an aziridinating agent for a range of alkenes (including methyl acrylate) by generation of the corresponding arenesulphenylnitrene 22 in situ on heating (Scheme 1.15). It appears that the sulphur substituent on the nitrene stabilises the singlet state since stereospecific aziridination of cis- and trans-butene is found.

Another well-studied aziridination uses ethoxycarbonylnitrene (Scheme 1.16); aziridine products obtained from these processes are the result of stereospecific singlet nitrene addition but require a large excess of the alkene.

There are additional limitations to the synthetic usefulness of this nitrene besides conversion of the first-formed nitrene into the triplet ground state at low
concentrations of alkene leading to loss of configuration of the parent alkene in the aziridine product by non-stereospecific addition. Thus competitive insertion reactions into C-H and other σ-bonds may occur.

\[ R - N_3 + \text{alkene} \rightarrow \text{aziridine} \]

Scheme 1.17

On heating azides with alkenes, 1,3-dipolar addition to give triazolines can occur; although deazetation of the triazoline may also lead to an aziridine, the reaction is not always stereospecific (Scheme 1.17).57

\[ \text{O} \]

\[ \text{N} \]

\[ \text{Z} \]

\[ \text{BHT} \]

\[ \text{CH}_2\text{Cl}_2, 109^\circ \text{C} \]

10%

\[ \text{NuIL}_2 \text{H}_2\text{O, MeOH, AcOH, AcSH, also PhLi/CuI, then H}_2\text{O} \]

Scheme 1.18

Intramolecular aziridination by thermolysis of appropriate alkoxy carbonyl azides has been accomplished but it is not certain that a nitrene is the intermediate (Scheme 1.18).58

For ethoxycarbonylnitrenes stabilisation of the singlet state (leading to inherent stereoselectivity in aziridination) and reduction of nitrene reactivity can be achieved by changing the carbonyl substituent. Thus aziridination of \textit{cis}- or \textit{trans}-4-methylpent-2-ene with \textit{N}-(methanesulphonyl)ethoxycarbimidoynitrene 23 (Scheme 1.19) is stereospecific even at low concentrations of the alkene.59
1.9 Aziridination via Michael addition

There are many examples of aziridination via Michael addition of a nitrogen nucleophile followed by elimination of a leaving group, but these are not inherently stereoselective: the configuration of the alkene is not usually retained in the product - especially with cis-alkenes. Only trans-aziridine 26 was isolated from Michael addition of diphenylsulphinimide 24 to cis- and trans-dibenzylethylene as loss of configuration occurs via intermediate 25 (Scheme 1.21).
Dai et al. have demonstrated that a mixture of cis- and trans-aziridines is obtained from addition of the anion derived from sulphonium salts to N-tosylimines (Scheme 1.22).

Stereoselective synthesis of aziridines from imines is obtained by using chiral imines, chiral nucleophiles or chiral catalysts. Condensation of enantiopure sulphinylimines with the lithium enolate of methyl-\(\alpha\)-bromoacetate allows cis-N-(p-toluenesulphinyl)aziridine-2-carboxylates to be isolated in 60-77 % yield; up to 98 % diastereoselectivity is observed in formation of the cis-diastereoisomer using methyl-\(\alpha\)-bromopropionate in this aza-Darzens type reaction.

A chair-like transition state is proposed (Scheme 1.23) in which the sulphinyl oxygen and imine nitrogen are co-ordinated to the lithium cation and both the enolate and \(N\)-sulphinylimine double bonds are required (sulphinylimines have low inversion barriers). As both enantiomers of the sulphinyl group are readily available from Anderson's reagent, synthesis of either aziridine enantiomer can be achieved.
1.11 Kinetic resolution of aziridines

Resolution of racemic aziridines can be achieved either chemically or enzymatically.

Enantiomeric excesses of up to 100% are observed from completely diastereoselective complexation of (-)-trans-2,3-bis(hydroxydiphenylmethyl)-1,4-dioxaspiro[5,4]decane 29 (derived from tartaric acid) with aziridine 30.68

Good enantiopurity is achieved in lipase-catalysed alcoholysis of aziridine-2-carboxylates69 and aziridine-2,3-trans-dicarboxylates70 with pig pancreatic lipase (PPL) or candida cylindracea lipase (CCL).

1.12 Diastereoselective aziridinations

As shown above, there are few general methods available for the highly diastereoselective aziridination of alkenes. Examples where the existing chiral element (chiral centre) is present in the alkene (substrate-controlled
diastereoselectivity) are rare and even fewer methods are available where the chiral element is contained in the reagent (reagent-controlled diastereoselectivity).

LTA-Mediated oxidative addition of N-aminophthalimide to α,β-unsaturated ester 31 bearing Oppolzer’s chiral auxiliary71 and to sugar-derived α,β-unsaturated esters e.g. 3272 both gave aziridines with excellent diastereoselectivity (Scheme 1.25). Aziridination of α-methylene-γ-butyrolactone by oxidative LTA-mediated addition of N-aminobenzimidazole gave aziridine 33 as a single diastereoisomer.73

![Scheme 1.25](image)

1.13 Enantiopure aziridines via other routes

If an enantiopure aziridine is required it is most likely to be prepared from chiral pool materials e.g. amino acids, amino alcohols or other readily available
starting materials such as single enantiomers of epoxides. These procedures usually involve multistep reactions and depend on the availability of the desired enantiopure precursors.

The absence of general methods for aziridination (by comparison with epoxidation) means that aziridine ring system is under-utilised and its synthetic potential (and potential advantages over the use of epoxides) has not yet been exploited.

1.14 Aziridination of alkenes using oxidative addition of N-aminoheterocycles

Work carried out at Leicester University in the late 1960s showed that LTA oxidation of e.g. N-aminoheterocycles 34-37 in the presence of alkenes often gave high yields of aziridine product (Scheme 1.26).74

![Chemical structures and Scheme 1.26](image)

Aziridines were obtained in good yield from oxidation of N-aminophthalimide (PNH₂) 34 using either electron rich alkenes – styrene, butadiene and trans-but-2-ene, or electron-deficient alkenes – methyl acrylate and methyl vinyl ketone. Only a small amount of aziridine 40 was obtained from aziridination of hex-1-ene and the major product was phthalimide 41.75
The intermediates in these aziridinations were assumed to be the corresponding N-nitrenes e.g. 38 (Scheme 1.27) stabilised by resonance, which were adding to alkenes via their singlet states, accounting for the stereospecific addition to cis- and trans-aziridines obtained. The unusually high yields in aziridination of electron deficient alkenes were ascribed to the nucleophilic character of the intermediate nitrenes (as expressed by 39 in Scheme 1.27).

The crystalline aziridine 42 (Scheme 1.28) isolated from LTA oxidation of N-aminophthalimide 34 in the presence of 2-acetylbenzofuran was itself shown by D. Jones in Leeds University to be an aziridinating agent and the intermediate in thermolysis of this product, presumably the N-nitrene, was assumed to be identical to that generated by oxidation of N-aminophthalimide with LTA.

Subsequently, generation of what appeared to be the same N-nitrene by a number of independent routes was thought to prove the identity of the aziridinating species (Scheme 1.29): the presumed nitrene species in all these reactions showed apparently the same ambiphilic reactivity in addition both to styrene and to methyl acrylate and reacted stereospecifically with alkenes.
Subsequent work in Leicester in the mid-1970s showed that aziridinations employing the supposed phthalimidonitrene derived from \( N \)-aminophthalimides in addition to being inherently diastereoselective (stereospecific) were completely diastereoselective in an unexpected sense (occasional diastereoselectivity).\(^{19}\)

Thus aziridination of styrene by oxidation of \( N \)-aminophthalimide with LTA in deuterochloroform at -20°C was monitored by NMR spectroscopy\(^{82}\) and showed that the kinetically-formed product was the \emph{endo}-\( N \)-inertomer 43 in which the phenyl group and phthalimide are \emph{cis}. On warming above 0°C, complete inversion occurred to give the more stable \emph{trans}-aziridine 44 as the thermodynamic product. Signals belonging to the \emph{cis}-aziridine were not present when the NMR spectrum was re-run at -20°C (Scheme 1.30). It was fortuitous for this observation that aziridines containing the electron-withdrawing phthalimido substituent have a sufficiently raised \( N \)-inversion barriers (\emph{cf.} 1.3) that their rates of \( N \)-inversion are effectively zero at -20°C.
A similar result was observed in aziridination of methyl acrylate with cis-invertomer 45 as the sole kinetically-formed product; a 5:1 mixture of trans : cis N-invertomers was present after thermodynamic equilibrium above 0°C in this instance. The kinetically-formed cis-aziridine 45 crystallised out of solution ~ -40°C; at ambient temperature conversion of crystalline cis 45 to the trans-N-invertomer 46 occurred slowly over several weeks.

The presence of an attractive secondary interaction (see below) between the phthalimide ring and π-electron-containing alkene substituent in the aziridination ts in Scheme 1.30, which accounts for the occasional diastereoselectivity above, was an unexpected but ultimately very important discovery.

1.15 LTA oxidation of 3-aminoquinazolinones

In the family of N-aminoheterocycles 34-37, 3-aminoquinazolinones 35 are particularly useful members as different R substituents can be incorporated at the 2-position of the quinazolinone ring. When the R-substituent contains a double bond, intramolecular aziridination can take place.83-84

![Scheme 1.31](image)

A key experimental observation in this work was made by Grimshire and subsequently developed by Kelly in the late 1980s: monitoring the intramolecular aziridination by LTA oxidation of 3-aminoquinazolinone 47 by NMR spectroscopy
revealed the presence of an intermediate which did not bring about aziridination of the double bond in the side chain until the temperature was raised (>0°C) (Scheme 1.31). Following on from this initial observation, LTA oxidation of 3-amino-2-ethylquinazolinone was also found to form a stable intermediate at -20°C (Scheme 1.32).

Scheme 1.32

The $^1$H and $^{13}$C NMR spectra of this intermediate at -30°C and an additional carbonyl stretching frequency at 1768 cm$^{-1}$ in its IR spectrum at -20°C revealed the identity of the aziridinating species as the corresponding 3-acetoxyaminoquinazolinone (Q$^2$NHOAc). The increase in the rate of disappearance of 49 with increased alkene concentration and with formation of aziridine 50 was consistent with 49 being the actual aziridinating species.

1.16 Aziridination of alkenes with QNHOAc

Scheme 1.33
It appears that aziridination of alkenes with QNHOAc mechanistically resembles epoxidation of alkenes via the Bartlett mechanism and this reagent QNHOAc, therefore, is the nitrogen analogue of peroxyacetic acid (Scheme 1.33).

Support for this analogy comes from aziridination of cyclohexen-2-ol with Q"NHOAc which shows a similar preference for syn-selectivity as observed by Henbest et al in peroxybenzoic acid epoxidation of the same alkene.

Hydrogen bonding between reagent and allylic hydroxy group is believed to direct addition from the syn-face of the olefin in both cases.

**1.17 Important features of aziridination of alkenes with QNHOAc**

3-Amino-2-substituted-quinazolinones are readily available and are prepared efficiently from acids including chiral acids; the corresponding 3-acetoxyamino
derivative is readily obtained in solution, usually dichloromethane or chloroform, in high yields by oxidation with LTA at -10°C → -20°C (Scheme 1.35).

Acetoxyamino-2-alkylquinazolinones are only stable for a few minutes above 0°C when prepared in situ. Decomposition of QNHOAc is accelerated by acetic acid; protonation of the carbonyl oxygen of the Q group leads to formation of 3H-quinazolinone 51 by the proposed mechanism shown in Scheme 1.36). Acetic acid is not only co-produced during acetoxylation but also in the aziridination step itself, limiting aziridine yields with less reactive alkenes.

![Scheme 1.36](image)

3-Acetoxyaminoquinazolinones bearing 2-alkyl substituents are efficient aziridinating agents for both electron-rich alkenes e.g. styrene and electron-deficient alkenes e.g. methyl acrylate. Hexamethyldisilazane (HMDS) is added to solutions of QNHOAc to scavenge acetic acid, prolonging the lifetime of the aziridinating agent and resulting in higher yields with less reactive alkenes e.g. hex-1-ene (Scheme 1.37).
Exceptionally, 3-acetoxyamino-2-trifluoromethylquinazolinone (QNHOAc) \( 52 \) is stable in solution at ambient temperature for several hours and also gives superior aziridine yields, especially with less reactive alkenes\(^{90} \) (Scheme 1.37).

1.18 Aziridination of alkenes with QNHOAc: mechanism

Our present transition state models for the aziridination differ subtly depending upon the electron availability of the alkene undergoing aziridination. Using styrene, an electron-rich alkene, the aziridination \( t^* \) has the quinazolinone ring and alkene contained in parallel planes with an attractive \( \pi-\pi \) interaction present between the phenyl ring and the quinazolinonyl carbonyl group\(^{91} \) (Fig 1.4) (cf. similar \( \pi-\pi \) interaction in Diels-Alder \( t^* \)).

\[
\text{Fig 1.4}
\]

In the 3-membered ring formation, \( C_2-N \) bond formation runs ahead of \( N-C_1 \) bond formation and thus with partial carbocation generation at the benzylic \( C_1 \) position: the exocyclic nitrogen, therefore, behaves primarily as an electrophile with backside displacement of the acetoxy group in an \( S_N2 \) sense, requiring this leaving group to be proximal to the quinazolinone carbonyl group during aziridination.
The particular configuration at the sp$^3$-hybridised exocyclic nitrogen specified by this mechanism is in accordance with the sense of diastereoselectivity obtained from aziridinations of α- and of γ-hydroxymethylstyrene derivatives (Scheme 1.38): hydrogen bonding is only possible with the departing acetoxy group in aziridination of the α-hydroxymethylstyrene. The sense and magnitude of the diastereoselectivity in aziridination of these α- and γ-hydroxymethylstyrenes is consistent with this interpretation.

In the transition state for aziridination of methyl acrylate, an electron-deficient alkene, an attractive interaction between the ester carbonyl oxygen and quinazolinone carbonyl carbon is believed to be present, requiring the α,β-unsaturated ester to adopt an s-cis conformation.
Evidence for this requirement comes from comparison of the aziridinations of s-trans-fixed α,β-unsaturated lactone 53 and s-cis-fixed α-methylene-γ-lactone 54; only the latter underwent aziridination.\textsuperscript{86} Thus the CO(OMe)–Q(C=O) interaction in the ts' in Fig 1.5 is secondary only in the sense that it does not lead to bonds in the product: in its absence no primary interaction leading to product formation occurs either.

![Scheme 1.39](image)

**Scheme 1.39**

Although in the ts' in Fig 1.5 both aziridine ring bonds are forming, N-C₃ bond formation runs slightly ahead of C₂-N formation, requiring the acetoxy group to assume a position distal to the quinazolinone carbonyl group for SN₂ displacement to occur at the exocyclic nitrogen. The secondary interaction in Fig. 1.5 activates electron deficient alkenes toward Michael addition at C₃ by the QNHOAc nitrogen whose lone pair of electrons becomes more available as a result of reduced electrophilicity from the quinazolinone carbonyl group - also owing to the secondary interaction.\textsuperscript{92}

![Scheme 1.40](image)

**Scheme 1.40**

In this ts', hydrogen bonding is possible between the departing acetoxy group and the hydroxy group of a γ-hydroxymethyl-substituted α,β-unsaturated ester (Scheme 1.40) and not of an α-hydroxymethyl-substituted α,β-unsaturated ester i.e. a
situation complementary to that above for the analogous styrene derivatives. Again the sense of diastereoselectivity in aziridination of these α,β-unsaturated ester alcohols (and their O-acetates) agrees with this interpretation.

The \(N\)-inversion barrier in \(N\)-(Q)-substituted aziridines is lower than in corresponding \(N\)-phthalimido analogues and inversion is taking place at the temperature required for aziridination to occur. Consequently it is not clear that the \(cis\)-\(N\)-invertomer is the exclusive first-formed product except where, exceptionally, the barrier to \(N\)-inversion is raised in the kinetically-formed \(cis\)-aziridine (see Chapter 2). However, the explanations above and all subsequent interpretations are based on the assumption that \(cis\)-\(N\)-invertomer formation is exclusive.

1.19 Aziridination in the presence of TFA

![Scheme 1.41](image)

It was found by Tughan\(^94\) that the diastereoselectivity of aziridination is greatly improved when carried out in the presence of trifluoroacetic acid (TFA).\(^94\) The yield of aziridine products obtained from aziridination of less reactive alkenes can also be increased by addition of QNHOAc to a solution of the alkene and TFA in dichloromethane at -40°C.\(^95\) A three molar excess of TFA is required to optimise these effects suggesting the formation of a diprotonated species as the reactive intermediate.

It was suggested by Tughan\(^93\) that protonation of both carbonyl oxygen and \(N_1\) positions of the quinazolinone ring had the effect of inverting the alkene orientation in the transition state as shown in Fig 1.6 so that the carbonyl oxygen of e.g. methyl acrylate now lies directly above/below the imine carbon of the Q group.
Fig 1.6

Experimental evidence to support this proposal has come recently from the work of Ulukanli who studied aziridination of $\alpha,\beta$-unsaturated esters using 3-acetoxyaminoquinazolinones and their 5-methyl congeners.$^{96}$

Scheme 1.42

Thus competitive reaction of methyl acrylate with a 1:1 mixture of aziridinating agents 49 and 55 gave a 3:2 mixture of aziridines 56 and 57 without TFA (ts' 60) and a 1:1 mixture on inclusion of TFA (ts' 61). However, tert-butyl acrylate gave aziridine 58 in the competitive reaction without TFA (ts' 60) with no aziridination by the 5-methyl congener, the result of a steric interaction between the Q-5-Me group and ester tert-butyl group in ts' 60. In the presence of TFA, a 1:1
mixture of aziridines 58 and 59 (via ts' 61) is produced as there is no steric interaction of the 5-Me group with the ester in the inverted ts'.

![Fig 1.7](image)

Competitive aziridinations using 3-acetoxyamino-2-trifluoromethyl-quinazolinone and its 5-methyl analogue show 1:1 mixtures of aziridines result from both methyl acrylate and tert-butyl acrylate which suggests that even in the absence of TFA, C=O(ester)-C=N(Q) overlap is preferred in aziridination ts' 62 as a result of the increased electrophilicity of the imine carbon.

1.20 Diastereoselectivity in aziridinations using 3-acetoxyaminoquinazolinones

![Scheme 1.43](image)

NMR analysis of Q^2NHOAc at -20°C showed the methylene protons of the ethyl group to be diastereotopic and appear as an ABX system. The chiral element responsible for this non-equivalence is the pyramidal exocyclic nitrogen which inverts
slowly on the NMR timescale, although inversion was shown by Williams\textsuperscript{97} to be fast on the timescale of aziridination. Incorporation of an additional chiral substituent in the 2-position of the quinazolinone ring gives rise to diastereoisomers, a 4:1 ratio from the NMR spectrum of Q\textsuperscript{8}NHOAc 63.\textsuperscript{93}

Aziridination of methyl acrylate gives a 2.4:1 mixture of diastereoisomers via a ts' believed to resemble 64 for formation of the major one (Scheme 1.44). The increase and change in sense of diastereoselectivity is observed on inclusion of TFA (Scheme 1.44) is presumed to be the result of a change in transition state geometry to that in 65 (cf. 61 above).

Here the more electrophilic (Q)-imine carbon holds methyl acrylate closer during aziridination and the preferred sites for the Bu', Me and H are as illustrated to accommodate the close proximity of the methoxycarbonyl group.\textsuperscript{96} Note that ts's 64
and 65 have opposite configurations for the \( N \)-acetoxyamino chiral centre but recall that this centre is stereolabile on the timescale of the aziridination.

Scheme 1.45

Diastereoselective aziridination of \( \beta \)-substituted styrenes was observed using \( Q^7 \)NHOAc 66: the required NAQ\(^7\) was prepared as a single enantiomer from (S)-lactic acid.\(^{98} \) The superior diastereoselectivity is ascribed to a conformational preference for the Q-2 chiral substituent and the C-O bond of the silyloxy group assuming a planar orientation with the quinazolinone ring. This conformational preference dictates the positions of the hydrogen and methyl groups, and alkene approach as shown in Scheme 1.46.

Scheme 1.46

Increased diastereoselectivity with increased electronegativity of the \( \beta \)-substituent (Scheme 1.46) was attributed to increasingly tighter transition states in the aziridinations.
1.21 Diastereoselectivity using chelation control

The highest levels of diastereoselectivity are obtained when the substituents on the chiral centre C* of the Q-2-substituent are fixed in the aziridinating agent QNHOAc by restricting rotation around the C*-Q bond. Aziridination of styrene with Q^6NHOAc 67 shows little diastereoselectivity, but in the presence of titanium(IV) tert-butoxide (TTB) gives a single diastereoisomer of aziridine 68 (Scheme 1.47).

![Scheme 1.47](image)

Initial titanium alkoxide formation with the hydroxy group in the side-chain followed by chelation with N\text{I} fixes the orientation of substituents on the chiral centre. In the aziridination, alkene attack from one face of the quinazolinone ring is eliminated by the tert-butyl group preventing approach due to steric factors. The configuration of the newly created chiral centre in aziridine 68 was confirmed by X-ray crystal structure analysis.

Aziridination of indene using 67 in the presence of TTB gave the (S)-C_2-configured cis-N-invertomer of aziridine 69 which slowly inverted to the trans-form at >0°C (Scheme 1.48). The barrier to N-inversion in aziridine 69a is sufficiently raised to confirm that it is the exclusive kinetically formed product (see earlier discussion 1.18).
1.22 Preparation of (2-substituted-3,4-dihydro-4-oxoquinazolin-3-yl)nitrene

Aziridination of alkenes via LTA oxidation of N-aminophthalimide is also thought to give the corresponding N-acetoxyaminophthalimide (PNHOAc) 70 but this intermediate is only stable in solutions at <-35°C. The aziridinating species from the thermal decomposition of aziridine 42 (Scheme 1.28) was formulated as the N-nitrene PN: 38 but its reactivity profile was very similar to that of PNHOAc.86

This problem was solved when it was found that competitive reactions of styrene and methyl acrylate (1:1 mixture) with PNHOAc 70 and PN: 38 gave different ratios of aziridines (1:1.3 v 1:1.8 respectively). Thus there are two aziridinating agents each with a separate existence but having very a similar but distinguishable reactivity profile.
It was found by E. Barker\textsuperscript{100} that reaction of $Q^3\text{NHOAc}$ 71 with triethylamine (TEA) at -30°C in dichloromethane gave an ammonium ylide 72: at this temperature slow spontaneous cleavage leads to generation of the nitrene $Q^3\text{N}$: 73 which adds \textit{in situ} to electron-rich or electron-deficient alkenes at lower temperatures than those required using authentic $Q^3\text{NHOAc}$ (Scheme 1.50). Thus it appears that, as in the phthalimide case above, 71 and 73 are both aziridinating agents and have similar but identifiably different reactivity.

### 1.23 Ring-opening of aziridines with C-N bond-cleavage: general

The regiosense of ring-opening by acids is controlled by ring-substituents better able to stabilise the developing positive charge. Attack of the nucleophile on the ‘not fully developed’ carbocation usually leads to (stereospecific) inversion of configuration but some loss of configuration may result where the ring-substituent is particularly carbocation-stabilising (Scheme 1.51a).\textsuperscript{101} Typically, aziridines which are $N$-H or $N$-alkyl-substituted undergo ring-opening by this mechanism and it is usually a phenyl or alkyl group on the ring that stabilises the developing carbocation.

Nucleophilic ring-opening is initiated by attack of the nucleophile on the aziridine ring-carbon (Scheme 1.51b) but is encouraged by the presence of an electron-withdrawing group on the ring-nitrogen, e.g. alkyl(aryl)sulphonyl [$R(\text{Ar})\text{SO}_2$], alkoxy carbonyl (RO$_2$C), phosphinoyl ($R_2$PO), etc., to stabilise the developing negative charge (so-called ‘activated’ aziridines).\textsuperscript{102} Although inversion of configuration at the ring carbon would be expected, and is usually found, it is not commonly observed because strict nucleophilic ring-opening (i.e. without assistance...
from N-protonation in the ts') normally occurs on unsubstituted ring-carbons (inversion here can be demonstrated using monodeuterium substitution of the aziridine ring-carbon undergoing attack).

![Scheme 1.51](image)

Although the ts' in nucleophilic ring-opening does not require protonation, it may be that a proton source in the reaction mixture is required when the nucleophile is also a good leaving group to eliminate reversibility of the ring-opening (Scheme 1.51b).

Of course, many ring-opening reactions of aziridines involve electrophilic and nucleophilic components and, for example, the reaction may occur by protonation of the ring-nitrogen and nucleophilic assistance to break the ring bond.

**1.24 Acid catalysed ring-opening**

Some examples of acid catalysed ring-opening are illustrated below:\textsuperscript{101,103}

![Scheme 1.52](image)
Ring opening of aziridine 74 is thought to proceed via an S_N1 mechanism (Scheme 1.52). Alcoholysis of cis-aziridine 76 also gave a single regioisomer with almost complete inversion of configuration. It seems likely that, in the absence of a strong nucleophile, acid-catalysed ring-opening of aziridines N-substituted with electron-withdrawing groups also occurs: the possibility that the small loss of configuration is the result of some epimerisation of the product was not excluded.

1.25 Nucleophilic ring-opening

Ring-opening of mono-substituted aziridines occurs predominantly at the methylene carbon as in (a), (c) and (d) (Scheme 1.53). In (b) the small negatively charged nucleophile is directed to the C_3 position by a repulsive interaction with the carboxylate anion and ring-opening occurs in an S_N2 sense with inversion of configuration. Wittig reagents have also been used in ring opening reactions as in (c). Nucleophilic ring opening of enantiopure N-tosyl aziridines (d) with anions derived from 1,3-dithianes proceeds regiospecifically at the lesser substituted carbon atom and the products can be converted easily to β-tosylamino-carbonyl compounds.

![Scheme 1.53](image-url)
Ring-opening via radical anion intermediates

Some examples of abnormal nucleophilic ring opening reactions at the more substituted ring carbon have been reported by Stamm\textsuperscript{108} and these are explained by a single electron transfer mechanism (Scheme 1.54).

\begin{center}
\textbf{Scheme 1.54}
\end{center}

1.26 Ring-opening of aziridine-2-carboxylates: regioselectivity

Regiospecific ring-opening reactions of enantiopure aziridine-2-carboxylates should allow routes to unusual enantiopure $\alpha$- or $\beta$-amino acids and hence are potentially of great use in organic synthesis.\textsuperscript{101}

In theory a C-3 \textit{trans}-mono-substituted aziridine ester can be ring-opened to deliver four amino acid derivatives (if $R_1 = R_2 =$ alkyl - Scheme 1.55) as a result of attack at $C_2$ or $C_3$ by the nucleophile ($\text{Nuc}^-$) with either inversion (a) or retention of configuration (b) in the ring-opening.

\begin{center}
\textbf{Scheme 1.55}
\end{center}
However, it is seldom that more than one of these modes of ring-opening can be achieved – usually with inversion of configuration (see below). Some ring-opening examples of both non-activated and activated aziridines are shown in Scheme 1.56.\textsuperscript{101}

![Scheme 1.56](image)

Clearly, not all these examples show complete regioselectivity and the ratio of regioisomers may depend on the exact conditions used.\textsuperscript{109,110} Zwanenburg \textit{et al} have shown that 3-substituted aziridine-2-carboxylates undergo regioselective ring-opening at C\textsubscript{3} using a range of nucleophiles (Scheme 1.56c).\textsuperscript{111}

![Fig 1.8](image)
Competition where it occurs from ring-opening at C₂, the ester bearing carbon, may be the result of σ*-π* interaction (Fig 1.8), facilitating overlap with the nucleophile and compensating for the greater steric hindrance in attack at this position [cf. (a) and (b), Scheme 1.55].

1.27 Ring-opening of aziridine alcohols

Enantiopure aziridino alcohols available from Sharpless asymmetric epoxidation are potentially of great use in the synthesis of “chirons” – small molecules with defined absolute configuration at two or three chiral centres and functional groups appropriate for use as starting materials. Control of regio/stereochemistry by ring-opening under mild conditions using organometallic reagents offers a range of possibilities for selective C-C bond formation.

\[
\text{Scheme 1.57}
\]

Tanner has shown that ring-opening in regio-complementary senses can be accomplished using aziridine 77: cuprate complexation to the hydroxy group and intramolecular delivery to the proximal ring carbon gives one regioisomer; using trimethylaluminium the attacking methyl is delivered from that aluminium coordinated to the butoxy group to give the other regioisomer (Scheme 1.57). Unusually, therefore, Scheme 1.57 illustrates two of the four possible modes of aziridine ring-opening (Scheme 1.55).
1.28 Aziridines in total synthesis

As enantiopure aziridines give access to a range of potentially useful building blocks in organic synthesis it is desirable to utilise them in the total synthesis of natural products. Chiral aziridine 78 was used by Oppolzer and Flaskamp in an enantioselective total synthesis of pumiliotoxin-C allowing unambiguous assignment of the natural product’s absolute configuration (Scheme 1.58). This methodology was one of the first to use an organometallic reagent for ring-opening of an activated aziridine.

![Scheme 1.58](image)

Carbapenem antibiotics 79-81 have been synthesised from 2,3-aziridino alcohols. Regio- and stereoselective ring-opening of suitable aziridines with Red-Al, LiEt₂Cu or AlMe₃ give reliable syntheses of three key intermediates - thienamycin 82, PS-5 83 and 1β-methylthienamycin 84; the first two use 2,3-trans-substituted aziridines and the third a 2,3-cis-aziridine where regioselective ring-opening is dictated by the bulk of the R-substituent (Scheme 1.59).
1.29 Biologically active aziridines

The potential for regio- and highly stereospecific ring-opening reactions of aziridines has not gone unnoticed in nature where potent biological activity is closely associated with reactions of the strained aziridine ring.
For example, naturally occurring mitosanes, mitomycin A, B & C together with pobiromycin are isolated from soil extracts of *Streptomyces verticillatus*. Their ability to cross-link DNA chains make them very useful as potent antitumour agents with the presence of an aziridine ring identified as essential for this activity. Much work has concentrated on increasing potency by synthesising derivatives of these natural products, making enantioselective synthesis of a range of aziridines a worthy target for the organic chemist.

Other aziridines have also been shown to have useful biological activity: 2-(4-amino-4-carboxybutyl)aziridine-2-carboxylic acid 85 is an irreversible inhibitor of the bacterial enzyme diaminopimelic acid epimerase and 2-(3-carboxypropyl)aziridine-2-carboxylic acid 86 is an irreversible inhibitor of glutamate racemase.

### 1.30 Ring-opening of N-Q^6^-substituted aziridines

From the enantiopure Q-substituted aziridines available, initial examination of their ring-opening reactions has demonstrated the use of the Q group to control regio- or stereo-chemistry. As in previous examples of electrophilic aziridine ring-opening, Gattrell showed that ring-opening of N-Q^6^-substituted aziridines is highly regioselective when the substituent(s) on one ring carbon can stabilise the developing carbocation in an acid-catalysed process (Scheme 1.60). Conversion of chloride product 87 back to aziridine in almost quantiative yield by sodium hydride in THF shows ring-opening occurs with complete inversion of configuration.
The greater stabilisation of the developing carbocation intermediate in ring-opening of the indene derived aziridine 69b leads to formation of both trans- and cis-ring-opened products i.e. indicating the carbocation is fully developed.

Whereas the trans-N-invertomer 69b is ring-opened with hydrogen chloride in ether to a mixture of stereoisomers 88 and 89, the cis-N-invertomer 69a gives only chloride 88 from inversion of configuration with hydrogen chloride in dichloromethane; the configuration of 88 was also confirmed by its re-conversion to aziridine 69. It is clear that the Q-group is in some way responsible for the change in stereochemistry in ring-opening of cis- and trans-N-invertomers of aziridine 69.119
Nucleophilic ring-opening of methyl aziridine-2-carboxylate 90 with iodide in the presence of samarium(III) metal and acetic acid gave iodide 91 as a single diastereoisomer from ring-opening at the ester bearing carbon (Scheme 1.61).\textsuperscript{120} Hydrolysis of the ester in 90 followed by lactonisation of the acid and subsequent ring-opening of the aziridine ring in lactone 92 gave iodide 93 resulting from attack at the methylene carbon i.e. changing the regiosense of attack. This is presumably, at least in part, due to the absence of a $\sigma^*-\pi^*$ interaction between the aziridine ring and ester moiety in lactone 92 during ring-opening (see Chapter 6).

1.31 Conversion of ring-opened $N$-(Q\textdegree)-aziridines to chiron

Quinazolinone rings are sufficiently electron-withdrawing substituents to allow nucleophilic ring-opening reactions to occur i.e. significant build up of negative charge on the exocyclic nitrogen in the ts' is stabilised. Thus ring-opening of aziridine 68 with sodium azide gave 94 in high yield (Scheme 1.62). Acetic acid was not involved in the ts' since the rate of disappearance of the starting material was almost
unaffected by an increase in its concentration. However, the presence of acetic acid is required to protonate the aziridine nitrogen in situ to prevent unwanted side reactions. It is possible to prepare diastereoisomer 94' by initial ring-opening with hydrogen chloride followed by nucleophilic displacement with azide in a double inversion sequence.\[1^\]

![Scheme 1.62](image)

Cleavage of the N-Q\(^6\) bond with samarium(II) iodide and in situ N-BOC-protection gave enantiomeric chiron 95 and 95' which are, therefore, both available from a single diastereoisomer of the parent aziridine.

Although the use of expensive samarium(II) iodide is prohibitive; less than molar quantities can be used by in situ reduction of Sm(III) → Sm(II) with magnesium during the reaction.\[12^1\] Where the N-atom in the Q-N bond is acylated or sulphonated, cleavage of the N-Q bond can be accomplished by aluminium amalgam. However, the difficulty in acylating or sulphonating this Q-N nitrogen when alkyl-substituted (QNHR) makes this method less widely applicable.\[12^2\]
Raney nickel or sodium in liquid ammonia have been shown to cleave $N$-$N$ bonds effectively; recent work has shown it is possible to cleave a $N$-$Q$ bond with lithium in liquid ammonia (Scheme 1.63) without affecting the aziridine ring.

1.32 Aims of this study

The aims of this study were:

1) to explore the aziridination of naphthalene with 3-acetoxyaminoquinazolinones and identify factors leading to the isolation of mono and bis-aziridines;

2) to apply the diastereoselective aziridination with $Q^6$NHOAc of ring-contained dienes and to investigate the potential of the products for conversion to useful chirons;

3) to investigate the ring-opening reactions of 1-(3,4-dihydro-4-oxoquinazolin-3-yl)aziridine-2-carboxylates and other aziridines including those obtained from intramolecular aziridination with a view to understanding factors affecting stereo- and regio-chemistry.
Chapter 2
Aziridination of Naphthalene
with 3-Acetoxyaminoquinazolinones
2.1 Introduction

Intermolecular reactions of simple naphthalenes which result in 1,2 addition to just one double bond are uncommon, as the remaining 3,4 (styrenoid) double bond in the functionalised ring will be more reactive than any bond in the parent naphthalene. Indeed, epoxidation with m-chloroperoxybenzoic acid\textsuperscript{125} or methyl (trifluoromethyl)dioxirane\textsuperscript{126} resulted in bis-epoxidation only (Scheme 2.1).

![Scheme 2.1](image)

Selective addition to just one double bond is a potentially valuable synthetic transformation as subsequent stereoselective addition to the second double bond, using a different reagent would lead to a variety of 1,2,3,4-tetrahydronaphthalenes as single diastereoisomers.

Preliminary experiments\textsuperscript{127} showed that in aziridination of naphthalene with 3-acetoxyaminoquinazolinones, the ratio of mono- : bis-aziridine produced can be controlled to a certain extent, by the size of the 2-substituent on the quinazolinone ring (Scheme 2.2). With R=H it is possible to prepare the mono-aziridination product as a mixture of \textit{N}-invertomers with no accompanying formation of bis-aziridine.

2.2 Aziridination of naphthalene with 3-acetoxyamino-2-alkylquinazolinones

After preparing the 2-alkyl-3-aminoquinazolinone compounds with methyl\textsuperscript{75} and with isopropyl\textsuperscript{128} groups in the 2-position of the quinazolinone ring, a detailed study of aziridination of naphthalene was undertaken.
Aziridination of naphthalene (3 mol eq.) with 3-acetoxyamino-2-methylquinazolinone (Q¹NHOAc 96) in dichloromethane in the presence of hexamethyldisilazane (HMDS, 2 mol eq.) gave a mixture of mono-aziridine 97 and bis-aziridine 98 in an 8:1 ratio in the crude product.

Scheme 2.2

However, the yield of aziridine from this reaction was poor with only 7% mono- and <1% bis-aziridine produced based on triphenylmethane as an internal standard (Scheme 2.2).

Experiments have shown that triphenylmethane does not participate in any process during aziridination. This makes it possible to add a known amount to the mixture and, using the integration of the C-H bond (@5.6δ), the aziridine yield (in mg) can be calculated as follows:

\[ \text{Mass(mg)} = \frac{\text{Integration(Azir)} \times \text{RMM(Azir)} \times \text{Mass(Triphenylmethane)(mg)}}{\text{Integration(TPM)} \times \text{RMM(TPM)} \times xH} \]

\[ xH = \text{number of protons in aziridine signal} \]
The aziridination was then repeated, using 3 mol eq. HMDS instead of the 2 mol eq. used previously and the NMR spectrum of the crude product showed that the ratio mono-bis-aziridine had fallen to 4:1, with yields of 29% and 4% respectively.

In the absence of HMDS, the same aziridination gave a mixture of mono- (6%) and bis-aziridine (10%) and the new compound 99 below in 22% yield (Fig 2.1). The formation of this product will be discussed later, but it is believed to be the acetic acid present in the reaction mixture which converts aziridine 97 into 99.

![Fig 2.1](image_url)

Having HMDS present in the reaction mixture removes acetic acid produced both in the acetoxylation of the 3-aminoquinazolinone by lead(IV) acetate and in the aziridination itself.

Using 3-acetoxyamino-2-ethylquinazolinone (Q'NHOAc 49), aziridination of naphthalene gave 28% mono-aziridine 100 and 19% bis-aziridine 101 from the NMR spectrum of the crude product and with triphenylmethane as the internal standard. When aziridination of naphthalene is carried out using 3-acetoxyamino-2-isopropylquinazolinone (Q'NHOAc 71) in the presence of HMDS (3 mol eq.), under the same conditions used above, the yield by NMR spectroscopy of the corresponding mono-aziridine 102 in the crude product was 29% together with 20% bis-aziridine 103. i.e. a significantly greater yield overall was obtained than in the aziridination with Q'NHOAc (cf. 29% above).

2.3 Aziridination of naphthalene with 3-acetoxyaminoquinazolinones: summary

In summary, the yields of mono- and bis-aziridine from aziridination of naphthalene using ethyl- and isopropyl- groups in the 2-position of the quinazolinone
ring of QNHOAc are similar, but changing to a methyl group greatly increased the proportion of mono-aziridine but at the same time reduces the overall yield. Attempts to aziridinate naphthalene with 3-acetoxyaminoquinazolinone (Q\textsuperscript{4}NHOAc) unsubstituted in the Q\textsuperscript{4}-2-position, were unsuccessful because, as was subsequently found, Q\textsuperscript{4}NHOAc was not sufficiently stable in solution under the conditions used. However, it was found that the reaction of Q\textsuperscript{4}NHOAc\textsuperscript{104}, prepared \textit{in situ}, by adding lead(IV) acetate and NAQ\textsuperscript{4} alternately in small portions to dichloromethane containing naphthalene and HMDS was effective. In the NMR spectrum of the crude product no signals from the bis-aziridine were present and only the mono-aziridination product was isolated as a 1:1 mixture of \textit{endo-} and \textit{exo-N}-invertomers \textsuperscript{105a} and \textsuperscript{105b} in 10% yield (Scheme 2.3).

\textbf{Scheme 2.3}

The absence of bis-aziridine in aziridination of naphthalene with Q\textsuperscript{4}NHOAc\textsuperscript{104} and the increased yields of bis-aziridination products with \textsuperscript{49} and \textsuperscript{71} by comparison with \textsuperscript{96} are consistent with the formation of bis-aziridine occurring only from the \textit{exo}-invertomer of the corresponding mono-aziridine (see later).

\textbf{2.4 Proposed mechanism for naphthalene aziridination}

Several low temperature NMR experiments were carried out to confirm that, as expected, the first formed product of aziridination is the \textit{endo-N}-invertomer of the mono-aziridine (Scheme 2.4).\textsuperscript{129} Solutions of the QNHOAc compounds were prepared in CDCl\textsubscript{3} at -20°C, then filtered, washed with cold saturated aqueous sodium
hydrogen carbonate solution and dried, keeping the temperature of the solution below 0°C throughout. The solution was then cooled to -20°C, naphthalene and HMDS (both 3 eq.) were added and the mixture transferred to an NMR tube, maintained at -20°C. Spectra were obtained from -20°C to ambient at 5°C intervals, monitoring the disappearance of the QNHOAc compound by the NH signal at -89.5 and the formation of aziridine products.

Aziridination was surprisingly slow: with Q\textsuperscript{1}NHOAc 96, formation of the endo mono-aziridine, for which there are two species present in 3:1 ratio, began at -5°C. This was followed at 0°C by the formation of bis-aziridine at the expense of the signals from the endo mono-aziridine above (Scheme 2.4). Signals belonging to the exo mono-aziridine only appear at 10°C when the aziridinating agent, Q\textsuperscript{1}NHOAc has almost been used up. At room temperature, signals from both endo mono-aziridine species had disappeared, being replaced by the signals belonging to the exo-N-invertomer of the mono-aziridine.\textsuperscript{129}

Scheme 2.4
The two species present in the *endo* mono-aziridine are believed to be *N*-*N* bond rotamers which disappear at the same rate i.e. interconversion of rotamers is fast on the timescale of *N*-inversion.

Similar observations were made for the aziridination of naphthalene with Q*N*HOAc 71. Signals belonging to the two *N*-*N* bond rotamers of the *endo* mono-aziridine (ratio 5:1) appeared at -10°C, followed by those of the bis-aziridine at -5°C. Signals from the *exo* mono-aziridine were detectable at 5°C.129 Bis-aziridination was complete at 10°C and all of the *endo* mono-aziridine had inverted to the *exo* form by room temperature (see Appendix 1.1).

These results suggest comparable rates for formation of the *endo*-mono-aziridine from naphthalene and Q*N*HOAc and faster *N*-inversion to give *exo* mono-aziridine with those bearing larger 2-substituents, from which fast bis-aziridination occurs. It is of interest that only one set of signals for the bis-aziridine are apparent, which is assumed to have the aziridine rings *trans* and the Q groups both *exo*. If the *endo*-*exo* bis-aziridine stereoisomer is an intermediate in the reaction, there are no signals assignable to it.

Following the aziridination of naphthalene with Q*N*HOAc 104 by VT NMR showed aziridine 105 was formed initially as just one *N*-*N* bond rotamer of the *endo* mono-aziridine at -20°C, followed by *N*-inversion to the *exo*-*N*-invertomer at 10°C. At room temperature a 1:1 ratio of *endo* and *exo* mono-aziridines is observed.

### 2.5 Purification of aziridine products

Separation of the mono- and bis-aziridines from the reaction of naphthalene with Q*N*HOAc and with Q3NHOAc by column chromatography proved to be straightforward. The former gave mono-aziridine 100 (19%) and bis-aziridine 101 (10%) and the latter, mono-aziridine 102 (20%) and bis-aziridine 103 (12%) as isolated yields. As can be seen from these results, some mono- and bis-aziridine is lost during separation. Column chromatography of the products from the aziridination of naphthalene with Q*N*HOAc was more problematic. Although the mono-aziridine was isolated, recovery was poor with only aziridine 97 (10%) being isolated and only a trace of bis-aziridine 98 obtained.
Removal of naphthalene from the crude reaction mixture was carried out by sublimation at 40°C in a high vacuum and naphthalene collected on a cold finger. Column chromatography of the residual crude aziridine still gave a poor isolated yield of mono-aziridine 97 (13%) after deactivation of the silica gel with triethylamine (TEA).

Attempts were made to obtain mono-aziridine 97 directly from the naphthalene-freed reaction product by crystallisation from a variety of solvents but in each case the recovered mono-aziridine was contaminated with either bis-aziridine or the ring-opened product 99 mentioned above.

Removal of naphthalene by sublimation of the crude products obtained from aziridination with Q2 NHOAc 49 or Q3 NHOAc 71 makes subsequent separation by chromatography of mono- and bis-aziridines much easier.

2.6 Reactivity of mono-aziridines

The possibility of using naphthalene derived mono-aziridines obtained previously to prepare 1,2,3,4-tetra-substituted naphthalenes as single stereoisomers was of interest.

Further aziridination of mono-aziridine 102 with Q2NHOAc 49 bearing a different 2-substituent on the quinazolinone ring was examined initially. Bis-aziridine 106 was obtained in 68% yield (by NMR) but the product was isolated in reduced yield (22%) from column chromatography, presumably as a result of decomposition during purification (Scheme 2.5).
Ring-opening of mono-aziridine 97 by acetic acid in deuterchloroform, gave 99 after stirring at room temperature for 3 hours presumably via the allylically and benzylically-stabilised carbocation (Scheme 2.6).

2.7 Thermal elimination of a nitrene species

Previous experiments had shown that the mono-aziridine 102 obtained from Q$_3$NH$_2$Ac 71, decomposes if heated above 80°C. It seemed possible that the mono-aziridine might eliminate nitrene 73 as a consequence of reforming naphthalene. This theory was tested by heating the mono-aziridine 102 in the presence of styrene and diethyl fumarate (1:1). If the nitrene was produced, it would be trapped in a 1:1 ratio by the two alkenes, a selectivity that had previously been diagnostic for this species generated by other means.\textsuperscript{100}
On heating aziridine 102 at 75°C in benzene-d$_6$ for 3 hours, aziridine products from styrene and diethyl fumarate were observed, together with bis-aziridine 103, in a 1:1:2:2 ratio in the crude product (Scheme 2.7).\textsuperscript{129}

By contrast, when Q$^\dagger$NHOAc 71 was reacted with the same two alkenes in a similar competitive process (-10°C → ambient), exclusive reaction with styrene was observed. It is likely that thermolysis of mono-aziridine 102 eliminates (3,4-dihydro-4-oxoquinazolin-3-yl)nitrene 73 which shows similar reactivity to Q$^\dagger$N prepared by Barker, since there is no possibility of QNHOAc being an intermediate in this decomposition.

The corresponding Q-nitrenes were presumably also intermediates when mono-aziridines 97 and 102 were heated to ~120°C and converted into their corresponding bis-aziridines 98 and 103: the major product from heating 97, however, was α-(Q$^\dagger$)-aminonaphthalene 99 (99 : 98 = 2:1) which is more likely to have been formed by an acid-catalysed decomposition.

2.8 Aziridination of naphthalene using Barker’s method

With a view to increasing the ratio of mono- : bis-aziridination products obtained, aziridination of naphthalene by Barker’s route\textsuperscript{100} was attempted. It is known that the aziridinating agent in this procedure, believed to be the Q-nitrene, reacts with alkenes at slightly lower temperatures than the corresponding 3-acetoxyaminoquinazolinone. Since inversion from endo to exo mono-aziridine will be slower at a lower temperature and bis-aziridination appeared to require the exo mono-aziridine, competition from bis-aziridination should be reduced. In Barker’s procedure the nitrene is generated at -20°C from the ylide obtained by adding triethylamine to a solution of the 3-acetoxyaminoquinazolinone at -20°C in the presence of an alkene (Scheme 1.50).

Generation of the nitrene in this way from Q$^\dagger$NHOAc 71 and triethylamine in the presence of naphthalene gave a ratio of mono : bis-aziridine products that had indeed risen from 3:2 using 71 (see earlier) to 4:1 using the nitrene route: the overall yield of products, however, was not as high as that from aziridination using 71.
Formation of the nitrene \( \text{73} \) from ylide \( \text{72} \) is presumably reversible and in the presence of unreactive alkenes (as in this case), a competitive reaction (discovered by Barker) is the decomposition of ylide \( \text{72} \) via a Stevens rearrangement (Scheme 2.9) to give imine \( \text{107} \) (20%) in this reaction. Yields of 19% mono-aziridine \( \text{102} \) and 5% bis-aziridine \( \text{103} \) were measured from the NMR spectrum of the crude product using triphenylmethane as an internal standard.

In an attempt to disfavour decomposition via Stevens rearrangement, the possibility of using trimethylamine instead of triethylamine in Barker’s procedure was explored: formation of the methyl radical in the rearrangement will be disfavoured relative to the ethyl radical, thus making the nitrene more available for aziridination. However, the amount of aziridine did not increase proportionally with 10% mono-aziridine \( \text{102} \) and 2% bis-aziridine \( \text{103} \) present in the NMR spectrum of the crude mixture by comparison with the internal standard.

### 2.9 Confirmation of trans-aziridine configuration in bis-aziridine \( \text{108} \)

Although it seemed likely that the two aziridine rings in the bis-aziridines obtained above were trans, definitive spectroscopic evidence to confirm this was not available. To obtain additional evidence, a sample of bis-aziridine was obtained from aziridination of naphthalene with \( Q^3 \text{NHOAc} \) using Gattrell’s method.\(^99\)

The bis-aziridine was obtained by crystallisation of the crude reaction mixture from ethanol, followed by recrystallisation from acetonitrile (Scheme 2.10). The \(^{13}\text{C}\)
NMR spectrum showed only 2 signals in the C-N bond region (~75 ppm) as expected. If the aziridine rings are *trans* to one another as in 108, then only 2 signals would be expected as the molecule has $C_{2v}$ symmetry.

If the rings are *cis* as in 108a, $C_{2v}$ symmetry is lost, the molecule has no plane of symmetry and we would expect to see either 3 or 4 signals in the C-N region of the $^{13}$C NMR spectrum. It is likely, therefore, that all bis-aziridines previously prepared have a *trans*-relationship of the two 3-membered rings.

### 2.10 Aziridination of naphthalene with 3-acetoxyamino-2-trifluoromethyl-quinazolin-4(3H)-one

The preparation of 3-amino-2-trifluoromethylquinazolin-4(3H)-one 110 was carried out as described by M. Coogan but it was found that the yield of the product was very low (20%) using this procedure, so several modifications were attempted. When the *crude* benzoxazinone 109 from reaction of anthranilic acid with trifluoroacetic anhydride (used without purification by crystallisation from light petroleum) was dissolved in ethanol and stirred for 1 h with hydrazine hydrate (1 eq.), 110 was obtained in 64% yield after crystallisation from methanol (Scheme 2.11).
Aziridination of naphthalene with 3-acetoxyamino-2-trifluoromethylquinazolin-4(3H)-one (Q^NHOAc) 52 in the presence of HMDS gave only mono-aziridine 111 in 33% yield (Scheme 2.12). This result was unexpected; with the bulky trifluoromethyl group in the 2-position of the quinazolinone ring, N-inversion of the first formed endo-N-invertomer was thought likely to be rapid, thus leading predominantly via the exo-N-invertomer to bis-aziridination. Mono-aziridine 111 was obtained in crystalline form from column chromatography. In this aziridination, the yield of 111 was unchanged when HMDS was omitted.

Following the reaction by NMR spectroscopy in CDCl₃ from -25°C to room temperature showed only one set of signals belonging to mono-aziridine 111, and these did not appear until 20°C. Indeed, at room temperature a significant amount of Q^NHOAc compound is still present; the stability of this compound is well documented.⁹⁷

Initially, the possibility that the first formed endo-N-invertomer of the mono-aziridine was stable at room temperature was considered. However, when this mono-aziridine product was heated to 130°C, just below its melting point, the NMR
spectrum of the recovered sample was unchanged. For the endo-\(N\)-invertomer to remain unconverted to the exo-\(N\)-invertomer at this temperature would require an unrealistically high energy barrier to \(N\)-inversion (see below) or some particular stabilising feature for the endo-\(N\)-invertomer in thermodynamic equilibrium with the exo-\(N\)-invertomer, the nature of which is not clear. It was subsequently shown that the barrier to \(N\)-inversion in \(N(\text{Q}^5)\)-substituted aziridines is, if anything, less than that of the corresponding Q-2-alkyl-substituted analogues (see below).

![Scheme 2.13](image)

Scheme 2.13

Strong support for assignment of the exo-configuration 111 to this isolated aziridine \(N\)-invertomer comes from conversion to bis-aziridine 112 by further aziridination with \(\text{Q}^3\text{NHOAc}\) 71 (Scheme 2.13). The conclusions from these experiments are that if the endo/o-\(N\)-invertomer is formed in the aziridination of naphthalene with \(\text{Q}^5\text{NHOAc}\) it must immediately \(N\)-invert to the exo-\(N\)-invertomer 111 and that further aziridination of this mono-aziridine with \(\text{Q}^5\text{NHOAc}\) does not occur.

![Fig 2.2](image)

Fig 2.2
A possible explanation for these results is as follows: the ts' for aziridination by Q^5NHOAc may be inverted (cf. aziridination of α,β-unsaturated esters with Q^5NHOAc, Fig 1.7) so that the secondary interaction is between the C=N and the aromatic ring (Fig 2.2A). If elimination of the OAc group is required to be syn to the (Q)C=O group, the partial positive charge formed in displacing this OAc group is not benzylically stabilised as would be the case in the corresponding ts' (B) with QNHOAc and R = alkyl. A syn-relationship between the acetoxy leaving group and the (protonated) quinazolinone carbonyl has been previously postulated by S. Ulukanli for aziridination of styrene.\textsuperscript{130}

2.11 Aziridination of indene with Q^5NHOAc 52

With the objective of measuring the N-inversion barrier for Q^5-substituted aziridines, indene was aziridinated with Q^5NHOAc 52. These endo mono-aziridines of indene have been shown to have higher barriers to N-inversion presumably because the transition state geometry for N-inversion of an aziridine fused to a five-membered ring is more strained. Therefore, if the endo-N-invertomer of the mono-aziridine were formed initially we would stand a better chance of observing its signals in an NMR spectrum at low temperature.

\[
\begin{align*}
&\text{NHOAc} \\
&\text{52} \\
&\begin{array}{c}
\text{O}^5 \\
\text{N} \\
\end{array}
\end{align*}
\]

\[
\begin{align*}
&\text{endomono-aziridine} \\
&\begin{array}{c}
\text{N} \\
\text{O}^5 \\
\end{array}
\end{align*}
\]

\[
\begin{align*}
&\text{exo-invertomer} \\
&\text{113, } R=H \\
&\text{114, } R=\text{Me}
\end{align*}
\]

\textbf{Scheme 2.14}

In the event, the results obtained with indene were the same as those with naphthalene; aziridination did not take place until \textasciitilde20°C and only the exo-invertomer of the corresponding mono-aziridine 113 appeared to be formed since the NMR spectrum was unchanged on heating to 140°C (Scheme 2.14).
A sample of 3-methyl-1H-indene was prepared\textsuperscript{131} and reacted with Q\textsuperscript{5}NHOAc \textbf{52} to give aziridine \textbf{114} as a 1.4:1 ratio of \textit{exo}- and \textit{endo}-\textit{N}-invertomers respectively after recrystallisation from light petroleum-ethyl acetate (azir. NCH at 85.23 when Q\textsuperscript{5} and Me are cis and 83.70 when Q\textsuperscript{5} and Me are trans).\textsuperscript{76} The crystals were dissolved in deuterochloroform at -40°C and NMR spectra obtained at 5°C intervals. The experiment showed that the minor \textit{N}-invertomer in solution at ambient temperature is the only one present in the crystalline form. Signals from the major \textit{N}-invertomer in the equilibrium mixture make their appearance at 20°C with slow establishment of the 1.4:1 ratio of \textit{N}-invertomers. Although the barrier for \textit{N}-inversion for this aziridine has not been measured, it is clear that it is not abnormally high by comparison with those of analogues in which the Q-2-substituent is an alkyl group.

\textbf{2.12 Aziridination of \(\alpha,\beta\)-unsaturated esters with Q\textsuperscript{5}NHOAc 52}

Aziridination of methyl acrylate with Q\textsuperscript{5}NHOAc \textbf{52} showed that the aziridine product, with the quinazolinone ring \textit{trans}- to the ester group was the thermodynamically preferred \textit{N}-invertomer (Scheme 2.15). Signals from only one \textit{N}-invertomer were present in the NMR spectrum of aziridine \textbf{115},\textsuperscript{96} but both \textit{N}-invertomers of aziridine \textbf{116} were present in 3:1 ratio by NMR analysis of the crude product from aziridination of methyl methacrylate.

\begin{equation}
\begin{array}{c}
\begin{array}{c}
\text{O}^5 \\
\text{NHOAc}
\end{array}
\begin{array}{c}
\text{H} \\
\text{CO}_2\text{Me}
\end{array}
\end{array}
\textbf{52}
\begin{array}{c}
\begin{array}{c}
\text{O}^5 \\
\text{NHOAc}
\end{array}
\begin{array}{c}
\text{Me} \\
\text{CO}_2\text{Me}
\end{array}
\end{array}
\begin{array}{c}
\begin{array}{c}
\text{Me} \\
\text{CO}_2\text{Me}
\end{array}
\end{array}
\end{equation}

\textbf{115}

\begin{equation}
\begin{array}{c}
\begin{array}{c}
\text{O}^5 \\
\text{NHOAc}
\end{array}
\begin{array}{c}
\text{Me} \\
\text{CO}_2\text{Me}
\end{array}
\end{array}
\begin{array}{c}
\begin{array}{c}
\text{Me} \\
\text{CO}_2\text{Me}
\end{array}
\end{array}
\end{equation}

\textbf{116}

\textbf{Scheme 2.15}
When aziridine 116 was crystallised from ethyl acetate-petroleum ether and the crystals then dissolved in CDCl$_3$ at -40°C an NMR spectrum of the solution at this temperature contained signals only from the minor $N$-inveromer having the Q$_5$ group and methyl cis (an example of second order asymmetric transformation). On warming to ambient temperature the 3:1 ratio of $N$-invertomers of 116 seen in the crude product was restored.

2.13 Conclusion

The rates of $N$-inversion of Q$_5$-substituted aziridines are not retarded by comparison with their Q$^1$, Q$^2$ and Q$^3$ analogues and the isolated naphthalene mono-aziridine 111 is believed to have Q$_5$-exo. Since further aziridination of the mono-aziridine 111 with Q$_3$NHOAc is successful it appears that the absence of bis-aziridination product 112 arises from an unexpected difficulty in further aziridination of 111 specifically with Q$_5$NHOAc.

In the $t^s$ for the formation of the bis-aziridine, it is assumed that again the endo-$N$-invertomer is the first formed product as a result of the favourable secondary interaction between the Q C=O and the aromatic ring (see Chapter 1).

![Fig 2.3](image)

Fig 2.3

It is well known that the endo mono-aziridine is the kinetically-formed product from syn-addition of 3-acetoxyaminoquinazolinones to aryl-substituted double bonds, presumably the result of an attractive interaction between the aryl and quinazolinone rings referred to in the Introduction.
It is not yet known whether the first-formed product from the second aziridination of a mono-aziridine is the endo-exo form or whether the exo-exo invertomer is formed directly (Scheme 2.16). Our rationalisation above for the absence of bis-aziridination in the case of Q^5NHOAc requires the endo-exo product to be formed initially: conversion to the isolated exo-exo form is expected to be rapid.
Chapter 3
Aziridination of Cyclic Dienes
with 3-Acetoxyaminoquinazolinones
3.1 Introduction

Work by W. Gattrell in Leicester, as described in the Introduction, has shown that aziridination of styrene, butadiene and indene with Q6NHOAc in the presence of titanium(IV) tert-butoxide (TTB) takes place completely diastereoselectively.

![Scheme 3.1](image)

Aziridination of isoprene with Q6NHOAc 67 in the presence of TTB gave a 1:1 ratio of regioisomers 117 and 118 (Scheme 3.1).

![Fig 3.1](image)

Completely diastereoselective aziridination of the unsubstituted double bond of isoprene was assumed to be result of a transition state (ts') resembling that using butadiene (see Introduction). Aziridination of the methyl-substituted double bond exhibits low diastereoselectivity (dr 1.6:1) which was assumed to result from competitive aziridination via ts's A and B (Fig 3.1).
Initial work in this area involved an investigation of aziridination of other acyclic alkyl-substituted dienes using Q\(^6\)NHOAc 67.

### 3.2 Aziridination of 1,3-pentadiene

Aziridination of trans-1,3-pentadiene in the presence of TTB gave aziridine 119 in 70% yield as a single diastereoisomer; no aziridine from addition to the methyl substituted double bond was evident in the NMR spectrum of the crude product.

Exclusive attack on the unsubstituted double bond as in Scheme 3.2, with the methyl-substituted double bond interacting secondarily with the quinazolinone, can be rationalised using previously deduced preferences in the aziridination ts\(^*\). Thus, with the OAc group syn to the Q-carbonyl and with partial carbocation formation at C\(_2\) of the diene in the ts\(^*\) (C\(_1\)-N bond formation runs ahead of N-C\(_2\)), the stabilising effect of the methyl group is called into play favouring attack on the unsubstituted double bond.
The Q₆ ring is directly involved in the ring-opening of aziridine 119 by acetic acid. Allylic acetate 120 and allylic alcohol 121 were isolated in 2:1 ratio, and are presumably formed with inversion and retention of configuration respectively (Scheme 3.3) based on the analogous ring-opening of the butadiene-derived aziridine described by W. Gattrell.¹¹⁹

A mechanism similar to that proposed by W. Gattrell accounts for the formation of allylic alcohol 121 with retention of configuration. Ring-opening of aziridine 122 by acetic acid leads to formation of a mixture of acetate 123 and alcohol 124. The mechanism for formation of alcohol 124 is believed to involve protonation of the Q-carbonyl initiating aziridine ring cleavage: capture of the C₂-carbocation by the Q₄-hydroxy group takes place before C₂-C₃ rotation can occur. Presumably the absence of rotation around the C₂-C₃ bond in 125 arises from its incorporation into the 1,3-dipole (Scheme 3.4).

Carrying out the reaction in the presence of hydrogen sulphide-saturated acetic acid gave some of the quinazolin-4-thione product 124', presumably by interception of 125 by H₂S.
The aziridination in Scheme 3.2 was carried out on a commercially available mixture of cis- and trans-1,3-pentadiene to give 119 (40%); presumably the unreactivity of the cis-isomer is a result of the low concentration of the s-cis conformation required in the aziridination ts' (Fig 3.2).

![Figure 3.2](image)

3.3 Aziridination of trans,trans-2,4-hexadiene

Aziridination of trans,trans-2,4-hexadiene with Q₆NHOAc 67 in the presence of TTB gave aziridine 126 in 56% yield as a mixture of products, which could not be separated by chromatography. Because of the complexity of the NMR spectrum it was not clear whether the two products were diastereoisomers or N-invertomers. From the NMR spectra of similarly substituted aziridines, the presence of both N-invertomers of aziridine 126 might be expected.⁸²

![Scheme 3.5](image)

The crude product from aziridination of trans,trans-2,4-hexadiene with Q₆NHOAc 71, which lacks a C₂-chiral centre, gave aziridine 127 which comprised a 3:1 mixture of N-invertomers by comparison of aziridine ring NMR signals at 82.90
and 3.18 (NCHC=C). Therefore, aziridine 126 is believed to exist as a mixture of diastereoisomers each of which exists as N-invertomers by comparison of aziridine ring NMR signals after chromatography; aziridination of trans,trans-2,4-hexadiene does not take place diastereoselectively via the transition state in Scheme 3.5.

3.4 Aziridination of cyclopentadiene

Cyclic dienes are liable to undergo aziridination readily as they already contain the s-cis conformation which is a prerequisite for the secondary interaction in the transition state between the quinazolinone ring and the alkene. The cyclopentadiene used in these reactions was freshly distilled and kept at -20°C to prevent polymerisation occurring. Aziridination of cyclopentadiene with Q3NHOAc 71 gave aziridine 128 as a white crystalline solid in 42% yield (Scheme 3.6). The NMR spectrum of this aziridine was very clean showing diagnostic signals in the NMR spectrum at δ 2.76 (1H, ddd, J 18.9, 5.0, 1.9, CHH), 2.95 (1H, ddd, J 18.9, 4.0, 1.9, CHH), 3.60 (1H, dd, J 5.0, 5.0, azir. NCHCH2), 3.79 (1H, dd, J 5.0, 1.0, azir. NCHC=C), 6.06 (1H, ddd, J 5.7, 1.9, 1.9, C=CHCH2) and 6.21 (1H, m, incl. J 5.7, CH=CCCH2); the sample contained only the one invertomer as expected.

\[
\text{Scheme 3.6}
\]

Aziridination of cyclopentadiene was then carried out using Q6NHOAc 67 in the presence of TTB following W. Gattrell’s conditions.90 Aziridine 130 was obtained
as a crystalline solid in 25% yield after crystallisation of the crude product from diethyl ether (Scheme 3.7).

A crystal was grown successfully for X-ray structure determination (see Appendix 2.1) and the absolute configuration of the product is in agreement with that predicted using Gattrell's ts model (see Introduction). The crystal structure showed unexpectedly that the quinazolinone and the cyclopentene rings were cis in this aziridine and this configuration at nitrogen was subsequently found to be retained in solution in the initial product. The quinazolinone-substituted nitrogen in these aziridines usually undergoes N-inversion at temperatures below -20°C, but in aziridine 130 the barrier to N-inversion is raised sufficiently for the first-formed endo-N-invertomer to be isolated.

A sample of aziridine 130 was dissolved in deuterochloroform and warmed in an NMR tube at 60°C for 30 min. Before heating NMR analysis showed signals at 83.58 (1H, dd, J 3.8, 3.8, azir. NCHCH₂), 4.21 (1H, m, azir. NCH=C), 5.38 (1H, ddd, J 5.7, 4.7, 2.2, C=CHCH₂) and 5.65 (1H, ddd, J 5.7, 2.2, 1.2, CH=CH₂). On cooling the NMR spectrum of the sample showed a 1:1 ratio of signals for the endo-N-invertomer of aziridine 130 and a new additional set belonging to the exo-N-invertomer having signals at 83.63 (1H, dd, J 5.7, 5.5, azir. NCHCH₂), 3.99 (1H, dd, J 5.7, 1.0, azir. NCH=CH), 6.03 (1H, ddd, J 5.7, 2.8, 1.0, CH=CH₂) and 6.19 (1H, ddd, J 5.7, 2.7, 1.2, C=CHCH₂)(Scheme 3.8). Heating the sample for longer was expected to provide the pure exo-invertomer of aziridine 130, but after several hours NMR analysis showed the 1:1 ratio of invertomers remained constant in the solution.
Aziridination of cyclopentadiene with Q\textsuperscript{6}NHOAc was repeated without TTB present to give a mixture of products from which no homogeneous product was separated. The NMR spectrum of this mixture suggested that both diastereoisomers of aziridine 130 were present.

It was previously assumed that aziridines 128 and 129 were isolated as their exo-invertomers, but in the light of the unexpected stability of endo-aziridine 130, samples of each aziridine were heated in deuterochloroform as above to see if any new signals appeared. Both aziridines 128 and 129 remained unchanged by NMR spectroscopy after heating at 60°C for 1 h and a sample of aziridine 128 remained unchanged after heating at 200°C for several minutes, so it can be concluded that conversion to the exo-N-invertomer in the aziridination had already occurred during warming to ambient temperature and that the barrier to N-inversion in the Q\textsuperscript{6}-analogue 130 is significantly higher and, for reasons as yet not clear, the endo and exo-N-invertomers are of comparable stability.

Aziridination of cyclopentadiene was also carried out using Q\textsuperscript{1}NHOAc 96 to investigate whether the size of the quinazolinone-2-substituent would affect the ratio of endo- and exo-N-invertomers present in the crude product. With a small methyl group in the Q\textsuperscript{1}-2-position it was possible that the endo-aziridine would be stable and remain at ambient temperature. In practice the NMR spectrum of aziridine 131 was very similar to those of aziridines 128 and 129 and, as with these compounds, heating for 1 h at 60°C showed no change by NMR analysis.

3.5 Ring-opening of aziridine 128 with cuprate

Our intention in aziridination of these dienes with enantiopure Q\textsuperscript{6}NHOAc 67 was to convert the product by ring-opening and N-N bond cleavage into a range of Q\textsuperscript{6}-
free chirons and the reaction of aziridine 128 with methyl cuprate was examined initially.

Aziridine 128 was added to a pre-mixed solution of copper(I) bromide-dimethyl sulphide (1 eq.) and methylmagnesium bromide in THF. Analysis of the crude product by NMR spectroscopy showed that the aziridine had been ring-opened giving a mixture of 132 and 133 in 71% yield. These products were separated from a minor amount of Q3H by chromatography but were not separated from each other. Therefore the mixture of amines 132 and 133 was oxidised with LTA in the normal way giving imines 134 and 135 (68%). These compounds were separated by Kieselgel chromatography and obtained in a 1:1 ratio (Scheme 3.9).

![Scheme 3.9](image)

The NMR spectra of imines 134 and 135 are distinguishable as the former shows a coupling ($J = 6.0$Hz) between a methylene proton and an olefinic proton, which is replaced by a coupling ($J = 2.5$Hz) between the CHMe and an olefinic proton in 135.

A similar reaction was carried out using phenylmagnesium bromide in an attempt to enhance the regioselectivity but NMR spectroscopy again showed a 1:1 ratio of SN2 and SN2' ring-opened amines present in the crude product.
3.6 Aziridination of 1,3-cyclohexadiene

1,3-Cyclohexadiene was the next diene whose aziridination was investigated and reaction with $Q^1\text{NHOAc}$ 71 gave aziridine 136 as a crystalline solid in 60% yield (Scheme 3.10). A sample of aziridine 136 heated on a Kofler block for several minutes at 200°C was recovered unchanged.

![Scheme 3.10](image)

Aziridination of 1,3-cyclohexadiene with $Q^5\text{NHOAc}$ 52 gave aziridine 137 as a colourless crystalline solid (59%). A crystal was grown successfully for X-ray structure determination (see Appendix 2.2). Evaporation of the mother liquor gave more aziridine 137 which contained an impurity that made up 50% of the residue. A small amount of the impurity was separated from aziridine 137 by Kieselgel chromatography and mass spectrometry showed that it had the same mass as the aziridine.

![Scheme 3.11](image)
Meanwhile, 1,3-cyclohexadiene was reacted with $Q^5$NHOAc 67 in the presence of TTB according to the method devised by W. Gattrell. After chromatography aziridine 138 was obtained as a 5:1 mixture with a minor product initially thought to be aziridine 141 (Fig 3.3): in some aziridinations this ratio fell (unaccountably) to 10:1. Aziridine 138 was isolated as a colourless solid by crystallisation from light petroleum-diethyl ether but with considerable loss in yield. Further elution in the chromatography above gave a fraction comprising a 2:1 mixture of tert-butoxyaminoquinazolinone 140 and a product subsequently identified as dienylamine 139 (Fig 3.3), the latter having signals at $\delta$ 2.37 (2H, m, incl. $J$ 6.4, 4.6, 1.4, C=$\text{CCH}_2$), 3.96 (1H, ddd, $J$ 6.4, 5.9, 5.1, CHNH), 5.37 (1H, d, $J$ 5.9, NH) and four olefinic signals, one of which was coupled to the CHNH proton (see Appendix 1.2). This structure assignment for 139 was eventually confirmed by chemical correlation (see below).

![Fig 3.3](image-url)

A comparison of NMR spectra of dienylamine 139 and that of the small amount of by-product obtained previously from aziridination of cyclohexa-1,3-diene with $Q^5$NHOAc 52 showed close similarities between them.

![Scheme 3.12](image-url)
An $^1$H spectrum on this by-product showed the presence of four olefinic protons plus a doublet ($J \sim 7$Hz) belonging to an NH which is exchangeable with deuterium oxide. There were no signals belonging to any aziridine ring protons in the NMR spectrum, so the impurity is formulated as dienylamine 142 (Scheme 3.12). The mechanism for formation of 139 and 142 will be discussed below.

### 3.7 Aziridination of 1,4-cyclohexadiene

Aziridination reactions of 1,4-cyclohexadiene with QNHOAc were investigated not only to see if there was any competitive formation of products analogous to the dienylamine seen in the case of 1,3-cyclohexadiene, but also to see if, in the reaction of Q$^6$NHOAc 67 with the latter, the impurity co-eluted with aziridine 138 was in fact aziridine 141. Aziridination of 1,4-cyclohexadiene with Q$^3$NHOAc 71 gave a mixture of three products which were separated by chromatography; dienylamine 143, aziridine 144 and Q$^3$H 145 were isolated in 13%, 27% and 12% yields respectively (Scheme 3.13).

![Scheme 3.13](image)

Not surprisingly the NMR spectrum of aziridine 144 was completely different to that of the dienylamine 143. The methylene group in 143 consisted of two further coupled doublets with a large ($J \sim 20$Hz) coupling constant between them. Aziridine 144 contained two identical methylene groups comprising two diastereotopic protons which gave rise to just two signals at $\delta$ 2.53 and 2.88 in the NMR spectrum, each with a large coupling ($J \sim 17$Hz).
Aziridination of 1,4-cyclohexadiene with $Q^6\text{NHOAc}$ 67 and TTB gave a mixture of aziridine 141 and dienylamine 146, isolated after chromatography in 23% and 27% yield respectively as crystalline solids. A crystal of 146 was grown successfully for X-ray structure determination (see Appendix 2.3). Aziridine 141 obtained from this reaction exhibited a completely different NMR spectrum to the minor compound co-eluted with aziridine 138 (Scheme 3.14)(the structure of this by-product is discussed in Chapter 4).

Scheme 3.14

3.8 Reaction of QNHOAc with cyclohexadienes via nitrene intermediates

Dienylamines 139, 142, 143 and 146 are formally insertion products into the allylic C-H bonds of cyclohexadienes by QNHOAc.

Insertion into C-H bonds is a reaction characteristic of more reactive singlet nitrenes and such products had never previously been obtained from reactions of QNHOAc compounds. Although unlikely, the insertion products obtained above could have resulted from the intermediacy of nitrene intermediates rather than QNHOAc compounds: certainly an increase in the insertion : aziridination ratio would be anticipated in the reaction of the cyclohexadienes with *bona fide* Q-nitrenes.

Scheme 3.15
The method of generating Q-nitrene intermediates devised by E. Barker\textsuperscript{100} previously described was employed to study the effect on this insertion: aziridination ratio of cyclohexa-1,3- and cyclohexa-1,4-dienes.

The method involves preparation of Q\textsuperscript{3}NHOAc \textsuperscript{71} in the normal way and then addition of triethylamine (TEA)(10 eq.) to give ylide, which spontaneously and probably reversibly gives the nitrene \textsuperscript{73} and TEA (Scheme 3.15)(see Chapter 2).

Using this route, reaction of the Q\textsuperscript{3}NHOAc-derived nitrene with 1,4-cyclohexadiene gave a higher proportion of aziridine \textsuperscript{144} (23\%) compared to dienylamine \textsuperscript{143} (5\%), suggesting that the nitrene is not the reactive intermediate giving rise to \textsuperscript{143} in Scheme 3.13. Likewise, reaction of 1,3-cyclohexadiene with the Q\textsuperscript{3}NHOAc-derived nitrene gave aziridine \textsuperscript{136} (35\%) and no dienylamine was isolated.

### 3.9 Swern oxidation of aziridine \textsuperscript{138}

As described previously, the reaction of cyclohexa-1,3-diene with Q\textsuperscript{6}NHOAc \textsuperscript{67} in the presence of TTB gave two products, aziridine \textsuperscript{138} (54\%) and dienylamine \textsuperscript{139} (10\%); aziridine \textsuperscript{138} contained an impurity, which varied in abundance from 10-25\% in a number of aziridinations based on the ration of signals at δ 3.57 and 3.79.

![Scheme 3.16](image_url)

\textsuperscript{dr 5:1} (some amsochronous signals for the aziridines epimeric at C₆ and C₇ visible)
A sample of aziridine 138 containing 20% of the impurity was oxidised by the Swern method to give ketone 147 in 51% yield, thus destroying the chiral centre in the side chain of the quinazolinone ring (Scheme 3.16). Ketone 147 was reduced with sodium borohydride to give back aziridine 138 in 36% yield with the bulk of the remaining material balance made up of unreduced ketone 147 (28%). NMR analysis of alcohol 138 showed a 3:2 ratio of the original aziridine 138 and the impurity, from comparison of signals at 83.57 and 3.79 respectively, showing that the abundance of the impurity had risen significantly. The identity of this impurity therefore can be assigned to the other diastereoisomer 138a (Fig 3.4) of aziridine 138 (and not a by-product from rearrangement as mentioned earlier). In the oxidation–reduction cycle in Scheme 3.16 there will be some small loss in the (presumed) enantiopurity of 138. Thus aziridination of 1,3-cyclohexadiene with Q^6NHOAc 67 in the presence of TTB is not completely diastereoselective.

![Diagrams of aziridine 138 and 138a](image)

**Fig 3.4**

### 3.10 Swern oxidation of dienylamine 139

The same oxidation–reduction cycle was carried out on dienylamine 139. Swern oxidation gave ketone 148 in 50% yield. Reduction of ketone 148 gave 139 in 67% yield whose NMR spectrum showed a new set of signals in addition to those from the original dienylamine 139 (ratio 1:1) by comparison of the NH signals at
δ5.37 and 5.16 respectively (Scheme 3.17). This additional set of signals, assigned to the other diastereoisomer of 139, is absent from the NMR spectrum of that originally isolated from reaction of 1,3-cyclohexadiene with Q₆NHOAc–TTB, therefore, 139 is produced completely diastereoselectively.

![Scheme 3.17](image)

3.11 Attempted insertion reactions using QNHOAc on other substrates

![Scheme 3.18](image)

Insertion reaction were attempted using Q₃NHOAc and Q₆NHOAc on 9,10-dihydroanthracene (DHA). Using Q₃NHOAc 71, the yield of amine 149 was only 10% with the bulk of the material balance made up of unreacted DHA and 2-isopropyl-quinazolinone (Q₃H) 145 (Scheme 3.18). Only 2% of insertion product 149 was obtained in the presence of TFA, the bulk of the material balance was again made up of 9,10-dihydroanthracene and Q₃H 145.
The reaction of DHA with Q\textsuperscript{6}NHOAc 67 in the presence of TTB gave only 12% of the corresponding insertion product 150 (Scheme 3.19).

9-Methyl-9,10-dihydroanthracene was obtained in 85% yield from the Birch reduction of 9-methylantracene (Scheme 3.20)\textsuperscript{133} but no insertion product was obtained from the reaction of Q\textsuperscript{3}NHOAc 71 with this substrate.

Insertion reactions of Q\textsuperscript{3}NHOAc were also attempted with three other substrates (Scheme 3.21). The reaction with fluorene and anthrone gave no insertion products with only the starting material and Q\textsuperscript{3}H 145 isolated in both cases. However with xanthene, in which the incipient carbocation is better stabilised by resonance, insertion product 151 was obtained in low yield (12%).

9,10-Dihydrophenanthrene was also tested as it would mimic 1,3-cyclohexadiene without competition from aziridination: no insertion products were isolated from the reactions with Q\textsuperscript{3}NHOAc, Q\textsuperscript{5}NHOAc and Q\textsuperscript{6}NHOAc (in the presence of TTB), with only the 9,10-dihydrophenanthrene and Q\textsuperscript{3}H (Q\textsuperscript{5}NHQ\textsuperscript{5} in the case of Q\textsuperscript{5}NHOAc)\textsuperscript{134} obtained after chromatography.
3.12 Discussion of insertion mechanism

Application of our ts' model to the reaction of the Q6NHOAc–TTB complex with 1,3-cyclohexadiene reveals that both double bonds of the diene can interact secondarily with C=O and C=N double bonds of the quinazolinone group.90, 99 The result is that the allylic C-H bond is ideally positioned to undergo insertion by NHOAc (Scheme 3.22).
In this reaction, hydride transfer to the $\sigma^*$-orbital of the N-OAc bond (with loss of OAc) occurs together with reaction of the $N$-lone pair with the C-H $\sigma^*$-orbital (Scheme 3.22).

The possibility that this insertion is non-concerted i.e. proceeds via hydride transfer and then capture of the cyclohexadienyl cation by NAQ seems unlikely since reaction could take place at either terminus of the cation to give diastereoisomeric insertion products (Scheme 3.23).

The proposed transition state geometry for insertion of Q$_3$NHOAc into the C-H $\sigma$-bond in cyclohexadiene (Scheme 3.22) resembles that of aziridination in having an attractive secondary interaction between the (Q)C=O and diene C=C. Additionally, in this insertion ts', an attractive interaction between the (Q)C=N and second double bond of the diene is postulated. Some precedent for secondary interaction of the imine carbon with the carbonyl oxygen of an ester comes from the work of S. Ulukanli described in the Introduction.

It may be significant that only the reactions of Q$_5$NHOAc and Q$_6$NHOAc/TTB with 1,3-cyclohexadiene gave insertion products: co-ordination of TTB to Q$_6$NHOAc has the effect of making the carbon of the imine more electrophilic as does the presence of a 2-trifluoromethyl group in 52.

The transition state for aziridination of 1,3-cyclohexadiene, viewed from above, shows the alkene overlapping with the carbonyl group of the quinazolinone ring and anchoring the diene in a position where aziridination can occur (Fig 3.5).
In the corresponding transition state for insertion, the diene has been rotated through $120^\circ$ so that both the original secondary interaction and a supplementary interaction of the diene with the imine double bond are present, allowing insertion into the dienylic C-H bond positioned directly underneath the exocyclic nitrogen of the quinazolinone ring.

The absolute configuration of the cyclohexadiene-derived aziridines 138 and hence of dienylamine 139 are assigned by analogy with that of cyclopentadiene-derived aziridine 130.

Similar transition states can be envisaged for aziridination and insertion reactions of $Q^b$NHOAc/TTB with 1,4-cyclohexadiene (Fig 3.6). For aziridination, it is possible that the non-conjugated double bond overlaps partially with both the carbonyl and imine double bonds of the quinazolinone ring giving aziridine 141 but in view of the results with 1,4-pentadiene (see below) this seems unlikely: aziridination may
even occur with the ring residue in the *exo* position. For insertion, the diene is again anchored by secondary interactions with the carbonyl and imine double bonds of the quinazolinone ring, with the dienylic C-H \( \sigma \)-bond located underneath the exocyclic nitrogen.

![Scheme 3.24](image)

Attention has been drawn previously to the analogy between aziridination using QNHOAc and epoxidation using peroxy(acetic)acid. However, a literature search did not reveal any examples of insertion into allylic C-H bonds by peroxyacids.

Allylic hydroxylation of oleanolic acid 152 by mCPBA does occur, but only in the presence of Fe(PFPP)Cl (Scheme 3.24).\(^{135}\) A mechanism involving an Fe-oxo-porphyrin intermediate, which brings about hydrogen abstraction followed by recombination of the resulting allylic radical was proposed.\(^{135}\)

### 3.13 Reactions of QNHOAc with acyclic non-conjugated dienes

![Scheme 3.25](image)

Several non-cyclic dienes were aziridinated with \( \text{Q}^3\text{NHOAc} \) and with \( \text{Q}^4\text{NHOAc} \) to see if insertion products were also formed during these reactions. Firstly 1,4-pentadiene was aziridinated with \( \text{Q}^3\text{NHOAc} \) giving aziridine 153 in 30% yield.
(Scheme 3.25). The yield of aziridine 153 obtained was similar to that obtained from aziridination of (excess) hex-1-ene with Q<sup>3</sup>NHOAc, suggesting that the additional double bond in 1,4-pentadiene does not play an important role. No bis-aziridine or insertion product was isolated from this reaction.

Neither was any insertion product obtained from reaction of Q<sup>5</sup>NHOAc 52 with 1,4-pentadiene in which 35% of aziridine 154 was formed. The reaction of 1,4-pentadiene with Q<sup>6</sup>NHOAc 67 with or without TTB present gave a 1:1 mixture of diastereoisomers of aziridine 155 in 29% yield (Scheme 3.26).

Reactions of allylbenzene with Q<sup>3</sup>NHOAc and with Q<sup>5</sup>NHOAc gave aziridines 156 and 157 in 28% and 34% yields respectively and no insertion products (Scheme 3.27). Again these aziridine yields are no higher than those observed for hex-1-ene which suggests that there is no stabilising secondary overlap of the phenyl group with the quinazolinone ring in the transition state for these aziridinations.

The results outlined above suggest that for insertion products to be formed from reaction of QNHOAc with a diene, the double bonds of the diene must be fixed in an orientation where overlap with the carbonyl and imine double bonds of the quinazolinone ring can occur, i.e. where they are contained in a six-membered ring.
3.14 Aziridination of 1,3-cycloheptadiene

The reaction of Q3 NHOAc 71 with 1,3-cycloheptadiene was also investigated to see if any insertion products were formed besides the expected aziridine product. Aziridine 158 (31%) was obtained as a crystalline solid by trituration of the crude product with light petroleum-ethyl acetate (Scheme 3.28).

No signals assignable to a dienylamine product were observed in NMR spectrum of the crude reaction and only a further small amount of aziridine 158 (5%) was recovered from the mother liquor after crystallisation from light petroleum-ethyl acetate.

The reaction was then carried out using Q6 NHOAc in the presence of TTB. A crystalline solid was obtained and after recrystallisation from light petroleum-ethyl acetate gave a single diastereoisomer of aziridine 159 in 25% yield (Scheme 3.29). Again no insertion product was obtained in this case.
3.15 Aziridination of cycloheptatriene

Work by D. W. Jones in Leeds has shown that aziridination of tropone by oxidative addition of N-aminophthalimide with LTA gives aziridine 160 as a single regioisomer. It is now known that the reactive intermediate in this aziridination is N-acetoxyaminophthalimide. The ts' for this aziridination presumably involves a double secondary interaction (cf. insertion ts', Fig 3.5 and 3.6) between 2,3 and 6,7 double bonds with each of the carbonyl groups on the phthalimide ring, leading to aziridination of only the 4-5 double bond (Scheme 3.30).

Scheme 3.30

The reaction of Q3 NHOAc 71 with cycloheptatriene, therefore, was of interest since either aziridination or insertion, with a double secondary interaction was possible. In practice aziridine 161 was obtained as a crystalline solid in 45% yield (Scheme 3.31). The other minor product isolated by chromatography of the crude reaction product was Q3H 145 (12%).

Scheme 3.31
A \textsuperscript{1}H-\textsuperscript{1}H COSY NMR spectrum of 161 showed that an aziridine ring proton at \(\delta 2.84\) (1H, dd, \(J 7.5, 3.8\), azir. NCHCH\(_2\)) was coupled to a methylene proton at \(\delta 2.99\) (1H, m. incl. \(J 3.8\), CHH), while the other aziridine ring proton at \(\delta 3.34\) (1H, dd, \(J 7.5, 4.8\), azir. NCHC=C) coupled with an olefinic proton at \(\delta 6.01\) (1H, ddd, \(J 11.2, 4.8\), NCHCH=C).

The absence of any insertion product in aziridination of cyclopentadiene with Q\(^8\)NHOAc might be construed as evidence for a two-step mechanism (cf. Scheme 3.23) involving hydride transfer from the diene and carbocation formation in the ts* with the anti-aromaticity of the cyclopentadienyl cation highly disfavoured. However, the same argument cannot account for the absence of insertion products from cycloheptatriene where hydride transfer would deliver the aromatic cycloheptatrienyl cation.

![Fig 3.7](image)

It seems more likely that the absence of insertion products from either cyclopentadiene, cycloheptadiene or cycloheptatriene is the result of the difficulty in overlapping two double bonds of the cyclic diene/triene with C=O and C=N double bonds of the quinazolinone (Fig 3.7).

3.16 Bromination of dienylamine 143

Dienylamine 143 was reacted with bromine in dichloromethane in expectation of forming dibromide 162. However, the mass spectrum of the product after
purification showed that the mass had increased by sixteen, suggesting the addition of a single oxygen atom; no diagnostic isotope peaks for the dibromide were visible.

![Scheme 3.32](image)

The NMR spectrum of the product showed signals at $\delta$ 2.42 (1H, ddd, $J$ 19.7, 5.3, 3.0, CHH trans to epoxide), 2.68 (1H, ddd, $J$ 19.7, 6.7, 1.3, CHH cis to epoxide), 3.33 (1H, ddd, $J$ 5.0, 4.1, 2.2, H-1), 3.44 (1H, ddd, $J$ 4.1, 3.0, 2.2, 1.3, H-6), 4.00 (1H, dd. $J$ 5.0, 4.4, 2.0, CHNH), 5.56 (1H, ddd, $J$ 10.6, 4.4, 2.2, H-3), 5.66 (1H, dddd, $J$ 10.6, 6.7, 5.3, 2.2, H-4) and 5.81 (1H, br s, NH); loss of two olefinic protons suggested epoxidation of one of the double bonds had occurred giving 164 (43%) (Scheme 3.32). A small W-coupling ($J$ 2Hz) between protons $H^1$ and $H^3$ and $H^4$ and $H^6$ is present which would not be favoured if the epoxide and the ($Q^3$)amino groups were trans to each other on the ring, the ($Q^3$)amino group is assumed to occupy a pseudo equatorial position.

![Scheme 3.33](image)
The formation of epoxide 164 can be explained by the route in Scheme 3.33 which clearly resembles that proposed for conversion of aziridine 122 → alcohol 124. Initially the bromonium ion is formed on the opposite face of the cyclohexadiene ring to the (Q³)amino group. Intramolecular attack of the Q³-carbonyl oxygen on the bromonium ion via 163 and capture of the Q-4 centred carbocation by adventitious water or bromide gives the epoxide on work up with sodium bicarbonate solution. This mechanism requires that the epoxide and (Q³)amino group are cis.

Aziridine 146 was also treated with bromine giving dibromide 165 (81%), with no evidence of epoxide formation; the quinazolinone ring in this case is too far removed for the carbonyl oxygen to intercept the bromonium ion before it is attacked by the bromide anion (Scheme 3.34).

[Diagram showing the mechanism of formation of epoxide 164]

Further evidence for the mechanism in Scheme 3.33 and hence the stereostructure of 164 was sought by saturating the reaction solvent with hydrogen sulphide gas before addition of bromine following the precedent of Gattrell.⁹⁹

[Diagram showing the reaction of aziridine 143 with bromine and hydrogen sulphide to give epoxide 166]

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This was expected to result in sulphur being incorporated into the quinazolinone ring instead of oxygen giving quinazolin-4-thione 166, thus showing that the carbonyl oxygen is involved in the reaction and that the quinazolinone ring and the epoxide are on the same face (Scheme 3.35).

However, instead of epoxide 166, bromohydrins 167 and 168 (Scheme 3.36) were isolated in 19% and 11% yields respectively with the bulk of the remaining product made up of unreacted aziridine 144 (34%).

![Scheme 3.36](image)

The regiostructure of bromohydrin 167 was supported by the coupling of \( \text{CHOH} \) (δ4.41) to both methylene protons and to \( \text{CHBr} \) (δ 3.83): the identity of this \( \text{CHOH} \) was confirmed by its cross peak in the COSY NMR spectrum with \( \text{CHOH} \). Moreover, the \( \text{CHBr} \) was coupled to the \( \text{CHNH} \) (δ 3.94) but not to the methylene signals (Fig 3.8). As in the NMR spectrum of epoxide 164, there are two olefinic protons at δ 5.59 and 5.81, and an \( \text{NHQ}^3 \) proton whose chemical shift (δ5.84) is close to that in 164.

![Fig 3.8](image)
The NMR spectrum of 168 includes non-aromatic signals at $\delta$ 4.08 (CHNH), 4.53 (CHOH), 4.85 (CHBr), 5.19 (COH), 5.65 (CH=CHCH$_2$), 5.88 (C=CHCH$_2$), 9.45 [1H, d, $J$ 8.0, H-5(Q)] and 12.59 (NH). Exchange of the Q$^1$-carbonyl oxygen by sulphur in bromohydrin 168 was shown by the H-5 doublet being moved downfield to $\delta$ 9.45 in the NMR spectrum supporting the proposal that the quinazolinone ring takes part in the intramolecular reaction. Interestingly, this doublet appeared to undergo partial conversion into an H-5 proton ($\delta$ 8.2) in a sample which had been shaken with D$_2$O. The stereostructure assignments of 167 and 168 require further investigation.

It is not clear why bromohydrins 167 and 168 were isolated in this experiment. Although, it appears that the corresponding epoxides 164 and 164' are intermediates in the formation of 167 and 168, which undergo ring-opening by HBr using these reaction conditions (Scheme 3.36). However, there is little doubt that participation of the quinazolinone is involved in the formation of epoxide 164.

3.17 Conclusion

Aziridination of cyclopentadiene, cyclohepta-1,3-diene and cycloheptatriene with Q$^6$NHOAc are highly diastereoselective but cyclohexa-1,3-diene is not completely diastereoselective and moreover, is accompanied by formation of a dienylamine from apparent insertion of Q$^6$N into an allylic C-H bond. However, the scope of the insertion reaction does seem to be limited at this time to cyclohexa-1,3- and 1,4-dienes, dihydroanthracene and xanthene. A mechanism for this insertion reaction, which takes place with complete diastereoselectivity is proposed.

Reaction of dienylamine 143 with bromine gives epoxide 166 by a mechanism involving intramolecular displacement by the quinazolinone carbonyl oxygen.
Chapter 4
Preparation of Insertion Products
from Diene-Derived \( N(Q) \)-Aziridines
4.1 Diastereoselectivity of aziridination/insertion reactions

In the previous chapter dienylamine 139 was obtained as a single diastereoisomer as a by-product in aziridination of 1,3-cyclohexadiene with Q^+NHOAc–TTB.

Conversion of aziridine 138 into dienylamine 139 was carried out to relate the configuration at the dienylamine ring carbon to one of the aziridine ring chiral centres in 138 and to determine the stereochemistry of the insertion reaction giving 139. In a model study, ring-opening of aziridine 144 by thiophenol, oxidation of sulphide 169 to sulfoxide 170 and elimination of sulphenic acid to give racemic dienylamine 171 was planned (Scheme 4.1).

In a preliminary study, aziridine 144 was mixed with p-chlorothiophenol in dichloromethane and heated; a temperature of 90°C was found necessary (Young’s tube) for ring-opening to occur and sulphide 169 was isolated in 40% yield.

This conversion of aziridine 144 to 169 was the first occasion to our knowledge that an N(Q)-substituted aziridine had been ring-opened by a thiol.

4.2 Synthesis of insertion product from aziridine 138

When aziridine 138 (dr 4:1) was ring-opened by p-chlorothiophenol under the same conditions the NMR spectrum of the crude product showed the presence of two ring-opened products, 172 (10%) and 173 (42%), the result of S_N2 and S_N2’ attack respectively (Scheme 4.2): the configuration at the sulphur-bearing ring carbon in 173 was not determined. The NMR spectra of the sulphide regioisomers differ largely; 172
having signals at δ 3.38 (2H, m, CHNH and CHSAr), 5.16 (1H, br s, NH), 5.81 (1H, dd, J 9.9, 1.8, CH=CCH₂), 5.99 (1H, d, J 9.9, 4.4, C=CHCH₂), 6.55 (2H, d, J 8.4, 2 x CH(Ar)) and 6.86 [2H, d, J 8.4, 2 x CH(Ar)]. The ¹H-¹H COSY spectrum of 172 showed the olefinic proton at δ5.81 coupled with CHSAr while the olefinic proton at δ5.99 coupled with a methylene group. Sulphide 173 showed diagnostic signals at δ 3.71 (1H, m, incl. J 5.5, CHNH), 3.78 (1H, d, J 3.5, CHSAr), 5.38 (1H, d, J 5.5, NH), 5.53 (1H, m, incl. J 9.5, CH=C), 5.91 (1H, dd, J 9.5, 2.5, C=CH), 7.28 [2H, d, J 8.4, 2 x CH(Ar)] and 7.33 [2H, d, J 8.4, 2 x CH(Ar)].

Scheme 4.2

Sulphide 173 was separated by chromatography and then oxidised with hydrogen peroxide (1.5 eq.) in glacial acetic acid, giving sulphoxide 174 in 31% yield. When the sulphoxide was heated in carbon tetrachloride at 85°C for two hours, dienylamine 139 (90%) was obtained (Scheme 4.2). After purification by chromatography, NMR analysis of the product showed that it contained 20% of the minor diastereoisomer (an epimer of 139 at the diene ring carbon centre) whose identity was previously confirmed by Swern oxidation/borohydride reduction of 139 (Chapter 3).
As aziridine 138 used in Scheme 4.2 contained ~20% of the minor diastereoisomer, this is presumably the origin of the minor diastereoisomer of dienylamine 139, i.e. there is no loss of diastereoselectivity in the conversion of aziridine 138 into dienylamine 139.

![Scheme 4.2](image)

To confirm that there is no loss of diastereoselectivity, a sample of the pure major diastereoisomer of aziridine 138 (recovered from a ring-opening reaction to be described in Chapter 5) was subjected to the same sequence of reactions (Scheme 4.3). Sulphides 172 and 173 were isolated in 5% and 20% yields respectively and 173 was converted into the corresponding sulphoxide 174 in 38% yield by stirring in glacial acetic acid containing hydrogen peroxide. Finally, heating in carbon tetrachloride gave only the major diastereoisomer of dienylamine 139 isolated from aziridination in 88% yield as expected.

The conclusion is, therefore, that dienylamine 139 is formed completely diastereoselectively and the configuration at the chiral centre on the cyclohexadiene ring carbon is the same as the corresponding chiral centre at C-6 in the major diastereoisomer of aziridine 138.

Oxidation of sulphide 172 was attempted under the same conditions used above but no sulphoxide was produced.
4.3 Ring-opening of aziridines with thiophenolate

Ring-opening of aziridine 144 was also attempted with p-chlorothiophenol under conditions successful for conversion of aziridine 138, but only starting aziridine was obtained after work up. Subsequent heating for longer periods also did not give any ring-opening. As the ring-opening of aziridine 144 was not achieved with thiophenol under these conditions, the possibility of using thiophenolate, a more nucleophilic anion, was examined initially with aziridine 144. Partial formation of phenyl thiophenolate anion was obtained by adding sodium hydroxide (0.5 eq.) to p-chlorothiophenol (1.5 eq.) in acetonitrile and aziridine 144 added subsequently: after heating the solution at 80°C for 30 min. and purification of the crude product by chromatography, sulphide 169 was isolated in 45% yield (Scheme 4.4).

Ring-opening of aziridine 141 under these conditions gave sulphide 170 in 46% yield as a mixture of diastereoisomers. Oxidation of sulphide 170 with hydrogen peroxide in glacial acetic acid, followed by elimination of thiophenol should give dienylamine 139 as a mixture of diastereoisomers as shown in Scheme 4.5. In fact a 1:1 mixture of diastereoisomers of dienylamine 139 was obtained from this reaction, in 64% isolated yield. The NMR spectrum of this product was almost identical to that from sodium borohydride reduction of ketone 148 (see Chapter 3).
Aziridine 138 (dr 4:1) was also ring-opened using the more nucleophilic thiophenolate anion using the same conditions described above, giving sulphide 172 in 41% yield. Interestingly, no sulphide 173 from S\textsubscript{N}2\textsuperscript{'} attack was evident from inspection of the NMR spectrum of the crude product (Scheme 4.6).

A crystal structure determination of sulphide 172 (see Appendix 2.4) confirmed the assigned stereostructure but, disturbingly, the space group (P \bar{1}) indicated that the crystal was composed of a 1:1 ratio of enantiomers. However,
sulphide 172 does exhibit an optical rotation ([α]₀ = 20, EtOH, c = 1.0) showing not all of the material is racemic. The X-ray crystal structure determination was carried out on one of a very small number of crystals of sulphide 172 formed from thebulk of the sample as an oil, which failed to produce further crystalline material on standing for several weeks. It is likely that only the crystalline material is racemic and the bulk of the oily sample comprises a single enantiomer, but the enantiopurity of aziridine 138 has not been quantified and the source of the racemisation has not been identified. It is unfortunate that the racemic nature of sulphide 172 does not allow assignment of absolute configuration to aziridine 138. The absolute configuration presently assigned to 138, therefore, rests on the assumption that the major diastereoisomer corresponds to that expected from Gattrell’s model for the aziridination.99

4.4 Oxidation of dienylamine 139 with lead(IV) acetate

![Scheme 4.7](image)

In an early attempt to characterise dienylamine 139, it was treated with LTA in the expectation of converting it to 3-phenylaminoquinazolinone 175 (Scheme 4.7). However, the only homogeneous product isolated after chromatography was aziridine 176 (30%)(Scheme 4.8). If the formation of aziridine 176 takes place by acetoxylation at the Q₆NH nitrogen and π-participation by the neighbouring double bond from one face in displacement of the N-acetoxy group, the configuration at the acetoxy bearing carbon would very likely be trans to the aziridine ring as a result of attack by acetic acid on the developing carbocation from the opposite face (Scheme 4.8).
The NMR spectrum of 176 showed signals at δ 2.38 (1H, dddd, J 20.0, 6.9, 4.5, 1.8, CHH-cis), 2.84 (1H, dddd, J 20.0, 4.2, 3.3, 2.1, CHH-trans), 3.77 (1H, dddd, J 7.7, 6.4, 3.3, 1.8, H-1), 4.35 (1H, dddd, J 7.7, 4.5, 1.3, H-6), 5.57 (1H, dddd, J 10.0, 4.0, 2.1, H-3), 5.63 (1H, dddd, J 6.4, 4.0, 2.2, H-2) and 5.74 (1H, dddd, J 10.0, 6.9, 4.2, 2.2, H-4) (see Appendix 1.3). The 1H-1H COSY showed the methylene protons and the CHOAc proton each couple to the adjacent aziridine ring proton and both olefinic protons; no W-coupling was evident between H1 and H3 and between H4 and H6, as seen in the case of epoxide 164, suggesting that although the two molecules are assumed to have similar conformations with the OAc or NHQ3 pseudo equatorial, they have different configurations at C1 and C6 (Fig 4.1).

4.5 Conversion of N(Q)-aziridines into allylamines as a general method

It was of interest to examine whether the methodology employed in the synthesis of dienylamine 139 from aziridine 138 was applicable to other aziridines and would allow conversion of N(Q)-aziridines to the corresponding allyl-
N(Q)amines. Work by J. Murphy has shown that when isophorol is aziridinated with Q\textsuperscript{3}NHOAc 49, the subsequent aziridine can undergo a radical-catalysed rearrangement giving allylic amine 177 (Scheme 4.9). Since methods for reductive N-Q cleavage are available, the allyl-N(Q)amines may be converted into the corresponding allylamines.

![Scheme 4.9](image)

Reagents: a, Q\textsuperscript{3}NH\textsubscript{2}, LTA, CH\textsubscript{2}Cl\textsubscript{2}; b, thiocarbonyldiimidazole (2 eq.), CH\textsubscript{2}Cl\textsubscript{2}, heat; c, Bu\textsuperscript{3}SnH, AIBN, THF, heat.

**Scheme 4.9**

### 4.6 Aziridination of cyclohexene

Aziridination of cyclohexene with Q\textsuperscript{3}NHOAc 71 gave aziridine 178 in 30% yield. As the yield was low, the reaction was repeated in the presence of TFA as this usually leads to a higher yield of aziridine product. Quenching of the reaction at -40°C with sodium hydrogen carbonate solution gave aziridine 178 in 80% yield after purification by chromatography (Scheme 4.10).

![Scheme 4.10](image)

Aziridine 178 was heated with p-chlorothiophenol (1 eq.) at 80°C in a sealed tube for 24 h. but only the starting material was isolated with no evidence of any ring-
opening from inspection of the NMR spectrum of the crude product. The reaction was repeated in the presence of sodium hydroxide (0.6 eq.), so that the reactive nucleophile was the thiophenolate anion and ring-opened sulphide 179 (56%) was isolated by chromatography (Scheme 4.10). Unfortunately, oxidation of sulphide 179 with hydrogen peroxide in glacial acetic acid, under the same conditions used previously (see Scheme 4.2) was unsuccessful.

4.7 Ring-opening of aziridine 178 with the selenide anion

\[ \text{NHOAc} \quad \text{PhSe} \quad 178 \quad \text{EtOH, NaSePh, 30 min. 44\%} \]

\[ \text{PhSa, NHQ}^+ \quad 180 \]

Scheme 4.11

Diphenyldiselenide was easily converted into the nucleophilic phenylselenolate by heating under reflux with sodium borohydride and sodium hydroxide in ethanol. Aziridine 178 was added to the solution of sodium phenylselenolate thus obtained which was stirred for 30 min. at ambient temperature. NMR analysis of the crude product showed that the aziridine had been ring-opened and selenide 180 was isolated in 44\% yield after chromatography (Scheme 4.11)

\[ \text{PhSe} \quad \text{NHOAc} \quad 180 \quad \text{(racemic)} \quad \text{H}_2\text{O}_2, \text{AcOH} \quad \text{HNO}_3 \quad 181 \quad \text{CCl}_4, \text{heat} \quad 182 \]

Scheme 4.12
Selenide 180 was oxidised with hydrogen peroxide in glacial acetic acid and allylamine 182 was the expected product from this reaction since selenoxides (e.g. 181) generally undergo syn-elimination at or below room temperature. In practice selenoxide 181 was isolated in 65% yield, its structure confirmed by accurate mass determination (Found: MH\(^+\) 458.1346. C\(_{23}\)H\(_{28}\)O\(_2\)N\(_3\)Se requires M 458.1345)(Scheme 4.12). However, allylamine 182 was obtained in 65% yield by heating selenoxide 181 in carbon tetrachloride at 80°C for two hours. The NMR spectrum of 182 shows diagnostic signals at \(\delta\) 3.70 (1H, br s, CHNH), 5.55 (1H, br s, NH), 5.63 (1H, m, incl. J 10.1, \(\text{C} = \text{CHCH}_2\)) and 5.92 (1H, dddd, J 10.1, 5.1, 3.5, 1.6, \(\text{CH} = \text{CCH}_2\)).

The stability of selenoxide 181 may be the result of hydrogen bonding of the oxygen with the QNH as in Fig 4.2, thus preventing the molecule from adopting a conformation where syn-elimination could occur.

![Fig 4.2](image)

4.8 Conversion of aziridine 183 into allylamine 185

Aziridine 183 was obtained in 30% yield from reaction of 1-methylcyclohexene with Q\(^2\)NHOAc 49 under normal reaction conditions (in the absence of TFA).

![Scheme 4.13](image)
Ring-opening of aziridine 183 using sodium phenylselenolate gave ring-opened 184 in 26% yield; the residue contained starting material 183. In this case oxidation of sulphide 184 gave allylamine 185 directly in 33% yield without the need for heating in carbon tetrachloride (Scheme 4.13). The NMR spectrum of 185 shows diagnostic signals at δ 1.53 (3H, br s, CH₃), 3.60 (1H, br s, H/HCCNMe), 4.75 (1H, br s, CH=C), 4.78 (1H, br s, C=CH) and 5.61 (1H, br s, NH).

4.9 Conclusion

Chemical correlation has related the configuration at the cyclohexadiene ring carbon chiral centre in dienylamine 139 to the configuration at C₆ in the major diastereoisomer of aziridine 138. The absolute configuration at this chiral centre in dienylamine 139 can be assigned as (R) if the major diastereoisomer of aziridine 138 is that expected from Gattrell’s aziridination model using Q⁶NHOAc−TTB. Although dienylamine 139 is formed as a single diastereoisomer, the work reported here does not prove it is formed with complete retention of configuration (as opposed to complete inversion). However, implicit in our discussion of the insertion mechanism is the assumption that dienylamine 139 is formed with complete retention of configuration.

Following on from the above chemical correlation, the ring-opening of N(Q)-aziridines 178 and 183 with phenylthiolate and phenylselenolate have been achieved. Oxidation of the resulting 1-(Q)amino-2-phenylselenocyclohexanes and elimination of phenylselenenic acid has yielded the corresponding cyclohexenyl-N(Q)amines. Although the yields in some of these conversions are low they have not been optimised.
Chapter 5
Preparation of Enantiopure Chirons from 1,3-Cyclohexadiene Derived $N(Q)$-Aziridines
5.1 Introduction

The ratio of aziridine : dienylamine obtained from the reaction of Q\textsuperscript{3}NHOAc 71 is ~1:1 with 1,4-cyclohexadiene and ~5:1 using 1,3-cyclohexadiene respectively. To probe into the mechanism of dienylamine formation (see Chapter 3), the effect on the aziridine/dienylamine ratios of changes in reaction conditions was explored.

5.2 Reaction of Q\textsuperscript{3}NHOAc with cyclohexa-1,4-diene in the presence of TFA

The effect of TFA on the ratio of aziridine/dienylamine produced was of interest since a) the formation of insertion products appeared to correlate with a more electrophilic Q-2-(imine) carbon in the reactions of the 3-acetoxyaminoquinazolinone (QNHOAc) reagent used with 1,3-cyclohexadiene, and b) the proposed mechanism of aziridination in the presence of TFA (Chapter 1) involves protonation at N-1 and consequently an increase in electrophilicity at C-2 in the quinazolinone ring.

Aziridinations in the presence of TFA can be carried out in dichloromethane at -40\textdegree C as the protonated QNHOAc species is more reactive. In the reaction of Q\textsuperscript{3}NHOAc with cyclohexa-1,4-diene at this temperature (Scheme 5.1) the reaction mixture was first allowed to warm to ambient temperature before addition of aqueous sodium hydrogen carbonate and trifluoroacetate 186 was isolated in 33% yield after
crystallisation from light petroleum. An X-ray crystal structure of 186 (see Appendix 2.5) shows that the initially formed aziridine had been opened by TFA in the expected S2 sense resulting in the QNH and trifluoroacetoxy groups being trans in the product.

The reaction was then repeated, but aqueous sodium hydrogen carbonate was added at -40°C after stirring the reaction mixture for 5 min. After work up, NMR analysis of the crude product showed that no ring-opening had occurred with dienylamine 143, aziridine 144 and unchanged starting material (NAQ3) 187 being isolated in 5%, 60% and 11% yields respectively after chromatography. As can be seen from this result, the ratio of aziridine to insertion product obtained from the reaction is 12:1, much higher than the 1:1 ratio afforded when TFA is omitted.

A sample of dienylamine 143 was stirred in dichloromethane with two drops of TFA for 30 min to ascertain its stability under these conditions. After work up, NAQ3 187 was obtained in 68% yield and no dienylamine was detected in the crude product by NMR analysis/mass spectroscopy. This is consistent with initial protonation of the (Q)amino group by TFA and elimination of 187 forming benzene (Scheme 5.2). Only NAQ3 187 was isolated from the crude product, benzene being lost during work up.

As 143 is unstable in the presence of TFA, the yield of NAQ3 isolated from the aziridination probably results from TFA degradation of dienylamine 143. However, even if all the NAQ3 is derived from decomposition of 143 this only amounts to a maximum of 16% dienylamine being formed in the reaction and hence a 1:4 ratio of dienylamine 143: aziridine 144. The effect of adding TFA to the aziridination is,
therefore, to depress the ratio of dienylamine : aziridine formed from the 1:2 ratio obtained in its absence.

5.3 Aziridination/insertion reactions of cyclohexadienes using acetonitrile as solvent

The proportion of aziridination: insertion product formed could be very dependent on the choice of reaction solvent. If the mechanism did involve hydride transfer and capture of the cyclohexadienyl cation in a second step (Scheme 3.23) then a more polar solvent than dichloromethane such as acetonitrile could increase the proportion of insertion product formed.

Aziridination of 1,4-cyclohexadiene with Q^3NHOAc 71 was carried out in the usual way with acetonitrile as the solvent. Aziridine 144, dienylamine 143 and Q^3H 145 were obtained in 30%, 9% and 5% yields respectively after chromatography (Scheme 5.3). Thus the overall yield of the reaction is lower than when dichloromethane is used as solvent and the ratio of aziridine : insertion product has risen to 3:1 from 1:1 in the crude product.

In the reaction of Q^3NHOAc 71 with 1,3-cyclohexadiene carried out in dichloromethane or acetonitrile, no dienylamine was isolated. However, in acetonitrile a new product was formed in addition to aziridine 136 (15%) which was identified as alcohol 188 (27%) and was separated by chromatography. Ring-opening of 136 was subsequently found to proceed with retention of configuration to give 188 (Scheme 5.4).
Scheme 5.4

The NMR spectrum of alcohol 188 showed signals at $\delta$ 2.85 (1H, ddd, $J$ 6.9, 6.9, 3.3, $CHNH$), 3.96 (1H, br s, $CHOH$), 4.83 (1H, br s, $OH$), 5.81 (1H, dddd, $J$ 11.9, 5.4, 3.3, 1.9, $CH=CCH_2$), 5.88 (1H, dddd, $J$ 11.9, 4.4, 2.0, $C=CHCH_2$) and 5.93 (1H, d, $J$ 6.9, NH). $^1$H-$^1$H COSY spectroscopy aided structure assignment of allylic alcohol 188.

Scheme 5.5

The aziridination of 1,4-cyclohexadiene with $Q^6$NHOAc in the presence of TTB was carried out in acetonitrile as shown in Scheme 5.5. A 2:1 ratio of dienylamine 146 : aziridine 141 was isolated from the reaction in 22% and 10% yields respectively. Thus using acetonitrile as solvent led to a lower overall yield of these products from the reaction (previously 27% and 23% respectively), but the ratio of dienylamine 146 : aziridine 141 obtained was higher than when dichloromethane was used.

Acetonitrile was then used as solvent in the aziridination of 1,3-cyclohexadiene with $Q^6$NHOAc in the presence of TTB. NMR analysis of the crude product showed the presence of aziridine 616 and dienylamine 617 along with two unknown products (Scheme 5.6).
Flash chromatography gave only the major diastereoisomer of aziridine 138 in 38% yield and dienylamine 139 in 7% yield. A third fraction eluted from the column contained a 4:1 mixture of diastereoisomeric alcohols 189a and 189b (Scheme 5.6) which were separated by Kieselgel chromatography and isolated in 12% and 6% yields respectively.

In the $^1$H-$^1$H COSY NMR spectrum of each alcohol diastereoisomer the proton on the Q$^6$NH-bearing carbon ($\delta$3.18 for 189a and $\delta$2.96 for 189b) showed a cross peak with the proton on the alcohol-bearing carbon of the six-membered ring and no coupling to either olefinic proton (see Appendix 1.4 and 1.5).

In the NMR spectrum of each alcohol, irradiation of the proton on the alcohol-bearing carbon ($\delta$4.17 for 189a and $\delta$4.63 for 189b) showed the loss of a coupling ($J$ ~3Hz) to the proton on the Q$^6$NH-bearing carbon and simplification of the olefinic signals. Since it is unlikely that both these protons are equatorial, the conclusion is that each diastereoisomer has the Q$^6$NH and OH groups cis with the alcohol group.
axial and Q\textsuperscript{6}NH group equatorial (the Q\textsuperscript{6}NH group is assumed to have a higher conformational preference for an equatorial position than an OH group)(Fig 5.1).

The absence of any of the minor diastereoisomer of aziridine 138 is of interest (dr ranges from 10:1 ~ 4:1 in dichloromethane). It is possible that aziridine 138 is formed as a mixture of diastereoisomers and conversion of the minor diastereoisomer to alcohol 189b occurs faster than the corresponding ring-opening of the major diastereoisomer leading to high diastereopurity in recovered aziridine 138.

5.4 Ring-opening of aziridine 138 with TFA

Aziridine 138 was stirred for 1 h with TFA (2 drops) in dichloromethane. On work up, NMR analysis of the crude product shows a mixture of a trifluoroacetate product and an alcohol which could not be separated by chromatography. The mixture was stirred in ethanol saturated with sodium carbonate, which converted the trifluoroacetate into alcohol 190 in an overall yield of 47% (Scheme 5.7). This result shows that the aziridine undergoes an \textit{S\textsubscript{N}2'} ring-opening by TFA.

<table>
<thead>
<tr>
<th>NMR Signal</th>
<th>CHNH(\delta)</th>
<th>CHX(\delta)</th>
<th>NH(\delta)</th>
<th>HC=CH(\delta)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol 190</td>
<td>3.75</td>
<td>4.19 (X=OH)</td>
<td>5.54</td>
<td>5.63, 5.97</td>
</tr>
<tr>
<td>Sulphide 173</td>
<td>3.71</td>
<td>3.78 (X=SAr)</td>
<td>5.38</td>
<td>5.53, 5.91</td>
</tr>
</tbody>
</table>
Structure confirmation of alcohol 190 comes from comparison of its NMR spectrum with that of sulphide 173 which are very similar suggesting that the regioisomer from $S_N2'$ ring-opening is formed and not the alternative from $S_N2$ ring-opening (see Table 5.1).

5.5 Ring-opening of aziridines 136 and 138 by weak acid

The origin of alcohols 189a and 189b in the aziridination of 1,3-cyclohexadiene with Q\textsuperscript{6}NHOAc–TTB in acetonitrile was not clear. In a separate reaction a sample of aziridine 136 was stirred in acetonitrile and water (25%) to investigate whether conversion to the corresponding alcohol occurred. NMR analysis of the crude product showed that none of the aziridine was ring-opened, so the reaction was repeated under the same conditions in the presence of glacial acetic acid (2 drops) (Scheme 5.8). Alcohol 188 was isolated from the process in 38% yield after chromatography. This is an interesting observation as no evidence of $S_N2'$ ring opening is present in the NMR spectrum of the crude product by comparison of the NMR spectrum of 190, suggesting the quinazolinone ring could be playing some role in this process (see below).

Aziridine 138 was also stirred initially in acetonitrile containing water (25%) for 1 h but the NMR spectrum of the crude product showed unchanged starting material. However, repetition of the procedure after addition of toluene p-sulphonic acid (2-3 crystals) followed by NMR analysis of the crude product showed the presence of a 4:1 mixture of the same alcohol diastereoisomers 189a and 189b as isolated previously, along with a minor amount of an unknown compound (Scheme 5.9). Flash chromatography separated these three compounds with the unknown
compound being eluted first. Close inspection of its NMR spectrum revealed the absence of an OH peak; the presence of NH was not confirmed as no exchange was observed after addition of deuterium oxide (1 drop), also the IR spectrum did not contain a characteristic NH signal.

Scheme 5.9

The structure of this product may be cyclic ether 191 which was obtained in 24% yield and could result from interception of the 1,3-dipolar species 192 by the hydroxy oxygen in the (Q)2-substituent (Scheme 5.10). The NMR spectrum of 191 showed diagnostic signals at δ3.23 (1H, struct. m, CHN), 4.53 (1H, br s, CHO), 4.81 (1H, s, Bu'CHO), 5.78 (1H, m, incl. J 10.3, CH=CCH₂), 6.06 (1H, ddd, J 10.3, 3.9, 2.0, C=CHCH₂) and 6.60 (1H, s, NH). A ¹H-¹H COSY spectrum shows that the olefinic protons are coupled to one methylene group and to CHO, which in turn couples to the CHNH proton.

Scheme 5.10
The alcohol diastereoisomers 189a and 189b were separated by column chromatography in 15% and 13% yield respectively, but a significant proportion diastereoisomer 189a was lost on chromatography as shown by analysis of the NMR spectrum of the crude product.

In a repetition of this experiment, flash chromatography was carried out on silica washed with triethylamine (2%) prior to the column being run. The same yields of cyclic ether 191 and the minor diastereoisomer 189b were isolated from the column. However, the yield of the major diastereoisomer 189a rose to 49% giving a more acceptable overall yield.

5.6 Mechanism of formation of cis-4-(Q6)amino-cyclohexen-3-ols 189a and 189b in ring-opening of aziridine 138 with toluene p-sulphonic acid in acetonitrile

Evidence for the involvement of the quinazolinone ring in formation of alcohols 189a and 189b under the title conditions came from a reaction in which aziridine 138 and toluene p-sulphonic acid were stirred for 4 h in acetonitrile saturated with hydrogen sulphide gas.\(^{119}\) The NMR spectrum of the crude product showed the presence of alcohols 189a and 189b together with a minor compound with a similar NMR spectrum to 189a (Scheme 5.11).

The most notable difference in the NMR spectrum of this minor compound was a doublet at ~8.78, indicating sulphur had replaced the quinazolinone ring carbonyl oxygen, giving quinazolin-4-thione 193 by a mechanism shown in Scheme
5.12. analogous to that given in Chapter 3. The products were separated by Kieselgel chromatography giving a mixture of alcohol diastereoisomers \textbf{189a} and \textbf{189b} (40\%) and quinazolinon-4-thione \textbf{193} (13\%). No cyclic ether was isolated in this reaction.

The isolation of thione \textbf{193} suggests that the stereochemistry of the ring-opening of aziridine \textbf{138} in acetonitrile by toluene p-sulphonic acid may result from participation by the quinazolinone ring as in Scheme 5.12. The mechanism of formation of \textbf{189a} and \textbf{189b} in the aziridination of 1,3-cyclohexadiene in acetonitrile is not clear although involvement of the $Q^6$ group seems likely.

\textbf{5.7 Conversion of cis-$Q^6$amino-cyclohexen-3-ols 189a and 189b to $Q^6$-chirons}

One of the objectives in this work was to use the products from aziridination of dienes with enantiopure QNHOAc reagents to prepare Q-free ring-opened enantiopure products containing two or more chiral centres (chirons).^{112}

The \textit{cis-}(Q)aminoalcohols \textbf{188}, \textbf{189a} and \textbf{189b} appeared to offer a route to easy $Q$-$N$ bond cleavage \textit{via} the corresponding oxazolidinones: it has been shown previously that reductive cleavage of these $Q$-$N$ bonds is facilitated when both nitrogens of the $N$-$N$ bond undergoing cleavage are acylated as would be the case in \textbf{194}, \textbf{195a} and \textbf{195b}. 

\begin{center}
\textbf{Scheme 5.12}
\end{center}
The cyclisation to oxazolidinone was tested on (Q$^3$)aminoalcohol 188, which was heated in THF at reflux (90°C) with sodium hydride (1.1 eq.) and 1,1'-carbonyldiimidazole for 3 h. On work up, NMR analysis of the crude product showed that the alcohol had undergone partial cyclisation and chromatography yielded oxazolidinone 194 (53%) together with unchanged starting material 188 (35%)(Scheme 5.13).

Likewise, the major diastereoisomer (Q$^6$)aminoalcohol 189a was converted into N-(Q$^6$)oxazolidinone 195a (49%) and unchanged 189a (43%) after separation by flash chromatography (Scheme 5.14).
The minor (Q₆)aminoalcohol diastereoisomer 189b was treated in a similar manner giving N-(Q₆)oxazolidinone 195b (44%) and unchanged 189b (48%). The similarity in rates of cyclisation of 189a and 189b by 1,1'-carbonyldiimidazole supports the previously drawn conclusion that both have the same (cis) relative configuration at Q₆N- and OH-substituted positions.

5.8 Cleavage of the N-N bond

The presence of an acyl group as a substituent on the exocyclic nitrogen of a Q-N bond undergoing reductive cleavage has previously meant that aluminium amalgam is a sufficiently strong reducing agent to accomplish this.

Aluminium amalgam was freshly prepared¹³⁸ and stirred at ambient temperature with N-(Q₆)oxazolidinone 195a in THF but no cleavage of the Q₆-N bond was obtained and the unchanged starting material was recovered.

5.9 Samarium(II) iodide mediated N-N bond cleavage

As reduction with aluminium amalgam was not successful, it was decided to switch to the method originally discovered by J. Williams and used by W. Gattrell for cleavage of the Q₆-N bond which uses samarium(II) iodide.¹³⁹ Following this procedure, the NMR spectrum of the crude product was very similar to that of oxazolidinone 195a, except for a singlet at ~8.96 assigned to Q₆H. Separation by chromatography was not straightforward as oxazolidinone 196a is not UV active and was undetectable on a TLC plate by developing in either PMA or vanillin. Using a mixture of ethyl acetate containing methanol (10%) for flash chromatography and collecting several fractions after Q₆H 197 had been eluted from the column was found to be the most satisfactory method for isolation of oxazolidinone 196a. 197 was obtained as a white solid (75%) and was separated from oxazolidinone 196a (62%) which had an optical rotation of -10.6 (Scheme 5.15).
The same procedure was applied to \(N\)-(Q\(^6\))oxazolidinone 195b giving 197 (60\%) and oxazolidinone 196b (72\%). This enantiomeric oxazolidinone 196b had an optical rotation of +13.2 i.e. each enantiomer of oxazolidinone 196 can be prepared from the corresponding diastereoisomer of alcohol 189 in acceptable yield.

The reduced form of oxazolidinone 196b has been synthesised via a route involving hydroxy carbamate 198 and utilising 196b as an intermediate; 199 had the 1R, 2S configuration and an optical rotation of +25.0 (Scheme 5.16) but the optical rotation of 196b was not reported.\(^{140}\)
Aziridinations of 1,3-cyclohexadiene and 1,4-cyclohexadiene with QNHOAc in acetonitrile and in dichloromethane are compared. The ratio of dienylamine (insertion) : aziridine decreases in the case of the 1,3-diene but increases in the case of the 1,4-diene. However, the overall yields of both aziridines are lower in acetonitrile.

Using $Q^6\text{NHOOAc-TTB}$, two alcohols are also obtained from the aziridination of 1,3-cyclohexadiene in acetonitrile and identified as \(189a\) and \(189b\). The same alcohols are obtained in ring-opening of aziridine \(138\) with toluene p-sulphonic acid by a mechanism which involves participation by the quinazolinone carbonyl oxygen, thus accounting for the \textit{cis}-relative configuration of OH and QNH groups. Conversion of alcohols \(189a\) and \(189b\) to $Q^6$-free chirons \(196a\) and \(196b\) has been accomplished, although the yields have not been optimised.
Chapter 6

Ring-Opening of $N(Q)$-Aziridines

with Iodide as the Nucleophile
6.1 Introduction

The work of Gattrell referred to in the Introduction has shown that the Q-group is sufficiently electron-withdrawing to allow nucleophilic ring-opening of \( N(Q) \)-aziridines i.e. the build up of negative charge on the ring nitrogen is stabilised by the Q-group. Nevertheless, good yields of ring-opened products very often required the presence of a proton source to react with the anionic nitrogen formed.

In \( N(Q) \)-aziridines, when the substitution at \( C_2 \) or \( C_3 \) is appropriate, both \( N \)-invertomers may be present in solution in comparable amounts and interconversion between them at room temperature, although slow on the NMR timescale, is likely to be fast on the timescale of most reactions. With this in mind, there are a number of ways in which the Q-group on the ring-nitrogen could affect the rate, regiochemistry or stereochemistry of ring-opening:

i) The two \( N \)-invertomers could have different reactivity e.g. the Q-group may interact with the \( cis-C_2 \) or \( C_3 \) substituent and thus influence the rate-/regiosense of ring-opening.

ii) The presence of strongly electron-withdrawing groups on the Q-group could accelerate the rate of nucleophilic attack.

iii) Ring-opening in acid may proceed via initial protonation of the Q-group rather than the weakly basic aziridine ring nitrogen: oxophilic Lewis acids mediating ring-opening will be even more likely to complex with the Q-carbonyl oxygen than the nitrogen lone pair.

The importance of some of these effects of the Q-group on aziridine ring-opening reactions largely by iodide was explored in this Chapter.

6.2 Preparation and ring-opening of aziridine 202

Work previously carried out at Leicester has examined intramolecular aziridinations by LTA oxidation of 3-aminoquinazolinones (NAQs) containing a double bond in the side-chain of the 2-substituent. Elaboration of this NAQ from the corresponding carboxylic acid was carried out in the usual way as exemplified by the synthesis of 3-aminoquinazolinone 201 by K. Woodthorpe (Scheme 6.1).
Oxidation of 3-aminoquinazolinone 201 with LTA gave aziridine 202 which K. Woodthorpe showed underwent ring-opening with hydrogen chloride gas giving a 3:1 mixture of chloride regioisomers 203 and 204 after chromatography as shown in Scheme 6.2.

One advantage of aziridines such as 202 is that N-inversion is geometrically prohibited. Therefore, it was decided to investigate the ring-opening of aziridine 202 further.

6.3 Ring-opening of aziridine 202 with hydriodic acid

Aziridine 202 was prepared according to the method employed by K. Woodthorpe. The crude product from ring-opening with hydriodic acid in THF contained a 1:1 ratio of the regioisomeric iodides 205 and 206 which were isolated in a combined yield of 71% (Scheme 6.3) analogous to the ring-opening in Scheme 6.2.
In the NMR spectrum of iodide 206, all of the signals are broadened except those for the quinazolinone aromatic ring. When the spectrum was recorded at 233K, sharp signals from two species were visible in a 2:1 ratio. By analogy with previous work\textsuperscript{122} these two species are likely to be $N$-$N$ bond rotamers (as opposed to $N$-invertomers) having ring-flipped conformations for the seven-membered ring but diastereoisomeric with the iodine in ‘equatorial’ or ‘axial’ positions (Scheme 6.4).

6.4 Aziridination of isobutene with $Q^3$NHOAc 71

The introduction of another alkyl substituent at the already substituted aziridine ring carbon in 202 would increase the stability of the developing carbocation in acid-catalysed ring-opening of aziridine 207 but at the same time increase steric hindrance to nucleophilic attack at this position (Scheme 6.5). The effect of these factors on the regioselectivity of ring-opening was of some interest.
Before making the corresponding 3-aminoquinazolinone and the derived aziridine 207 to investigate its ring-opening, it was decided to prepare the aziridine derived from isobutene and investigate its ring-opening reactions as a preliminary. Aziridine 208 was obtained as a crystalline solid in 70% yield (Scheme 6.6).

### Scheme 6.6

#### 6.5 Ring-opening reactions of aziridine 208

Aziridine 208 was stirred in THF with hydriodic acid (5 eq.) for 5 mins giving a single product identified as iodide 209 which was purified by chromatography and isolated in 54% yield (Scheme 6.7).
The NMR spectrum of the crude product showed a doublet at δ5.62 for NH and the diastereotopic methylene protons as broad singlets due to retarded rotation around the N-N bond.\textsuperscript{122}

The effect of reducing acid concentration was probed by ring-opening of aziridine 208 with sodium iodide (3 eq.) and acetic acid (1 eq.) in acetonitrile. After stirring for 10 min the starting material had disappeared (TLC) and, after work up, the crude product was shown by NMR spectroscopy to contain a 10:1 ratio of regioisomeric iodides 209 and 210, the latter exhibiting an NH triplet at δ5.89. The major product 209 was identical with that isolated above but could not be completely separated from the small amount of the regioisomeric iodide 210 by chromatography (Scheme 6.8). Iodide 210 was subsequently isolated in pure form (see below).

\[
\text{HNQ}^3 \quad 1) \text{NaI, CH}_3\text{CN} \quad \begin{array}{c} \rightarrow \end{array} \quad 209 + 210 \\
2) \text{AcOH} \\
\]

\textbf{Scheme 6.8}

The reaction was repeated in the presence of excess acetic acid (3 eq.) to determine whether a change in acid concentration would affect the regioselectivity of ring-opening, but the resultant crude product still contained a 10:1 ratio of regioisomeric iodides 209 and 210.

6.6 Ring-opening of 208 catalysed by samarium(III) chloride

Unpublished work in this Department by I. Lochrie has shown that N(Q)-aziridines ring-opening by iodide in the presence of acetic acid is catalysed by samarium(III). The conditions devised by Lochrie were applied to ring-opening of aziridine 208 (Scheme 6.9) and a 1:1 mixture of regioisomeric iodides 209 and 210 was separated by chromatography.
The mechanism of samarium(III) catalysed ring-opening will be discussed later, but it is clear that regioselectivity is dramatically affected by the presence of samarium(III) chloride. Co-ordination of samarium with the quinazolinone carbonyl oxygen and ring-opening at least in part via a mechanism involving partial carbocation character on the ring carbon explains the (lack of) regioselectivity.

On standing for several weeks, NMR analysis showed that iodide 209 had undergone conversion to alcohol 211 exhibiting signals at $\delta$3.08 and 3.18 (both dd) for the methylene protons and an NH singlet at $\delta$5.60 (Scheme 6.10). Conversion of iodide 210 into alcohol 211 could occur via a mechanism where iodide is displaced by the quinazolinone carbonyl oxygen followed by attack of adventitious water (Scheme 6.10).
6.7 Ring-opening of aziridine 208 with glacial acetic acid

![Chemical structure]

Aziridine 208 was ring-opened by stirring in neat glacial acetic acid (~1 h) to give acetate 212 (69%) and alcohol 213 (17%) in a 4:1 ratio which were separated by chromatography (Scheme 6.11). The NMR spectrum of each compound showed the methylene protons as a broad singlet (due to restricted N-N bond rotation) and the NH as a triplet ($J \approx 7.5$ Hz). These are typical conditions which encourage ring-opening via carbocation formation and as expected the regiochemistry is in agreement with such a mechanism (Scheme 6.12).

![Chemical structure]

Alcohol 212 is presumably formed by interception of the carbocation in Scheme 6.12 by the Q-C$_4$ hydroxy group, as in formation of alcohol 124 (Chapter 3).

6.8 Synthesis of 3-amino-2(3-methylbut-3-ene-1-yl)quinazolinone 218

3-Aminoquinazolinone 218, the precursor of aziridine 207 bearing an additional methyl group at the more substituted aziridine ring carbon (cf. aziridine 202) was synthesised by a modified procedure to that used by K. Woodthorpe.$^{83}$ Dimethyl malonate was deprotonated by sodium ethoxide and addition of 3-chloro-2-
methylpropene gave diester 214 in 58% yield. Decarboxylation gave mono-ester 215 in 82% yield which was hydrolysed giving acid 216 in 78% yield (Scheme 6.13). Acid 216 was converted into the corresponding acid chloride under acid-free conditions and reacted with methyl anthranilate to give \( N \)-acylanthranilate 217 in 30% yield. The desired 3-azoniquinazolinone 218 was obtained as a white crystalline solid in 46% yield after treatment with hydrazine.
The subsequent intramolecular aziridination reaction was carried out (in dilute solution) to minimise the yield of intermolecular aziridination – aziridine 207 was isolated in 66% yield as a crystalline solid (Scheme 6.14).

6.9 Ring-opening of aziridine 207 with hydriodic acid

Ring-opening of aziridine 207 with hydriodic acid in THF gave a single product which was the result of ring-opening at the less substituted carbon of the aziridine ring; iodide 219 was isolated as a crystalline solid in 78% yield from chromatography (Scheme 6.15). The NMR spectrum of 219 shows the methylene protons as doublets at δ3.30 and 3.32 (J = 10.3), and the NH(s) at δ6.86.

These results suggest that there is little development of carbocation character in the ring-opening reactions of aziridines 207, 208 and presumably 202. Ring-opening under these conditions would be expected to involve protonation of the aziridine ring nitrogen (or Q-group), but nucleophilic attack at the less hindered ring-carbon by iodide determines the regioselectivity. Curiously, the small amount of iodide 210 from ring-opening of aziridine 208, is produced under the least acidic conditions in which carbocation formation is expected to be least favoured.
6.10 Ring-opening of $N(Q)$-aziridine carboxylic acid esters with iodide

The ring-opening of $N(Q)$-aziridine acid esters with iodide was explored with particular attention to the involvement of the Q group in influencing the stereo- and regiochemistry of ring-opening. Control of the ring-opening of aziridine acid esters is of particular interest since these compounds are obvious precursors of substituted $\alpha$- or $\beta$-amino acids.

There are a few literature examples where ring-opening of aziridines at $C_2$ bearing the ester group is favoured. The reaction of aziridine 220 by lithium bromide (a soft nucleophile) in the presence of a Lewis acid leads to exclusive ring-opening at $C_2$ to give bromide 221 (Scheme 6.16). This is in contrast to aziridine 222, where $C_3$ ring-opening under similar conditions is almost always observed. The reaction of 220 with methanol (a hard nucleophile) in the presence of a Lewis acid gave the product resulting from aziridine ring-opening at $C_3$. It was concluded that the regioselectivity of attack by soft nucleophiles was determined by the centre having the highest LUMO coefficient ($C_2$) whilst hard nucleophiles react with centres having the highest charge.

![Scheme 6.16](image)

![Scheme 6.17](image)
The ring-opening of aziridine 223 with sodium azide gave a 4:1 ratio of regioisomers 224 and 225 resulting from attack at C\textsubscript{2} and C\textsubscript{3} respectively (Scheme 6.17).\textsuperscript{1} Ring-opening with thiol gave a 1:1 mixture of regioisomers, but the use of other reagents for ring-opening, such as benzylamine or alkyl cuprate, led to attack at C\textsubscript{1} only.

However, the great majority of aziridine acid esters, unsubstituted at position 3, undergo highly regioselective attack at C\textsubscript{3}.

### 6.11 Ring-opening reactions of aziridine 226

Aziridine 226 (see Chapter 2) was obtained in a 45% yield from the aziridination of methyl acrylate with Q\textsuperscript{3}NHOAc 71. A number of ring-opening reactions were carried out on aziridine 226 with iodide under different conditions and the results summarised in Table 6.1.

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Rxn. Time (min.)</th>
<th>Ratio 227:228</th>
<th>Yield (%)</th>
<th>Yield 229 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HI (2 drops), THF</td>
<td>45</td>
<td>3:2</td>
<td>61</td>
<td>-</td>
</tr>
<tr>
<td>NaI(3 eq.), AcOH(1 eq.), CH\textsubscript{3}CN</td>
<td>25</td>
<td>&gt;50:1</td>
<td>55</td>
<td>10</td>
</tr>
<tr>
<td>NaI(3 eq.), AcOH(10 eq.), CH\textsubscript{3}CN</td>
<td>120</td>
<td>&gt;50:1</td>
<td>48</td>
<td>15</td>
</tr>
</tbody>
</table>

Aziridine 226 was stirred in acetonitrile with hydriodic acid for 30 min.; the crude product contained a 3:2 mixture of regioisomers 227 and 228, isolated in a combined yield of 61\% (Scheme 6.18) and distinguishable by NH signals at δ5.91(t) and δ5.94(d) respectively in their NMR spectra, were not separated by chromatography.
Ring-opening of aziridine 226 with sodium iodide (3 eq.) and acetic acid (1 eq.) gave iodide 227 after stirring for 5 min in acetonitrile. Analysis of the crude product by NMR spectroscopy showed that iodide 227 was accompanied by the de-iodinated methyl ester 229 which was assumed to be formed by the mechanism shown in Scheme 6.19. The abundance of 229 varied from 10-15% under the different conditions used for ring-opening; it was not separated from iodide 227 by Kieselgel chromatography. Loss of product during chromatography gave the lower isolated yield of iodide 227 (55%) still contaminated with 229.

Ring-opening with sodium iodide/acetic acid was repeated with stirring at ambient temperature for 2 h. Analysis of the crude product by NMR spectroscopy showed little difference to that above, although the isolated yield of iodide 227 (48%) was marginally lower. The regioselectivity of ring-opening was unaffected by increasing the concentration of acetic acid ten-fold.
6.12 Ring-opening reactions of aziridine 115

Aziridine 115 was obtained as a colourless crystalline solid from the aziridination of methyl acrylate with Q$^5$NHOAc 52 in 54% yield. Ring-opening reactions were carried out on aziridine 115 under various conditions; the results are summarised in Table 6.2.

Table 6.2: Ring-opening of aziridine 115 under different conditions

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Rxn. Time (min.)</th>
<th>Ratio 230:231</th>
<th>Yield (%)</th>
<th>By-products (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HI (2 drops), THF</td>
<td>30</td>
<td>1:1</td>
<td>78</td>
<td>-</td>
</tr>
<tr>
<td>NaI(3 eq.), AcOH(1 eq.), CH$_3$CN</td>
<td>2</td>
<td>6:1</td>
<td>68</td>
<td>-</td>
</tr>
<tr>
<td>NaI(3 eq.), AcOH(1 eq.), CH$_3$CN</td>
<td>60</td>
<td>5:1</td>
<td>53</td>
<td>110 (21), 232 (17)</td>
</tr>
</tbody>
</table>

Ring-opening of aziridine 115 with hydriodic acid in THF gave a 1:1 mixture of regioisomers 230 and 231 in the crude product, isolated in a combined yield of 78% after chromatography, during which 231 partly decomposed (Scheme 6.20). Iodides 230 and 231 are distinguishable by NMR, having NH signals at δ 5.76(t) and 6.15(d) respectively. A pure sample of 230 was obtained by Kieselgel chromatography.

![Scheme 6.20](image)

The reaction of aziridine 115 with sodium iodide and glacial acetic acid in acetonitrile was complete after only 2 min. Chromatography gave a 6:1 mixture of iodides 230 and 231 in the crude product, isolated in 68% yield.

When the reaction mixture was stirred for a further hour before work up a lower isolated yield of iodides 230 and 231 (53%) was obtained together with NAQ$^5$ 110 (21%) and de-iodinated ester 232 (17%), both presumably resulting from
deiodination of iodide 230 (Scheme 6.21) \textit{via} a mechanism analogous to that proposed for formation of ester 229 (Scheme 6.19).

Scheme 6.21

The more rapid reaction of aziridine 115 compared with that of 226 suggests that ring-opening is the result of nucleophilic attack at C$_2$ and that the acetic acid present in the mixture is protonating the nitrogen anion after opening by iodide and is not involved in the ts' for ring-opening. Ring-opening with hydriodic acid could involve prior protonation of the aziridine ring nitrogen (or the quinazolinone ring) and less selective nucleophilic attack by iodide.

6.13 Stability of iodides 227 and 230

Samples of iodides 227 and 230 were stirred separately in acetonitrile with sodium iodide (3 eq.) and glacial acetic acid (1 eq.) to probe the suggested mechanism of deiodination to give esters 229/232 (Schemes 6.19, 6.21). In each experiment the mixture was stirred for 2 h, but NMR analysis showed no decomposition of iodides 227 or 230 after this time. This result was unexpected as exposure of these iodides to the reaction conditions for longer (Tables 6.1, 6.2) does lead to increased amounts of deiodination products: further investigation is required to account for these results.
6.14 Ring-opening reactions of aziridine 233

Aziridine 233 was obtained as an oil from the aziridination of methyl methacrylate with Q\(^3\)NHOAc 71 in 39% yield; NMR analysis showed the aziridine was present in solution as a 4:1 mixture of N-invertomers with the major one having Q\(^3\) and CO\(_2\)Me cis.\(^7\) Thus, the N-invertomer having the aziridine ring methyl signal at higher field (shielded by the Q\(^3\) group) was the minor one. The results of ring-opening reactions carried out on this aziridine are summarised in Table 6.3.

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Rxn. Time (min.)</th>
<th>Ratio 234:235</th>
<th>Yield (%) 233 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HI(2 drops), THF</td>
<td>30</td>
<td>1:1</td>
<td>38</td>
</tr>
<tr>
<td>NaI(3 eq.), AcOH(1 eq.), CH(_3)CN</td>
<td>240</td>
<td>2:3</td>
<td>49</td>
</tr>
<tr>
<td>NaI(3 eq.), AcOH(10 eq.), CH(_3)CN</td>
<td>60</td>
<td>2:3</td>
<td>46</td>
</tr>
</tbody>
</table>

The effect of introducing a methyl group at C\(_2\) in aziridine 233 by comparison with 226 is to slow the rate of hydriodic acid ring-opening as starting aziridine 233 (55%) was isolated under conditions where 226 completely reacted: iodides 234 and 235 (Scheme 6.22) were distinguishable by NMR having NH signals at 86.08(t) and 5.83(s) respectively. A pure sample of iodide 234 was obtained from chromatography, during which 235 decomposed.

\[
Q^3\begin{array}{c} \text{HNQ}^3 \\ \text{CO}_2\text{Me} \end{array} \begin{array}{c} \text{HNQ}^3 \\ \text{CO}_2\text{Me} \end{array} _\text{30 min} \rightarrow \begin{array}{c} \text{HNQ}^3 \\ \text{CO}_2\text{Me} \end{array} + \begin{array}{c} \text{HNQ}^3 \\ \text{CO}_2\text{Me} \end{array}
\]

Scheme 6.22

Ring-opening of aziridine 233 with sodium iodide (3 eq.) and acetic acid (1 eq.) in acetonitrile gave iodide regioisomers 234 and 235 and unchanged aziridine 233 in 19, 30 and 35% isolated yields respectively after column chromatography. The ratio of iodides 234:235 was unaffected by using 10 eq. of acetic acid in the ring-opening.
Ring-opening reactions of methyl methacrylate-derived aziridine 233 by sodium iodide–acetic acid is also much slower than the corresponding reactions of methyl acrylate-derived aziridines under the same conditions judging by starting material recovered: conditions for complete consumption of the aziridine were not found.

6.15 Ring-opening of aziridine 116

Aziridine 116, obtained as a white crystalline solid described in Chapter 2, was subjected to similar ring-opening reactions; the results of which are tabulated below (Table 6.4). NMR analysis showed that the aziridine is present in solution as a 3:1 ratio of \( \text{N} \)-invertomers at ambient temperature, the major \( \text{N} \)-invertomer having \( \text{Q}\) and ester cis.

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Rxn. Time (min.)</th>
<th>Ratio 236:237</th>
<th>Yield (%)</th>
<th>116 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HI (2 drops)</td>
<td>30</td>
<td>1:1</td>
<td>57</td>
<td>31</td>
</tr>
<tr>
<td>NaI(3 eq.), AcOH(1 eq.)</td>
<td>2</td>
<td>1:1</td>
<td>45</td>
<td>42</td>
</tr>
</tbody>
</table>

Ring-opening of aziridine 116 with hydriodic acid gave a 1:1 ratio of iodide regioisomers 236 and 237 in the crude product, from attack at \( \text{C}_2 \) and \( \text{C}_3 \) by comparison of \( \text{NH} \) signals at 5.78 and 5.88 in the NMR spectrum respectively; starting material was recovered in 31\% yield (Scheme 6.23).

![Scheme 6.23](image)
A 1:1 mixture of iodide regioisomers 236 and 237 was also observed in the crude product when aziridine 116 was ring-opened by mixing with sodium iodide (3 eq.) and glacial acetic acid together with unchanged aziridine (42%). Stirring the reaction mixture for a further hour had no effect on the yield or ratio of products.

6.16 Stability of iodide products

Mixtures of iodides 234 and 235 and of 236 and 237 were stirred separately with sodium iodide (3 eq.) and glacial acetic acid (1 eq.) to investigate the stability of these products to the reaction conditions. After 2 h. NMR analysis of the recovered products showed them to be identical to the starting material in each reaction.

6.17 Discussion of results

The ring-opening reactions described in the previous pages show that attack of 1-(Q)-aziridine-2-carboxylic esters 226 and 115 by iodide at C2, the ester-bearing carbon is favoured over C3. This is the opposite regiosense to that expected as nucleophiles usually attack the less hindered C3 methylene in aziridine-2-carboxylic acid bearing esters other N-substituents (see Introduction). Therefore, another factor must promote attack at C2 and this may be the consequence of an enhanced interaction between the anti-bonding σ* orbital of the ester-bearing carbon C2 and the π* anti-bonding orbital of the ester carbonyl group. The energy of the σ* orbital is lowered and attack by the nucleophile is thereby facilitated (Fig 6.1A).

![Fig 6.1](image-url)
The conformation adopted by the ester group allowing $\sigma^*-\pi^*$ overlap may be favoured as a result of an interaction between the ester carbonyl oxygen and the Q carbonyl group which resembles the secondary interaction in the aziridination ts of methyl acrylate by QNHOAc (Fig 6.1B) except that in the latter case the two components are envisaged as being closer together.

![Diagram](image)

**Fig 6.2**

An attractive interaction like that proposed in Fig 6.1A has been suggested to account for the unexpected change in N-invertomer ratios as the size of the ester alkyl group was increased (Fig 6.2). X-Ray crystallography of an N(Q)-aziridine carboxylic acid ester shows a stereostructure for the molecule which resembles that in A (Fig 6.1).

6.18 Aziridination of $\alpha$-methylene-$\gamma$-butyrolactone

As discussed above, ring-opening at C$_2$ in $\alpha,\beta$-unsaturated ester-derived aziridines is assumed to be promoted by overlap of the C$_2$-N $\sigma^*$ anti-bonding orbital with the $\pi^*$ anti-bonding orbital of the ester carbonyl group. If this overlap is disturbed, nucleophilic attack by iodide will occur predominantly at the methylene carbon, C$_3$, as discussed in the Introduction. Aziridination of $\alpha$-methylene-$\gamma$-butyrolactone with Q$^\circ$NHOAc will produce an aziridine spiro-fused to a five membered lactone ring and whilst $\sigma^*-\pi^*$ overlap may still be present, the rigidity of the molecule could interfere with the optimum interaction of the lactone carbonyl with the Q-group, thus the regioselectivity of ring-opening may be affected (Fig 6.3).
Fig 6.3

A 33% yield of aziridine 238 was isolated from the reaction of α-methylene-γ-
butyrolactone with Q\(^3\)NHOAc. Aziridine 239 was also obtained in 33% yield from
aziridination of the lactone with Q\(^5\)NHOAc (Scheme 6.24). Both aziridines were
colourless crystalline solids and NMR analysis showed that each was present in
solution as a single \(N\)-inveromer, presumably with the lactone carbonyl and
quinazolinone ring \(cis^{144}\): this is certainly the preferred \(N\)-inveromer in the crystal
structure of aziridine 239 (see Appendix 2.6).

Scheme 6.24

6.19 Ring-opening of aziridines 238 and 239

Aziridine 238 was stirred for 30 min. with sodium iodide (3 eq.) and glacial
acetic acid (1 eq.) in acetonitrile to give iodide 240 (38%) after column
chromatography (Scheme 6.25); 48% of aziridine 238 was recovered from the
reaction. There was no evidence in the NMR spectrum of the crude product for the presence of the regioisomeric iodide from ring-opening.

\[
\begin{align*}
\text{Nal (3 eq.),} \\
\text{AcOH (1 eq.),} \\
\text{CH}_3\text{CN}
\end{align*}
\]

20 min.

\[
\begin{align*}
Q=Q^3 \\
Q=Q^5
\end{align*}
\]

Scheme 6.25

Aziridine 239 was ring-opened with sodium iodide and acetic acid under the same conditions giving iodide 241 and unchanged aziridine 239 in 45% and 41% isolated yields respectively. As above, no signals from the regioisomeric ring-opened iodide were visible in the NMR spectrum of the crude product.

The high regioselectivity in ring-opening of aziridines 238 and 239 may reflect the less favourable interaction of lactone carbonyl and Q-group, but it may also be the result of the \textit{s-trans}-enforced conformation of the lactone which may affect the \(\sigma^*\text{-}\pi^*\) overlap.

6.20 Ring-opening of aziridines in the presence of samarium(III) chloride

Aziridines 226, 115, 233, 116, 238 and 239 were also ring-opened by sodium iodide (3 eq.) and acetic acid (1 eq.) in acetonitrile in the presence of samarium(III) chloride; the results of these experiments are summarised in Table 6.5.

The presence of samarium (III) chloride leads to a small increase in the rate of ring-opening (progress was monitored by TLC) and to the yields of isolated products compared to reactions in its absence (see Tables 6.1-6.4). Regioselectivity of ring-opening of aziridines 226, 233, 238 and 239 is not affected by the presence of samarium (III) chloride with attack by iodide occurring at C2 still favoured for 226 and 233 (Scheme 6.26).

Preparation of \textit{tert}-butyl methacrylate\textsuperscript{145} and subsequent aziridination with Q\textsuperscript{3}NHOAc gave aziridine 242 (56%) as a 4:1 mixture of invertomers.\textsuperscript{93} Ring-opening
with sodium iodide and acetic acid in the presence of samarium(III) chloride was complete after 5 min. Column chromatography gave iodides 243 and 244 as a 1:2 mixture (from nucleophilic attack at C\textsubscript{3} and C\textsubscript{2} respectively) in 79% isolated yield, by comparison of NH signals at δ 5.95 and 5.86 in the NMR spectrum.

Table 6.5: **Ring-opening of aziridines in the presence of samarium(III) chloride**

<table>
<thead>
<tr>
<th>Aziridine</th>
<th>Rxn. Time (min.)</th>
<th>Ratio C\textsubscript{2}:C\textsubscript{3}</th>
<th>Yield (%)</th>
<th>By-product (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>226</td>
<td>10</td>
<td>≥50:1</td>
<td>59</td>
<td>229 (20)</td>
</tr>
<tr>
<td>115</td>
<td>2</td>
<td>2:3</td>
<td>39</td>
<td>110 (21), 232 (17)</td>
</tr>
<tr>
<td>233</td>
<td>60</td>
<td>&gt;50:1</td>
<td>37</td>
<td>233 (39)</td>
</tr>
<tr>
<td>116</td>
<td>20</td>
<td>1:3</td>
<td>68</td>
<td>-</td>
</tr>
<tr>
<td>238</td>
<td>20</td>
<td>(C\textsubscript{3} only)</td>
<td>45</td>
<td>238 (39)</td>
</tr>
<tr>
<td>239</td>
<td>20</td>
<td>(C\textsubscript{3} only)</td>
<td>62</td>
<td>239 (27)</td>
</tr>
<tr>
<td>242</td>
<td>5</td>
<td>1:2</td>
<td>79</td>
<td>-</td>
</tr>
</tbody>
</table>

Additional evidence for an increase in the rate of ring-opening in the presence of samarium(III) chloride was the complete reaction of aziridines 116 and 242. The results in Table 6.5 also show that ring-opening of Q\textsuperscript{5}-substituted aziridines 115, 116 and 242 at C\textsubscript{3} is more favoured in the presence of samarium(III) chloride.

6.21 **Mechanism of N(Q)-aziridine ring-opening in the presence of samarium(III) chloride**

The effect of including samarium(III) chloride is to increase the rate of ring-opening of 1-(Q\textsuperscript{3})-aziridine-2-carboxylic esters by iodide compared to the same
reaction in its absence. It seems likely that the highly oxophilic samarium will co-
ordinate with the carbonyl oxygen. Since the regioselectivity of ring-opening is
affected, it seems that samarium may play a further role by co-ordinating with one of
the C-N (banana) bonds of the aziridine ring (Scheme 6.27). Attack of iodide would
then take place on the samarium(III)-co-ordinated C-N bond.

\[
\begin{align*}
\text{Scheme 6.27}
\end{align*}
\]

The effect of samarium(III) inclusion on the Q^5-substituted aziridines bearing a
C_2-trifluoromethyl group does appear to increase the proportion of C_3- over C_2-attack
although the effect is not large. As described in the Introduction, the trifluoromethyl
group brings about a change in the ts^* for aziridination of acrylates from (Q)C=O to
(Q)C=N overlap by the ester carbonyl oxygen. If it is assumed that this preference
carries over to the N(Q^5)-aziridines then the enhanced level of attack at C_3 could be
the result of significant reaction via the ts^* shown in Scheme 6.28. Here unhindered
samarium(III) co-ordination of the C_3-N σ bond and (Q)C=O leads to competitive
ring-opening at C_3.

\[
\begin{align*}
\text{Scheme 6.28}
\end{align*}
\]
6.22 Conclusion

As discussed in the Introduction, there are few literature examples of ring-opening of aziridines at the ester bearing carbon, C₂. An important observation from this work is that ring-opening of 1-(Q³)-aziridine-2-carboxylic esters by iodide in the absence of strong acid occurs predominantly at C₂. Enhanced σ*-π* overlap of the aziridine C₂-N σ bond with the ester carbonyl group may encourage nucleophilic attack at this position, stabilised by an interaction between the ester moiety and the quinazolinone ring (resembling that present in the aziridination ts') when these groups are syn during ring-opening. In the case of α-methylene-γ-butyrolactone derived N(Q)-aziridines, exclusive iodide attack at the methylene carbon takes place.

Ring-opening reactions of N(Q³)-aziridine-2-carboxylic acid esters proceed at a faster rate than Q³-substituted aziridines, as the intermediate exocyclic nitrogen anion is stabilised by the electron deficient quinazolinone ring. Ring-opening of N(Q)-2-methyl-2-aziridine-2-carboxylic acid esters is much slower although the CF₃ group as a Q₂ substituent does accelerate the reaction; however conditions were not found where all the aziridine was ring-opened in the absence of samarium(III).

The reactions described in this Chapter have also shown that the regioselectivity of ring-opening may be influenced by co-ordination of the (Q)C=O to samarium(III) chloride. The weakened aziridine C-N σ-bond adjacent to the quinazolinone carbonyl group is then assumed to be favoured for ring-opening.

A combination of these factors will allow methodology to be developed for regioselective ring-opening of aziridines. N-N bond cleavage of these products will access a range of chiral α- and β-amino acids for use as starting materials in stereoselective synthesis of larger molecules.
EXPERIMENTAL
General Experimental

All 250 MHz proton and 62.9 MHz carbon NMR spectra were recorded on a Bruker ARX 250 spectrometer at ambient temperature in deuterated chloroform unless otherwise stated. 400 MHz NMR proton and 75 MHz carbon NMR spectra were recorded on a Bruker DRX 400 spectrometer. Standard mass spectra and accurate mass measurements were recorded on a Kratos Concept 1H spectrometer, the former using electron ionisation at 70 eV. Elemental analysis was carried out by CHN analysis, Wigston, Leicester. Melting points were determined using a Kofler hot block and are uncorrected. Flash chromatography was carried out using silica gel C60 (35-70) or Kieselgel 60 (230-400 mesh) manufactured by Merck & Co.. TLC was conducted on pre-coated silica sheets (60-254) with a 0.2 mm thickness, manufactured by Merck & Co.. IR spectra of crystalline compounds were recorded as solutions in dichloromethane and of liquids as thin films using a Perkin Elmer 298 spectrometer. Optical rotations were determined on a Perkin Elmer 341 Polarimeter at 589nm. All X-ray structure determinations were carried out by Dr J. Fawcett and Dr D. R. Russell at the University of Leicester.

Light petroleum refers to the 60-80°C fraction. Dry tetrahydrofuran (THF) was obtained by distillation from sodium metal in the presence of benzophenone. Dry triethylamine and dichloromethane were obtained by distillation from calcium hydride. Ether refers to diethyl ether, dried with sodium. Organic solvents were dried by methods described by Perrin and Armarego. Routine drying of organic solvents was carried out using magnesium sulphate unless otherwise indicated. Evaporation under reduced pressure was carried out using a Buchi rotary evaporator and a water pump (~ 16mm Hg).

Lead(IV) acetate was purchased (Lancaster) as a solid under acetic acid and was freed from residual acetic acid before use. Titanium(IV) tert-butoxide was purchased from Merck & Co., (L)-tert-leucine from Degussa or kindly donated by Roche and 1.0M solutions of methyl magnesium bromide and samarium diiodide in THF from Aldrich. Argon gas was zero grade. All other reactants were reagent grade unless stated and used as received.
Samples were routinely freed from traces of solvent using an oil pump (~2mm Hg) before carrying out spectroscopic/polarimetry measurements.

**Physical data**

In NMR spectra, chemical shifts expressed in ppm on the δ scale relative to an internal standard (TMS). The following abbreviations are used: s-singlet; d-doublet; t-triplet; q-quartet; m-multiplet; dd; doublet of doublets; ddd; doublet of doublet of doublets; h-heptet; br-broad; Ar-aryl; azir.-aziridine; Ph-phenyl; Q-quinazolinone; J-coupling constant (Hz). Assignments of chemical shifts for $^{13}$C resonances was assisted by DEPT.

Mass spectra were determined in units of mass relative to charge $(m/z)$ with fast atomic bombardment (FAB) ionisation. Except for the molecular ion $\text{MH}^+$, only peaks $>20\%$ of the base peak are given.

IR spectra were measured in units of $\text{cm}^{-1}$ and the following abbreviations used: s-strong, m-medium and w-weak.

Optical rotation values are given in units of $10^1 \text{deg cm}^2 \text{g}^{-1}$.
Experimental relating to Chapter 2
Synthesis of 3-Amino-2-methylquinazolin-4(3H)-one

3-Amino-2-methylquinazolin-4(3H)-one was prepared from methyl anthranilate and acetic anhydride according to the literature procedure and obtained as a colourless solid (73%), mp 147-148°C (from ethanol) (lit. mp 148-149°C).75

Preparation of 3-amino-2-isopropylquinazolin-4(3H)-one

3-Amino-2-isopropylquinazolin-4(3H)-one was prepared according to the literature procedure and obtained as a colourless solid (80%), mp 99-100°C (from ethanol) (lit. mp 101-102°C).128

Preparation of 3-amino-2-trifluoromethylquinazolin-4(3H)-one

3-Amino-2-trifluoromethylquinazolin-4(3H)-one was prepared using a modification of the literature procedure.90 Thus the crude trifluorobenzoxazinone (17.66g), without purification, was dissolved in ethanol (75 cm³) and hydrazine hydrate (3.8g, 0.075 mol) was added dropwise at 0°C and stirred at ambient temperature for 1 h. After evaporation of the solvent under reduced pressure, the residual solid was crystallised from boiling methanol to give 3-amino-2-trifluoromethylquinazolin-4(3H)-one as white crystals (11.06g, 66%), mp 149-151°C (from methanol) (lit. mp 150-151°C). When the trifluorobenzoxazinone above was purified by crystallisation from light petroleum according to the published procedure, the yield of the title compound was only 20%.

Preparation of 3-aminoquinazolin-4(3H)-one

3-Aminoquinazolin-4(3H)-one was prepared according to the literature procedure and obtained as a colourless solid (4.6 g, 26%), mp 207-209°C (lit. mp 210-211°C).147
General procedure A for aziridination of naphthalene with 3-acetoxyamino-
quinazolin-4(3H)-ones

Dry dichloromethane (1 cm$^3$ for each 0.1g 3-aminoquinazolinone) was added to a 25
cm$^3$ round bottom flask, suspended in a dry ice/acetone bath at -12°C and
magnetically stirred. Lead(IV) acetate (LTA, 1.05 mol equiv.) was added to the flask
in one portion. When the LTA had dissolved, the temperature of the bath was lowered
to -20°C. The appropriate 3-aminoquinazolinone (1.0 mol equiv.) was added
continuously in small portions over 10-15 min. at this temperature, stirring
throughout. The temperature of the bath was allowed to rise to -10°C and the solution
filtered into a flask maintained at -10°C, removing the solid lead di-acetate present
(end of general procedure for Q$^n$NHOAc preparation).

To this filtered solution naphthalene (3 mol equiv.), triphenylmethane (20 mg, as
internal standard), and hexamethyldisilazane (HMDS, 3 mol equiv.) were added, the
cooling bath removed and the temperature allowed to reach ambient (~15 min.),
stirring throughout. The reaction mixture was filtered, the filtrate washed with
saturated aqueous sodium hydrogen carbonate solution, dried and the solvent
 evaporated under reduced pressure.
Aziridination of naphthalene with 3-acetoxyamino-2-methyl-4(3H)quinazolinone

General procedure A for aziridination above was followed using LTA (0.796g, 1.79 mmol), 3-amino-2-methyl-4(3H)-quinazolinone (0.3g, 1.71 mmol), naphthalene (0.656g, 5.13 mmol), triphenylmethane (20mg) and HMDS (0.872g, 5.13 mmol) in dichloromethane (6 cm³). Analysis of the NMR spectrum of the crude product shows that the yield of mono-aziridine is 29% (151mg) and of bis aziridine is 4% (36mg) by comparison of the signals at δ 4.35 and 4.21 respectively with that of the internal standard. Flash column chromatography using 2:1 light petroleum-ethyl acetate gave the mono-aziridine 97 as colourless crystals (63mg, 12%), mp 128-131°C (from acetonitrile), Rf 0.44, (Found: M⁺ 301.1215. C₁₉H₁₅N₃O requires M 301.1215; ν_max/cm⁻¹ 2960m, 1680s and 1585s; δ_H 2.72 (3H, s, CH₃), 3.73 (1H, dd, J 7.8 and 4.7, azir. NCH=CH), 4.35 [1H, d, J 7.8, azir. NCH(Ar)], 6.45 [1H, dd, J 9.4 and 4.7, NCHCH=CH], 6.68 [1H, dd, J 9.4, NCHCH=CH], 7.25-7.35 (1H), 7.37-7.55 (3H) and 7.68-7.90 (3H) [4 x H(Ar) and 3 x H(Q)] and 8.23 [1H, d, J 8.0, H-5(Q)]; δ_C 22.7 (CH₃), 50.5, 52.9 (2 x NCH), 120.4 [CCO(Q)], 121.4, 125.8, 126.4, 126.5, 127.6, 128.6, 128.7, 129.0, 130.4 [4 x CH(Ar), 3 x CH(Q), C=C], 132.0, 132.1, 133.8 [2 x C and CH(Q)], 146.0 [CN=C(Q)] and 154.0, 159.5 [C=N(Q), CO(Q)]; m/z(%) 301 (M⁺, 35), 175 (23), 160 (28), 146 (20), 142 (27), 141(23), 128 (100) and 115 (22).

Further elution with the same solvent gave a trace of bis-aziridine 98 (18mg, 2%) as a colourless oil. R_f 0.28. (Found: M⁺ 474.1804. C₂₈H₂₂N₆O₂ requires M 474.1804; ν_max/cm⁻¹ 2980m. 1675s and 1590m; δ_H 2.84 (6H, s, 2 x CH₃), 3.68 (2H, d, J 8.0, azir. NCHCHN), 4.21 [2H, d, J 8.0, 2 x azir. NCH(Ar)], 7.10-7.90 [10H, m, 4 x CH(Ar) and 6 x CH(Q)] and 8.32 [2H, d, J 8.0, 2 x H-5(Q)]; m/z(%) 474 (M⁺, 51), 301 (88), 175 (48), 160 (22) and 128 (100).
Aziridination of naphthalene with 3-acetoxyamino-2-ethyl-4(3H)-quinazolinone

Aziridination of naphthalene with 3-acetoxyamino-2-ethyl-4(3H)-quinazolinone

General aziridination method A was followed using LTA (0.740g, 1.66 mmol), 3-amino-2-ethylquinazolin-4(3f/>one (0.300g, 1.59 mmol), naphthalene (0.611g, 4.77 mmol), triphenylmethane (20mg) and HMDS (0.769g, 4.77 mmol) in dichloromethane (6 cm³). Analysis of the NMR spectrum of the crude product shows that the yield of mono-aziridine was 28% (112mg) and of bis-aziridine was 19% (130mg) by comparison of signals at δ 4.39 and 4.22 respectively with those of the internal standard. Flash column chromatography using 2:1 light petroleum-ethyl acetate gave mono-aziridine 100 as colourless crystals (80mg, 20%), mp 121-123°C, Rf 0.43. (Found: C, 74.2; H, 5.5; N, 13.0%. C₂₀H₁₇N₃O requires C, 74.0; H, 5.6; N, 13.0%); νmax/cm⁻¹ 2980m, 1680s and 1590s; δH 1.42 (3H, t, J 7.0, CH₃), 3.10 (2H, m, CH₂), 3.81 (1H, dd, J 7.6 and 4.5, azir. NCHCH=CH), 4.39 [1H, d, J 7.6, azir. NCH(Ar)], 6.48 (1H, dd, J 10.0 and 4.5, NCHCH=CH), 6.72 (1H, d, J 10.0, NCHCH=CH₂), 7.18-7.81 [7H, m, 4 x CH(Ar) and 3 x CH(Q)] and 8.24 [1H, d, J 8.0, H-5(Q)]; δC 11.2 (CH₃), 28.1 (CH₂), 50.8, 53.1 (2 x NCH), 120.8 [C=O(Q)], 121.8, 123.6, 126.0, 126.1, 126.4, 127.6, 129.1, 132.6 [6 x CH(Ar), C=CH], 135.1, 141.1 (2 x C), 146.5 [CN=C(Q)] and 158.2, 160.1 [C=N(Q), CO(Q)]; m/z (%) 315 (M⁺,53), 174 (86), 173 (100), 143 (66), 142 (34), 141 (28), 128 (100), 119 (33) and 115 (41).

Further elution gave bis-aziridine 101 as colourless crystals (75mg, 11%), mp 217-220°C (from light petroleum-ethyl acetate), Rf 0.36. (Found: M⁺ 502.2117. C₂₆H₂₆N₆O₂ requires M 502.2118); νmax/cm⁻¹ 1675s and 1600s; δH 1.40 (6H, t, J 7.5, CH₃), 2.85 (4H, q, J 7.5, CH₂), 3.77 (2H, d, J 8.5, azir. NCHCHN), 4.22 [2H, d, J 8.5, 2 x azir. NCH(Ar)], 7.1-7.8 [10H, m, 4 x H(Ar), 6 x H(Q)] and 8.33 [2H, m, 2 x H-
Aziridination of naphthalene with 3-acetoxyamino-2-isopropylquinazolin-4(3H)-one

![Diagram of reaction](image)

General procedure A given earlier was followed using LTA (0.688g, 1.55 mmol), 3-amino-2-isopropylquinazolin-4(3H)-one (0.301g, 1.48 mmol), naphthalene (0.568g, 4.42 mmol), triphenylmethane (20mg) and HMDS (0.713g, 4.42 mmol) in dichloromethane (6 cm³). The yield of mono-aziridine (30%,113mg) and bis-aziridine (33%, 127mg) was calculated by comparison of signals at δ 4.41 and 4.18 with those of the internal standard by NMR analysis of the crude reaction product.

Flash column chromatography using 2:1 light petroleum-ethyl acetate gave mono-aziridine 102 as colourless crystals (75mg, 20%), mp 128-129°C (from ethyl acetate-light petroleum) (lit. mp 128-129°C)¹⁴⁸, Rf 0.49. (Found: M⁺ 329.1528. C₂₁H₁₉N₃O requires M 329.1528); ν max/cm⁻¹ 2970m, 1670s and 1580s; δ H 1.46, 1.50 (6H, 2 x d, J 6.7, CH₃(CHCH₃), 3.75 (1H, h, J 6.7, CH₃CHCH₃), 3.86 (1H, dd, J 7.5, 4.6, azir. NCHC≡C), 4.41 [1H, d, J 7.5, azir. NCH(Ar)], 6.55 (1H, dd, J 9.6, 4.6, NCHCH=CH), 6.78 (1H, d, J 9.6, NCHCH=CH), 7.25-7.37 [1H, m, CH(Ar)], 7.39-7.58 [3H, m, 3 x CH(Q)], 7.68-7.80 [2H, m, 2 x CH(Ar)], 7.83-7.90 [1H, m, CH(Ar)] and 8.32 [1H, dd, J 7.7 and 0.9, H-5(Q)]; δ c 21.5, 21.6 (2 x CH₃), 31.5 (CH₃CHCH₃), 50.8, 53.2 (2 x NCH), 121.7 [CCO(Q)], 121.0, 121.1,126.4, 126.7, 126.9, 127.2 [4 x CH(Ar)/Q, C≡C], 127.4 (C), 129.2 [CH(Ar)/Q], 129.5, 130.5, 132.6, 135.0 [C and 3 x
Further elution gave bis-aziridine 103 as colourless crystals (62mg, 16%), mp 222-224°C (from ethyl acetate-light petroleum)(lit. mp 223-224°C), $^{148}$ Rf 0.35. (Found: M$^+$ 530.2431. C$_{32}$H$_{30}$N$_6$O requires M 530.2431); $\nu_{max}$/cm$^{-1}$ 1675s and 1595s; $\delta_H$ 1.28, 1.32 (12H, 2 x d, $J$ 6.7, 2 x CH$_3$CH$_3$), 3.59 (2H, h, $J$ 6.7, 2 x CH$_3$CH$_3$), 3.74 (2H, d, $J$ 8.3, azir. NCHCHN), 4.18 [2H, d, J 8.3, 2 x azir. NCH(Ar)], 7.28-7.39 [4H, m, 4 x CH(Ar)], 7.52-7.69 [6H, m, 6 x CH(Q)] and 8.11-8.27 [2H, m, 2 x H-5(Q)]; $\delta_C$ 21.5, 21.6 (4 x CH$_3$), 31.6 (2 x CH$_3$CH$_3$), 46.6, 47.8 (4 x NCH), 121.6 [2 x CCO(Q)], 126.7, 126.8, 127.5, 129.7 [8 x CH(Ar)/Q], 130.8 (C=C), 131.6, 134.8 [4 x CH(Ar)/Q], 146.6 [2 x CN=C(Q)] and 160.6, 161.3 [2 x CN(Q), 2 x CO(Q)]; m/z(%) 530 (M$^+$,27), 329 (59), 201 (100), 187 (38), 142 (60) and 128 (77).

**Aziridination of naphthalene with 3-acetoxyaminoquinazolin-4(3H)-one**

![Diagram](image_url)

General aziridination procedure B: LTA (144mg, 0.32 mmol) and 3-aminoquinazlin-4(3H)-one (50mg, 0.31 mmol) were added continuously and alternately in small portions to a stirred solution of dichloromethane (1 cm$^3$) containing naphthalene (119mg, 0.931 mmol), triphenylmethane (10mg) and HMDS (150mg, 0.931 mmol) maintained at -10°C. The cooling bath was removed, the mixture allowed to warm to room temperature and filtered, the filtrate washed with saturated aqueous sodium hydrogen carbonate solution, dried and the solvent evaporated under reduced pressure to give the crude product.
The yield of mono-aziridine 105 was 5% (29 mg) by comparison of the signals at δ 4.31 and 4.53 with those of the internal standard in the crude reaction product using NMR spectroscopy. Flash column chromatography using light petroleum-ethyl acetate (2:1) gave mono-aziridine 105 as colourless crystals (12 mg, 2%), Rf 0.23. (Found: M⁺ 287.1059. C₁₂H₁₀N₆O requires M 287.1059); νmax/cm⁻¹ 2960 m. 1665 s and 1595 s; δH (1:1 mixture of N-invertomers) 3.92 (1H, dd, J 7.5, 4.7, azir. NCH=C), 4.22 (1H, dd, J 5.0, 5.0, azir. NCH=C), 4.31 [1H, d, J 7.5, azir. NCH(Ar)], 4.53 [1H, d, J 5.0, azir. NCH(Ar)], 6.30 (1H, dd, J 9.4, 5.0, NCHCH=CH), 6.45 (1H, d, J 9.4, NCHCH=CH), 6.48 (1H, dd, J 9.8, 4.7, NCHCH=CH), 6.71 (1H, d, J 9.8, NCHCH=CH), 7.09 [1H, d, J 7.2, H-6(Q)], 7.15-7.85 [13H, m, 8 x CH(Ar) + 5 x CH(Q)], 8.15 [1H, d, J 6.9, H-5(Q)] and 8.33 [1H, m, H-5(Q)]; m/z(%) 287 (M⁺29), 159 (100), 145 (88) and 128 (79).

Further aziridination of mono-aziridine 102 using Q₂NHOAc

![Chemical structure](image)

General aziridination procedure A was followed using LTA (57 mg, 0.128 mmol), 3-amino-2-ethylquinazolin-4(3H)-one (25 mg, 0.126 mmol), mono-aziridine 102 (20 mg, 0.061 mmol) and HMDS (59 mg, 0.36 mmol) in dichloromethane (1 cm³). Column chromatography (3:1 light petroleum-ethyl acetate) of the crude product gave bis-aziridine 106 (13 mg, 42%) as a colourless oil, Rf 0.35. (Found: M⁺ 504.2274. C₃₁H₂₈N₆O₂ requires M 504.2274); νmax/cm⁻¹ 1680 s and 1595 s; δH 1.30 (3H, d, J 6.6, CH₃CHCH₃), 1.33 (3H, s, CH₂CH₃), 1.30 (3H, d, J 6.6, CH₃CHCH₃), 3.05 (2H, m, CH₂CH₃), 3.63 (1H, h, J 6.6, CH₃CHCH₃), 3.74 (2H, dd, J 7.8 and 1.3, 2 x azir. NCHCHN), 4.13 [1H, dd, J 7.8 and 1.3, azir. NCH(Ar)], 4.26 [1H, dd, J 7.8 and 1.3, azir. NCH(Ar)], 7.35-7.50 [4H, m, 4 x CH(Ar)], 7.55-7.80 [6H, m, 6 x CH(Q)] and
8.25 [2H, br d, 2 x H-5(Q)]; m/z(%) 504 (M+21), 315 (41), 303 (29), 201 (52), 189 (30), 188 (26), 187 (39), 174 (22) and 128 (100).

**General procedure C for aziridination via (3,4-dihydro-4-oxoquinazolin-3-yl) nitrenes QN:**

A solution of N-acetoxyaminoquinazolinone, freed from lead diacetate was prepared from the appropriate 3-aminoquinazolinone following general procedure A. Following the procedure of E. Barker, trialkylamine (10 mol equiv.) was added and the solution set aside at -20°C for 10 min. before addition of the alkene (naphthalene). After warming to ambient temperature, work up was carried out as in general procedure A.

**Aziridination via a nitrene intermediate in the presence of triethylamine**

![NMR spectrum](image)

General procedure C was followed LTA (0.687g, 1.55 mmol), 3-amino-2-isopropylquinazolin-4(3H)-one (0.3g, 1.47 mmol), naphthalene (0.565g, 4.43 mmol), triphenylmethane (20mg) and triethylamine (1.49g, 14.7 mmol) in dichloromethane (6 cm³). Analysis by NMR of the crude product showed that mono-aziridine 102 (19%, 88mg) and bis-aziridine 103 (5%, 22mg) were present by comparison with the internal standard. Another product was the imine 107, present in 20% yield (Rf 0.31) mp. 60-61°C (from ethanol)(lit. mp 60-62°C).
Aziridination via a nitrone intermediate in the presence of trimethylamine

General procedure C was followed using the same quantities of reagents used in the previous experiment except that trimethylamine (1.18g, 14.7 mmol) replaced triethylamine. The NMR spectrum of the crude product showed that mono-aziridine 102 (10%) and bis-aziridine 103 (2%) were present by comparison of the internal standard with the same signals used previously (see above).

Aziridination of naphthalene with 3-acetoxyamino-2-(1-hydroxy-2,2-dimethylprop-1-yl)-quinazolin-4(3H)-one

General aziridination procedure A was followed using LTA (1.116g, 2.56 mmol), 3-amino-2-(1-hydroxy-2,2-dimethylprop-1-yl)-quinazolin-4(3H)-one (0.600g, 2.42 mmol), naphthalene (0.310g, 2.42 mmol) and HMDS (1.162g, 7.26 mmol) in dichloromethane (6 cm³) but omitting the triphenylmethane. The crude product was dissolved in ethanol and cooled in ice to give bis-aziridine 108 as a colourless crystalline solid (53mg, 70%), mp 221-222°C (from acetonitrile). [α]₀ +131.4 (c=1.0, EtOH); (Found: M⁺ 619.3033. C₃₆H₃₈N₆O₄ requires M⁺ 619.3033); υₘₐₓ/cm⁻¹ 3450w, 1665s and 1580m; δH 1.87 [18H, s, 2 x C(CH₃)₃], 3.55 (2H, d, J 10.0, 2 x CHO), 3.72 (2H, d, J 7.5, azir. NCHCHN), 4.60 [2H, d, J 7.5, 2 x azir. NCH(Ar)], 4.96 (2H, d, J 10.0, 2 x CHO), 7.38-7.55 (4H, m) and 7.62-7.87 (6H, m), [6 x CH(Q), 4 x CH(Ar)] and 8.33 [2H, d, J 9.5, 2 x H-5(Q)]; δC (75 MHz) 26.3 [2 x (CH₃)₃], 38.5 [2 x C(CH₃)₃], 48.0, 48.3 (4 x NCH), 75.0 (2 x CHO), 121.9 [2 x CCO(Q)], 127.1, 127.4, 129.7 [6 x CH(Ar)/Q], 130.8 (2 x C), 131.6, 134.5 [4 x CH(Ar)/Q], 145.2 [2 x
CN=C(Q) and 157.7, 159.7 [2 x C=N(Q), 2 x CO(Q)]; m/z(%) 619 (MH\(^+\),72), 374 (52), 245 (66), 231 (38) and 128 (100).

Bis-aziridine 108 was first prepared by W. Gattrell in Leicester but its characterisation was not reported.

**Aziridination of naphthalene with 3-acetoxyamino-2-trifluoromethyl-4(3H)-quinazolinone**

![Chemical structure of 3-acetoxyamino-2-trifluoromethyl-4(3H)-quinazolinone](image)

General aziridination procedure A was followed using LTA (0.607g, 1.37 mmol), 3-amino-2-trifluoromethyl-quinazolin-4(3H)-one (0.300g, 1.31 mmol), naphthalene (0.506g, 3.92 mmol), triphenylmethane (20mg) and HMDS (0.632g, 3.92 mmol) in dichloromethane (6 cm³). The yield of mono-aziridine 111 was 38% (118mg) from comparison from the signal at δ 4.25 with that of the internal standard in the NMR spectrum of the crude reaction product.

Flash column chromatography using 2:1 light petroleum-ethyl acetate gave mono-aziridine 111 as colourless crystals (16mg, 5%), mp 138-139°C, R\(_f\) 0.44. (Found: C, 64.0; H, 3.55; N, 11.8%. C\(_{10}\)H\(_{12}\)N\(_3\)F\(_3\)O requires C, 64.2, H, 3.4; N, 11.8%); \(\nu_{max}/\text{cm}^{-1}\) 1685s and 1600s; δ\(_H\) 4.25 (1H, dd, J 7.8, 4.4, azir. NCHC=C), 4.82 [1H, d, J 7.8, azir. NCH(Ar)], 6.32 (1H, dd, J 9.4, 4.4, NCHCH=CH), 6.66 (1H, d, J 9.4, NCHCH=CH), 7.15-7.28 [1H, m, H-6(Q)], 7.30-7.42 (2H, m), 7.60-7.70 (1H, m), 7.72-7.85 (3H, m)[4 x CH(Ar), 3 x CH(Q)] and 8.31 [1H, d, J 9.0, H-5(Ar)]; m/z(%) 355 (M\(^+\),12), 214 (20), 145 (24), 142 (59), 141 (100), 128 (45), 115 (52), 90 (25) and 76 (27).
Further aziridination of mono-aziridine 111 using $\text{Q}^3\text{NHOAc}$

\[
\text{Q}^3\text{NHOAc} \quad 71, \\
\text{HMDS, CH}_2\text{Cl}_2 \\
36\%
\]

General aziridination procedure A was followed using LTA (46mg, 0.11mmol), 3-amino-2-isopropylquinazolin-4(3H)-one (20mg, 0.10mmol), mono-aziridine 111 (36mg, 0.10mmol) and HMDS (48mg, 0.30mmol) in dichloromethane (0.5 cm$^3$). Column chromatography of the crude product (2:1 light petroleum-ethyl acetate) gave bis-aziridine 112 (20mg, 36%) as a colourless oil, $R_f$ 0.39. (Found: $M^+$ 556.1819. $C_{30}H_{23}F_3N_6O_2$ requires $M^+$ 556.1819); $\nu_{\text{max/cm}^{-1}}$ 1685s and 1600s; $\delta_H$ 1.25 (6H, m, $CH_3CHCH_3$), 3.61 (1H, h, $J$ 6.0, $CH_3CHCH_3$), 3.66 [1H, d, $J$ 7.8, azir. NCH(Ar)], 4.01 (1H, dd, $J$ 7.8, 1.6, azir. NCHCH), 4.55 (1H, d, $J$ 7.2, azir. NCHCH), 4.81 [1H, dd, $J$ 7.2, azir. NCH(Ar)], 7.00-7.45 [6H, m, 6 x CH(Q)], 7.50 [4H, m, 4 x CH(Ar)] and 8.24 [2H, d, $J$ 7.6, 2 x H-5(Q)]; $m/z$ (%) 556 (M$^+$,26), 355 (28), 329 (31), 227 (41), 213 (38), 201 (41), 188 (21), 187 (56) and 128 (100).

Aziridination of indene with 3-acetoxymono-2-trifluoromethylquinazolin-4(3H)-one

General aziridination procedure A was followed using LTA (609mg, 1.37 mmol), 3-amino-2-trifloromethylquinazolin-4(3H)-one (300mg, 1.31 mmol), indene (456mg, 3.93 mmol), triphenylmethane (20mg) and HMDS (634mg, 3.93 mmol) in dichloromethane (6 cm$^3$). The NMR spectrum of the crude product showed that 59%
(241mg) of aziridine 113 was present from comparison of the signal at δ 4.29 with that of the internal standard.

Flash column chromatography (1:1 light petroleum-ethyl acetate) gave indene (Rf 0.88) followed by aziridine 113 (Rf 0.70) as colourless crystals (191mg, 43%) mp 159-161°C. (Found: C, 62.7; H, 3.6; N, 12.2%. C_{18}H_{12}ON_{3}F_{3} requires C, 62.9; H, 3.5; N, 12.2%); ν max/cm⁻¹ 1690s and 1600m; δ H 3.28 (1H, dd, J 18.0 and 5.0, CHH), 3.45 (1H, d, J 18.0, CHH), 4.29 (1H, dd, J 5.5 and 5.0, azir. NCHCH₂), 4.75 [1H, d, J 5.5, azir. NCH(Ar)], 7.20-7.30 [3H, m, 2 x CH(Ar), H-6(Q)], 7.54-7.68 [2H, m, H-7 and H-8(Q), 7.75-7.85 [2H, m, 2 x CH(Ar)] and 8.27 [1H, d, J 8.0, H-5(Q)]; m/z(%) 343 (M⁺,6), 214 (10), 130 (32) and 128 (100).

Aziridination of 3-methyl-1H-indene with 3-amino-2-trifluoromethylquinazolin-4(3H)-one

[Chemical structure image]

3-Methyl-1H-indene was prepared by the literature method¹³¹ and obtained as a colourless liquid (68%) after Kugelrohr distillation. δ H 2.11 (3H, s, CH₃), 3.25 (2H, br s, CH₂), 6.10 (1H, br s, C=CHCH₂), 7.05-7.32 [3H, m, 3 x CH(Ar)] and 7.41 [1H, d, J 8.0, CH(Ar)].

General aziridination procedure A was followed using LTA (0.406g, 0.916 mmol), 3-amino-2-trifluoromethylquinazolin-4(3H)-one (0.200g, 0.873 mmol), 3-methyl-1H-indene (0.341g, 2.62 mmol), triphenylmethane (20mg) and HMDS (0.422g, 2.62 mmol) in dichloromethane (4 cm³). Flash column chromatography of the crude product using 2:1 light petroleum-ethyl acetate first eluted indene (Rf 0.69) then aziridine 114 (Rf 0.42), which crystallised from ethyl acetate-light petroleum as a colourless solid (102mg, 32%), mp 111-112°C. (Found: M⁺ 357.1089. C_{19}H_{14}N_{3}F_{3}O₃)}
requires $M$ 357.1088; $\nu_{\text{max/cm}}$ 2970m, 1665s and 1590s; $\delta_{\text{H}}$(400 MHz)(2:1 mixture of $N$-inverteders) major $N$-invertedomer - 1.62 (3H, s, CH$_3$), 3.34 (1H, dd, $J$ 17.3, 4.8, CHH), 3.42 (1H, d, $J$ 17.3, CHH), 5.23 (1H, d, $J$ 4.8, azir. NCH), 7.29 [1H, m, CH(Ar)], 7.40 [1H, dd, $J$ 7.5, 1.5, CH(Ar)], 7.64 [2H, m, CH(Ar) and H-6(Q)], 7.73 [1H, d, $J$ 7.5, CH(Ar)], 7.82 [2H, m, H-7 and H-8(Q)] and 8.30 [1H, d, $J$ 8.2, H-5(Q)]; minor $N$-invertedomer (observable signals) - 2.05 (3H, s, CH$_3$), 2.90 (1H, br d, $J$ 19.3, CHH), 3.24 (1H, dd, $J$ 19.3, 4.8, CHH), 3.70 (1H, d, $J$ 4.8, azir. NCH), 6.69 [1H, d, $J$ 7.5, CH(Ar)], 6.91 [1H, dd, $J$ 7.5, 7.5, CH(Ar)], 7.03 [1H, dd, $J$ 7.5, 7.5, CH(Ar)], 7.37 [1H, dd, $J$ 7.0, 7.0, H-6(Q)], 7.58 [1H, d, $J$ 7.5, CH(Ar)], 7.63 [1H, d, $J$ 8.0, H-8(Q)] and 7.66-7.70 [2H, m, H-5 and H-7(Q)]; m/z(%) 357 (M$^+$,13), 144 (41), 143 (100), 129 (21), 128 (57), 116 (31) and 115 (29).

Aziridination of methyl acrylate with 3-amino-2-trifluoromethylquinazolin-4(3H)-one

\[
\begin{align*}
\text{F}_3\text{C} & \quad \text{N} \quad \text{N} \\
& \quad \text{\text{OAc}} \\
\text{H} & \quad \text{\text{CO}_2\text{Me}} \\
\text{CH}_2\text{Cl}_2 & \quad 44\% \\
\end{align*}
\]

Methyl 1-(2-trifluoromethyl-3,4-dihydro-4-oxoquinazolin-3-yl)aziridine-2-carboxylate 115 was prepared by the literature method$^{96}$ and obtained as a colourless solid (44%), mp 105-107°C (lit. mp 107-108°C)
Aziridination of methyl methacrylate with 3-acetoxyamino-2-trifluoromethyl-quinazolin-4(3H)-one

General aziridination procedure A was followed using LTA (2.05g, 4.62 mmol), 3-amino-2-trifluoromethylquinazolin-4(3H)-one (1.00g, 4.40 mmol) and methyl methacrylate (0.88g, 8.80 mmol) in dichloromethane (10 cm³) but omitting HMDS and triphenylmethane. The crude product was dissolved in ethanol, the colourless crystals formed from the solution on cooling were separated and dried giving aziridine 116 (0.576g, 40%) as a colourless solid, mp 99-101°C. (Found: M+ 327.0830. C₁₄H₁₂N₃F₃O requires M 327.0830; νmax/cm⁻¹ 1685s, 1605m and 1470m; δₚH(3:1 mixture of N-invertomers) major N-invertomer - 1.65 (3H, s, CH₃), 2.76 (1H, br s, azir. NCH), 3.40 (1H, br s, azir. NCH), 3.49 (3H, s, CO₂Me), 7.43-7.55 [1H, m, H-6(Q)], 7.65-7.80 [2H, m, H-7 and H-8(Q)] and 8.10 [1H, d, J 8.0, CH-5(Q)]; δC 18.9 (CH₃), 48.0 (C), 53.2 (CO₂CH₃), 120.6 (CF₃), 122.6 [CCO(Q)], 126.8, 128.7, 129.5, 134.8 [4 x CH(Q)], 144.0 [CN=C(Q)] and 160.0, 169.2 [CN(Q), CO(Q)] - (CO₂CH₃ not visible); minor N-invertomer (observable signals) - δₚH 1.47 (3H, s, CH₃), 3.12 (1H, br s, azir. NCH), 3.70 (3H, s, CO₂Me), 4.36 (1H, br s, azir. NCH), 7.43-7.55 [1H, m, H-6(Q)], 7.65-7.80 [2H, m, H-7 and H-8(Q)] and 8.20 [1H, d, J 8.0, H-5(Q)]; δC 13.3 (CH₃), 43.0 (CH₂), 46.5 (C), 53.1 (CO₂CH₃), 116.2 (CF₃), 120.5 [CCO(Q)], 123.3 [CN=C(Q)], 127.2, 128.9, 129.1, 135.2 [4 x CH(Q)] and 161.6, 170.9 [CN(Q), CO(Q)] - (CO₂CH₃ not visible); m/z(%) 327 (45), 240 (81), 197 (22), 171 (27), 145 (25), 130 (39), 114 (46), 104 (82), 102 (24), 90 (22) and 76 (61).
Aziridination of naphthalene with QNHOAc: low temperature NMR experiments.

The following procedure was carried out so that the progress of the aziridination of naphthalene could be monitored by NMR. A lead di-acetate-free solution of the 3-acetoxyaminoquinazolinone Q*NHOAc at -20°C was prepared in CDCl₃ (2 cm³) using the general procedure A in a “cool box” which was pre-cooled to -35°C using solid carbon dioxide. This solution was washed briefly with ice-cold saturated aqueous sodium hydrogen carbonate before addition of naphthalene and HMDS (both 3 mol equiv.). A small quantity of this solution was transferred to an NMR tube maintained at -35°C in a Dewar flask and subsequently without warming, to the probe of a Bruker DRX 400 spectrometer with the probe temperature initially -25°C. Spectra were obtained at 5°C intervals.

Aziridination at low temperature with 3-acetoxyamino-2-methylquinazolin-4(3H)-one

The method above was followed LTA (133mg, 0.30mmol), 3-amino-2-methylquinazolin-4(3H)-one (50mg, 0.285mmol), naphthalene (108mg, 0.86mmol) and HMDS (0.138mg, 0.86mmol) in deuterochloroform (1 cm³). Q¹NHOAc exhibited a singlet at δ~11(NH). Signals belonging to the two N-N bond rotamers of the endo-mono-aziridine first appeared at -5°C with (observable signals); major rotamer: δ 4.40 (1H, dd, J 6.1 and 4.7, azir. CHC=C), 4.48 [1H, d, J 6.1, azir. CH(Ar)], 6.36 [1H, dd, J 9.9 and 4.7, CH=CH(Ar)] and 6.40 [1H, d, J 9.9, CH=CH(Ar)]; minor rotamer: δ 4.04 (1H, dd, J 5.4 and 4.6, azir. CHC=C), 4.86 [1H, d, J 5.4, azir. CH(Ar)], 6.17 [1H, dd, J 9.3 and 4.6, CH=CH(Ar)] and 6.66 [1H, d, J 9.3, CH=CH(Ar)]. The rotamers were present in a 3:1 ratio which did not change measurably as the signals from both rotamers decreased in intensity (see below).

Slow growth of signals from bis-aziridine 98 at δ3.68 (2H, d, J 8.0, azir. NCHCHN) and 4.21 [2H, d, J 8.0, 2 x azir. NCH(Ar)] were observed at -5°C. At 5°C, the signal at δ~11 from Q¹NHOAc had decreased to 10% of its original intensity and signals from exo-mono-aziridine first appeared at δ3.73 (1H, dd, J 7.8 and 4.7, azir. NCHCH=CH), 4.35 [1H, d, J 7.8, azir. NCH(Ar)], 6.45 (1H, dd, J 9.4 and 4.7,
NCH\(\text{CH} = \text{CH}\) and 6.68 (1H, d, \(J\ 9.4\), NCH\(\text{CH} = \text{CH}\)). By 10°C all of the \(\text{Q}^1\)NHOAc had reacted and some \text{endo}-\text{mono-aziridine} remained; there was no increase in \text{bis-aziridine} concentration. At room temperature all of the \text{endo}-\text{mono-aziridine} had inverted to the \text{exo}-form.

**Aziridination at low temperature with 3-acetoxyamino-2-isopropylquinazolin-4(3\(H\))-one**

The method above was followed using LTA (114mg, 0.26mmol), 3-amino-2-isopropylquinazolin-4(3\(H\))-one (50mg, 0.24mmol), naphthalene (95mg, 0.74mmol) and HMDS (119mg, 0.74mmol) in deuterochloroform (1 cm\(^3\)).

Signals belonging to two rotamers of the \text{endo}-\text{mono-aziridine} appeared at -10°C together with those of \text{bis-aziridine} with (observable signals):

- Major rotamer: \(\delta\)4.39 (1H, dd, \(J\ 7.2\) and \(5.3\), azir. CH\(\text{C}=\text{C}\)), 4.48 (1H, d, \(J\ 7.2\), azir. \text{CH} (Ar)), 6.25 [1H, d, \(J\ 9.5\), \text{CH} = \text{CH}(\text{Ar})] and 6.35 [1H, dd, \(J\ 9.5\) and \(5.3\), \text{CH} = \text{CH}(\text{Ar})]; minor rotamer: \(\delta\)4.07 (dd, \(J\ 7.45\) and \(4.9\), azir. CH\(\text{C}=\text{C}\)), 4.87 [1H, d, \(J\ 7.45\), azir. \text{CH} (Ar)], 6.10 [1H, dd, \(J\ 9.3\) and \(4.9\), \text{CH} = \text{CH}(\text{Ar})] and 6.63 [1H, d, \(J\ 9.3\), \text{CH} = \text{CH}(\text{Ar})]; \text{bis-aziridine}: \(\delta\)3.74 (2H, d, \(J\ 8.3\), azir. NCHCH\(\text{N}\)) and 4.18 [2H, d, \(J\ 8.3\), 2 x azir. NCH(\text{Ar})]. The rotamers were present in a 5:1 ratio which did not change as the signals from both rotamers decreased in intensity (see below);

At 5°C, signals from the \text{exo}-\text{mono-aziridine} at \(\delta\)3.86 (1H, dd, \(J\ 7.5\), \(4.6\), azir. NCH\(\text{C}=\text{C}\)), 4.41 (1H, d, \(J\ 7.5\), azir. NCH), 6.55 (1H, dd, \(J\ 9.6\), \(4.6\), NCH\(\text{CH} = \text{CH}\)) and 6.78 (1H, d, \(J\ 9.6\), NCH\(\text{CH} = \text{CH}\)) began to form at the expense of those of the \text{endo} form. By 20°C, the concentration of \text{bis-aziridine} had reached a maximum and all of the \text{endo} product had inverted to the \text{exo} -\text{mono-aziridine}.

**Aziridination at low temperature with 3-acetoxyamino-2-quinazolin-4(3\(H\))-one**

The method above was followed using LTA (144mg, 0.32mmol), 3-amino-2-quinazolin-4(3\(H\))-one (50mg, 0.31mmol), naphthalene (119mg, 0.93mmol) and HMDS (150mg, 0.93mmol) in deuterochloroform (1 cm\(^3\)).

Signals from the \text{endo}-invertomer formed at -20°C as a single \text{N-N} bond rotamer at \(\delta\)4.22 (1H, dd, \(J\ 5.0\), 5.0, azir. NCH\(\text{C}=\text{C}\)), 4.53 [1H, d, \(J\ 5.0\), azir. NCH(\text{Ar})], 6.30
(1H, dd, J 9.4, 5.0, NCHCH=CH) and 6.45 (1H, d, J 9.4, NCHCH=CH). The Q^tNHAc singlet at $\delta$=11 had disappeared by 0°C: conversion to $N$-exo-invertomer of the mono-aziridine was observed at 10°C by the appearance of signals at $\delta$3.92 (1H, dd, J 7.5, 4.7, azir. NCH=C), 4.31 [1H, d, J 7.5, azir. NCH(Ar)], 6.48 (1H, dd, J 9.8, 4.7, NCHCH=CH) and 6.71 (1H, d, J 9.8, NCHCH=CH) and at room temperature, a 1:1 ratio of N-invertomers was present. No signals attributable to bis-aziridine were evident in the NMR spectra.

Aziridination at low temperature with 3-acetoxyaminoo-2-trifluoromethylquinazolin-4(3H)-one

The method above was followed using LTA (101mg, 0.23mmol), 3-amino-2-trifluoromethylquinazolin-4(3H)-one (50mg, 0.21mmol), naphthalene (84mg, 0.65mmol) and HMDS (106mg, 0.65mmol) in deuterochloroform (1 cm$^3$). Signals from the presumed exo-$N$-invertomer of aziridine appeared slowly at $\delta$4.25 (1H, dd, J 7.8, 4.4, azir. NCH=C), 4.82 [1H, d, J 7.8, azir. NCH(Ar)], 6.32 (1H, dd, J 9.4, 4.4, NCHCH=CH) and 6.66 (1H, d, J 9.4, NCHCH=CH) only when the temperature was raised to 20°C: no signals assignable either to the endo-$N$-invertomer or to the bis-aziridine were evident.

Aziridination of 1-methyl-1H-indene at low temperature with 3-acetoxyaminoo-2-trifluoromethylquinazolin-4(3H)-one

The method above was followed using LTA (101mg, 0.24mmol), 3-amino-2-trifluoromethylquinazolin-4(3H)-one (50mg, 0.22mmol), 1-methyl-1H-indene (76mg, 0.66mmol) and HMDS (106mg, 0.66mmol) in deuterochloroform (1 cm$^3$). Signals from the major and minor aziridine $N$-invertomers first appeared at 20°C in the same ratio (1:1) as observed for the crystalline aziridine 114 at $\delta$3.34 (1H, dd, J 17.3, 4.8, CHH), 3.42 (1H, d, J 17.3, CHH), 5.23 (1H, d, J 4.8, azir. NCH) for the major $N$-invertomer and at $\delta$2.90 (1H, br d, J 19.3, CHH), 3.24 (1H, dd, J 19.3, 4.8, CHH), 3.70 (1H, d, J 4.8, azir. NCH) for the minor $N$-invertomer.
Experimental relating to Chapter 3
General procedure D for aziridination of alkenes in the presence of titanium(IV) tert-butoxide

Following the procedure of W. Gattrell, powdered LTA (1.05 eq.) was added in one portion to dry dichloromethane (1 cm³/100 mg NAQ⁶) stirred at -12°C (bath temperature). After dissolution the reaction mixture was cooled to -20°C and NAQ⁶ (1 eq.) added in small portions over 10-15 min. Stirring was continued for 5 min. before filtering through a cotton wool plug into a stirred solution of titanium(IV) tert-butoxide (TTB)(2.1 eq.) held at -20°C. After stirring at this temperature for 2 min. the alkene (2 eq.) was added and the reaction mixture allowed to reach ambient by removal of the cooling bath.

Saturated sodium hydrogen carbonate solution was added to the vigorously stirred reaction mixture and a gelatinous precipitate formed immediately. The solution was filtered through Celite and the organic layer of the filtrate separated, washed with brine, dried, and the solvent evaporated under reduced pressure to give the crude product.

Aziridination of 1,3-pentadiene with Q⁶NHOAc

General aziridination procedure D was followed in this reaction using NAQ⁶ (1.00 g, 4.00 mmol), LTA (1.98 g, 4.50 mmol), 1,3-pentadiene (0.40 g, 6.00 mmol) and TTB (2.72 g, 8.20 mmol) in dichloromethane (12 cm³). Work up gave the crude product as a yellow solid. Column chromatography (3:1 light petroleum-ethyl acetate) gave aziridine 119 (876 mg, 70%) as a pale yellow solid, (Rf 0.59) mp 94-96°C (from light petroleum-ethyl acetate). (Found: M⁺ 313.1789. C₁₈H₂₃O₂N₃ requires M⁺ 313.1789); [α]D +240.4° (c=1.4, EtOH); νmax/cm⁻¹ 3500w, 1675s, 1610m and 1590s; δH 1.02 [9H,
Aziridine 119 (43 mg, 0.13 mmol) was dissolved in neat glacial acetic acid (1 cm³) and stirred at ambient temperature for 1 h. Addition of ethyl acetate (10 cm³) and washing with saturated aqueous sodium hydrogen carbonate (5 cm³) followed by drying and evaporation of the solvent gave the crude product as a colourless oil. Column chromatography (3:1 light petroleum-ethyl acetate) gave acetate 120 (27 mg, 53%) as a colourless oil. Rf 0.30. (Found: MH⁺ 374.2080. C₂₀H₂₇O₄N₃ requires M 374.2080); νmax/cm⁻¹ 2950, 1745, 1650, 1590; δH 0.94 [9H, s, C(CH₃)₃], 1.16 (3H, dd, J 6.6, 1.6, C=CCH₃), 2.06 (3H, s, OCOCH₃), 2.89 (2H, m, incl. J 16.8, 6.3, 1.6, CH₂), 3.35 (1H, ddd, J 10.9, 3.8, 3.8, CHOAc), 3.56 (1H, d, J 10.3, OH), 4.89 (1H, d, J 10.3, CHOH), 5.24 (1H, dd, J 6.3, NH), 5.50 (1H, ddd, J 14.9, 10.9, 1.6, CH=CCH₃), 5.77 (1H, dt, J 14.9, 6.6, C=CHCH₃), 7.41 (1H, ddd, J 8.2, 6.9, 1.2, H-6(Q)), 7.62 (1H, d, J 8.2, H-8(Q)), 7.70 (1H, ddd, J 8.2, 6.9, 1.2, H-7(Q)) and 8.18 (1H, dd, J 8.2, 1.2, H-5(Q)); m/z(%) 397 (MNa⁺, 100), 374 (MH⁺, 36) and 355 (61).
Further elution gave alcohol 121 (12mg, 26%) as a colourless oil, Rf 0.13. (Found: MH+ 332.1974. C18H26O3N3 requires M 332.1974); νmax/cm⁻¹ 3450w, 2960m, 1740s, 1680s, 1590s; δH 0.96 [9H, s, C(CH₃)₃], 1.62 (3H, dd, J 6.6, 1.2, C=CCH₃), 2.88 (1H, dd, J 14.4, 5.9, CHH), 3.07 (1H, ddd, J 14.4, 8.5, 3.8, CHH), 3.57 (1H, br s, OH), 4.03 [1H, d, J 10.4, OH(Q)], 4.24 (1H, m, incl. J 7.6, 3.8, CHO), 4.96 [1H, d, J 10.4, CHO(Q)], 5.45 (1H, ddd, J 15.4, 7.6, 1.6, CH=CHCH₃), 5.66 (1H, dd, J 8.5, 5.9, NH), 5.71 (1H, dd, J 15.4, 6.6, C=CHCH₃), 7.42 [1H, ddd, J 8.2, 6.9, 1.0, H-6(Q)], 7.65 [1H, dd, J 8.0, 1.0, H-8(Q)], 7.70 [1H, ddd, J 8.0, 6.9, 1.2, H-7(Q)] and 8.18 [1H, dd, J 8.2, 1.2, H-5(Q)]; m/z(%) 355 (MNa⁺,100) and 332 (MH⁺,22).

**Aziridination of 2,4-hexadiene with Q6NHOAc**

![Diagram of aziridination reaction](image)

General aziridination procedure D was followed in this reaction using NAQ⁶ (200mg, 0.81 mmol), LTA (378mg, 0.85 mmol), trans,trans-2,4-hexadiene (100mg, 1.22 mmol)(Aldrich) and TTB (578mg, 1.71 mmol) in dichloromethane (4 cm³). After work up in the normal way the crude product was isolated as a yellow oil. Column chromatography (2:1 light petroleum-ethyl acetate) gave aziridine 126 (148mg, 56%) as a colourless oil, Rf 0.48. (Found: MH⁺ 327.1947. C_{19}H_{25}O_{2}N_{3} requires M 327.1947); νmax/cm⁻¹ 3400w, 2970m, 2940m, 1665s, 1580s, 1465m, 1380m; δH - (mixture of diastereoisomers) major diastereoisomer: 0.89 [9H, s, C(CH₃)₃], 1.49 (3H, d, J 5.8, NCHCH₃), 1.76 (3H, dd, J 6.6, 1.4, C=CCH₃), 2.87 (1H, dd, J 9.5, 5.8, azir. NCH=CH=CH₂), 2.95 (1H, dd, J 5.8, azir. NCHCH₃), 3.58 (1H, d, J 10.4, OH), 4.68 (1H, ddd, J 15.6, 9.5, 1.4, NCH=CH=CH₂), 5.01 (1H, d, J 10.4, CHO), 6.01 (1H, dd, J 15.6, 6.6, C=CHCH₃), 7.41 [1H, ddd, J 8.2, 6.9, H-6(Q)], 7.56 [2H, m, H-7 and H-8(Q)] and 8.21 [1H, d, J 8.2, H-5(Q)]; minor diastereoisomer (observable signals): 1.02 [9H, s, C(CH₃)₃], 1.57 (3H, dd, J 6.3, 1.2, NCHCH₃), 1.78 (3H, dd, J 7.0, 1.2, C=CCH₃), 3.20 (1H, dd, J 10.3, 6.3, NCH=CH=CH₂), 3.75 (1H, d, J 10.4, OH), 4.56 (1H, ddd, J 10.3,
1.4, 1.2, NCHCH=Cl, 4.87 (1H, d, J 10.4, CHOCH), 5.68 (1H, dd, J 10.7, 7.0, C=CHCH3); m/z(%) 327 (MH+, 91), 245 (56) and 231 (100). Comparison of the signals at δ2.87 and 3.20 show a 1:1 ratio of diastereoisomers is present in solution.

Aziridination of 2,4-hexadiene with Q3NHOAc

General aziridination procedure A was followed in this reaction using NAQ3 (165mg, 0.81 mmol), LTA (378mg, 0.85 mmol), trans,trans-2,4-hexadiene (100mg, 1.22 mmol) and HMDS (328mg, 2.03 mmol) in dichloromethane (3 cm³). After work up in the normal way the crude product was isolated as a yellow oil. Column chromatography (2:1 light petroleum-ethyl acetate) gave aziridine 127 (108mg, 47%) as a colourless oil, Rf 0.40. (Found: MH+ 284.1763. C17H22ON3 requires M 284.1763); νmax/cm⁻¹ 2980m, 2935m, 1660s, 1580s, 1465m and 1380m; δH (mixture of N-invertomers) major N-invertomer, Q³ and Me trans: 1.17 (3H, d, J 6.9, CH₃CHCH₃), 1.26 (3H, d, J 6.9, CH₂CHCH₃), 1.51 (3H, d, J 5.7, NCHCH₃), 1.58 (3H, dd, J 6.6, 1.6, C=CHCH₃), 2.90 (1H, dd, J 9.4, 5.7, azir. NCHCH=C), 2.99 (1H, dd, J 5.7, azir. NCHCH₃), 3.44 [1H, h, J 6.9, CH(CH₃)₂], 4.68 (1H, ddd, J 15.4, 9.4, 1.6, NCHCH=C), 5.87 (1H, dd, J 15.4, 6.6, C=CHCH₃), 7.31 [1H, ddd, J 8.0, 6.8, H-6(Q)], 7.58 [2H, m, H-7 and H-8(Q)] and 8.13 [1H, d, J 8.0, H-5(Q)]; minor N-invertomer, Q³ and Me cis (observable signals): 1.18 (3H, d, J 6.9, CH₃CHCH₃), 1.27 (3H, d, J 6.9, CH₂CHCH₃), 1.74 (3H, dd, J 6.2, 1.5, NCHCH₃), 1.79 (3H, dd, J 7.0, 1.5, C=CHCH₃), 3.18 (1H, dd, J 10.5, 6.2, azir. NCHCH=C), 3.34 [1H, h, J 6.9, CH(CH₃)₂], 4.53 (1H, ddd, J 10.5, 1.5, NCHCH=C) and 5.74 (1H, dd, J 10.5, 7.0, C=CHCH₃); m/z(%) 284 (MH+, 100), 230 (24), 189 (51) and 173 (22). Comparison of the signals at δ2.90 and 3.18 show a 3:1 ratio of invertomers is present in solution.
Aziridination of cyclopentadiene using $Q^3NHOAc$

\[
\begin{align*}
\text{O}^3NHOAc & \quad \text{HMDS, CH}_2\text{Cl}_2 \\
\text{71} & \quad \text{42\%} \\
\end{align*}
\]

General aziridination procedure A was followed using NAQ$^3$ (300mg, 1.47 mmol), LTA (687mg, 1.55 mmol), HMDS (474mg, 2.94 mmol) and cyclopentadiene (194mg/0.24 cm$^3$, 2.94 mmol) in dichloromethane (6 cm$^3$). Crystallisation of the crude product (457mg) from ethyl acetate-light petroleum gave aziridine 128 (159mg, 42%) as a colourless solid, mp 126-128°C (from ethyl acetate-light petroleum).

(Found: C, 71.5; H, 6.4; N, 15.7%. $C_{16}H_{17}ON_{3}$ requires C, 71.8; H, 6.4; N, 15.7%);

$\nu_{\text{max}}/\text{cm}^{-1}$ 1670s, 1470m and 1380s; $\delta_{\text{H}}$ 1.40 (3H, d, $J_{6.6}$, CH$_2$CH$_3$), 1.42 (3H, d, $J_{6.6}$, CH$_3$CHCH$_3$), 2.76 (1H, ddd, $J_{18.9}$, 5.0 and 1.9, CHH), 2.95 (1H, ddd, $J_{18.9}$, 4.0, 1.9, CHH), 3.60 (1H, dd, $J_{5.0}$, 5.0, azir. NCHCH$_2$), 3.67 [1H, h, $J_{6.6}$, CH(CH$_3$)$_2$], 3.79 (1H, dd, $J_{5.2}$, 1.0, azir. NCHC=C), 6.06 (1H, ddd, $J_{5.7}$, 5.0, 1.9, C=CHCH$_2$), 6.21 (1H, m, incl. $J_{5.7}$, CH=CHCH$_2$), 7.40 [1H, ddd, $J_{8.2}$, 6.9, 1.5, H-6(Q)], 7.62 [1H, dd, $J_{8.2}$, 1.5, H-8(Q)], 7.68 [1H, ddd, $J_{8.2}$ 6.9, 1.0, H-7(Q)] and 8.19 [1H, dd, $J_{8.2}$, 1.0, H-5(Q)]; $\delta_{\text{C}}$ 21.6, 32.7 (2 x CH$_3$), 36.7 (CH$_2$), 49.5 [CH(CH$_3$)$_2$], 52.5, 58.1 (2 x C-N), 121.8 [CCO(Q)], 126.4, 126.5, 127.3, 128.4, 133.9, 138.5 [4 x CH(Q) and HC=CH], 146.6 [CN=C(Q)] and 160.4, 161.8 [CN(Q), CO(Q)]; $m/z$(%) 267 (M$^+$.10), 189 (12), 188 (43), 187 (27) and 173 (100).
Aziridination of cyclopentadiene using Q⁵NHOAc

General procedure aziridination A was followed in this reaction using NAQ⁵ (300mg, 1.31 mmol), LTA (609mg, 1.38 mmol) and cyclopentadiene (173mg/0.22 cm³, 2.62 mmol) in dichloromethane (6 cm³). Crystallisation of the crude product (309mg) from ethyl acetate-light petroleum gave aziridine 129 (212mg, 55%) as a colourless solid, mp 125-127°C (from ethyl acetate-light petroleum). (Found: M⁺ 293.0775. C₁₄H₁₀N₃F₃ requires M 293.0775; ν_max/cm⁻¹ 1665s, 1390s and 1470m; δ_H 2.70 (1H, ddd, J 18.8, 2.0, 1.0, CHH), 2.85 (1H, ddd, J 18.8, 5.5, 2.0, CHH), 4.04 (1H, dd, J 5.7, 5.5, azir. NCHCH₂), 4.28 (1H, d, J 5.7, azir. NCHC=C), 6.01 (1H, ddd, J 5.7, 2.0, 1.0, C=CHCH₂), 6.11 (1H, dd, J 5.7, 2.0, CH=CCH₂), 7.59 [1H, ddd, J 8.2, 5.8, H-6(Q)], 7.67 [1H, m, H-8(Q)], 7.80 [1H, dd, J 5.8, 1.0, H-7(Q)] and 8.24 [1H, dd, J 8.2, 1.0, H-5(Q)]; δ_C 38.6 (CH₂), 49.1, 55.0 (2 x C-N), 123.3 [CCO(Q)], 127.0, 128.8, 129.0, 129.5, 134.9, 138.4 [4 x CH(Q) and HC=CH], 144.3 [CN=C(Q)] and 160.5, 170.2 [CN(Q), CO(Q)]; m/z(%) 293 (M⁺,7), 215 (100), 214 (70) and 213 (38).

Aziridination of cyclopentadiene with Q⁶NHOAc

General aziridination procedure D was followed in this reaction using NAQ⁶ (200mg, 0.80 mmol), LTA (376mg, 8.50 mmol), TTB (576mg, 1.71 mmol) and cyclopentadiene (105mg/131 cm³, 1.59 mmol) in dichloromethane (5 cm³).
Crystallisation of the crude product from diethyl ether gave *endo-aziridine 130* (60mg, 25%) as a colourless solid, mp 126-128°C (from diethyl ether-light petroleum). \([\alpha]_D = +1.3^\circ\) (c=1.1, EtOH): (Found: C, 69.1; H, 6.8; N, 13.4%. C\(_{18}\)H\(_{21}\)O\(_2\)N\(_3\) requires C, 69.4; H, 6.8; N, 13.4%); \(v_{\text{max}}/\text{cm}^{-1}\) 1675s, 1610m and 1590s; \(\delta_H\) 1.00 [9H, s, C(CH\(_3\))\(_3\)], 2.43 (1H, ddd, \(J\) 20.1, 3.8, 2.2, CHH), 2.63 (1H, ddd, \(J\) 20.1, 4.7, 2.2, CHH), 3.58 (1H, dd, \(J\) 3.8, 3.8, azir. NCHCH\(_2\)), 3.84 (1H, d, \(J\) 10.6, CHOH), 4.21 (1H, m, azir. NCHC=C), 4.75 (1H, d, \(J\) 10.6, CHOH), 5.38 (1H, ddd, \(J\) 5.7, 4.7, 2.2, C=CHCH\(_2\)), 5.65 (1H, ddd, \(J\) 5.7, 2.2, 1.2, CH=CCH\(_2\)), 7.42 [1H, ddd, \(J\) 8.2, 6.9, 1.0, H-6(Q)], 7.62 [1H, dd, \(J\) 8.2, 1.0, H-8(Q)], 7.70 [1H, ddd, \(J\) 8.2, 6.9, 1.0, H-7(Q)] and 8.17 [1H, dd, \(J\) 8.2, 1.0, H-5(Q)]; \(\delta_C\) 26.3 [C(CH\(_3\))\(_3\)], 38.6 (C), 39.4 (CH\(_2\)), 50.6, 57.0 (2 x C-N), 75.3 (C-OH), 121.9 [CCO(Q)], 126.2, 126.6, 126.8, 127.2, 132.8, 134.0 [4 x CH(Q) and H=C=CH], 145.1 [CN=C(Q)] and 156.9, 158.2 [CN(Q) & CO(Q)]; \(m/z(\%)\) 311 (M\(^+\),4) and 176 (100).

**Thermolysis of *endo-aziridine 130***

*Endo-aziridine 130* (50mg, 0.16 mmol) was heated in CDCl\(_3\) at 60°C for 30 min. On cooling the NMR spectrum showed, in addition to signals belonging to *endo-aziridine 130*, those assignable to *exo-aziridine 130* at \(\delta_H\) 1.02 [9H, s, C(CH\(_3\))\(_3\)], 2.58 (1H, ddd, \(J\) 18.8, 2.8, 1.2, CHH), 2.99 (1H, ddd, \(J\) 18.8, 5.5, 2.7, CHH), 3.63 (1H, dd, \(J\) 5.7, 5.5, azir. NCHCH\(_2\)), 3.76 (1H, d, \(J\) 10.4, CHOH), 3.99 (1H, dd, \(J\) 5.7, 1.0, azir. NCHC=C), 5.01 (1H, d, \(J\) 10.4, CHOH), 6.03 (1H, ddd, \(J\) 5.7, 2.8, 1.0, CH=CCH\(_2\)), 6.19 (1H, ddd, \(J\) 5.7, 2.7, 1.2, C=CHCH\(_2\)), 8.21 [1H, dd, \(J\) 8.2, 1.0, H-5(Q)]; \(\delta_C\) 25.9 [C(CH\(_3\))\(_3\)], 32.5 (CH\(_2\)), 38.1 (C), 51.2, 56.6 (2 x C-N), 75.0 (C-OH), 121.5 [CCO(Q)],...
Aziridination of cyclopentadiene using $Q^1$NHOAc

General aziridination procedure A was followed using NAQ$^1$ (300mg, 1.71 mmol), LTA (796mg, 1.80 mmol), HMDS (550mg, 3.42 mmol) and cyclopentadiene (225mg/0.28 cm$^3$, 3.42 mmol) in dichloromethane (6 cm$^3$). Work up in the normal way gave the crude product as a yellow oil. Column chromatography (2:1 light petroleum-ethyl acetate) gave 2-methylquinazolin-4(3H)-one (168mg, 61%) as a white crystalline solid, $R_t$ 0.34, mp 238-240°C (from ethanol)(lit. mp 239-241°C). Further elution gave aziridine 131 (50mg, 12%) as a yellow oil, $R_t$ 0.08. (Found: MH$^+$ 239.1059. C$_{14}$H$_{13}$ON$_3$ requires M 239.1059); $\nu_{\max }$/cm$^{-1}$ 1665s, 1475m and 1380s; $\delta_H$ 2.67 (1H, ddd, $J$ 18.6, 5.4, 2.2, CHH), 2.68 (3H, s, CH$_3$), 2.84 (1H, ddd, $J$ 18.6, 1.9, CHH), 3.49 (1H, dd, $J$ 5.4, 5.4, azir. NCHCH$_2$), 3.72 (1H, dd, $J$ 5.4, 1.0, azir. NCHC=C), 5.96 (1H, ddd, $J$ 5.6, 2.2, 1.9, C=CHCH$_2$), 6.10 (1H, ddd, $J$ 5.6, 1.0, CH=CCH$_2$), 7.31 [1H, ddd, $J$ 8.2, 6.9, 1.3, H-6(Q)], 7.47 [1H, d, $J$ 8.2, H-8(Q)], 7.58 [1H, ddd. $J$ 8.2, 6.9, 1.5, H-7(Q)] and 8.08 [1H, dd, $J$ 8.2, 1.5, H-5(Q)]; $\delta_C$ 36.4 (CH$_2$), 40.7 (CH$_3$), 52.8, 58.0 (2 x C-N), 120.9 [CCO(Q)], 126.6, 126.8, 127.4, 128.6, 133.9 [4 x CH(Q) and HC=CH], 138.5 (HC=CH), 146.3 [CN=C(Q)] and 160.4, 161.8 [CN(Q), CO(Q)]; m/z(%) 239 (MH$^+$,100), 238 (M$^*$,54), 212 (51), 197 (21) and 186 (47).
Ring-opening of aziridine 128 with a cuprate reagent

A flame dried 2-necked flask equipped with a septum cap and 3-way tap was flushed with nitrogen, degassed, flushed with argon, degassed and filled with argon. Methylmagnesium bromide (101 mg/ 0.1 cm³, 0.84 mmol) dissolved in THF (1 cm³) was added via a syringe to a suspension of copper(I) bromide-dimethyl sulphide (58 mg, 0.28 mmol)(prepared by literature procedure) dissolved in THF (1 cm³). Aziridine 128 (75 mg, 0.28 mmol), dissolved in THF (1 cm³), was added dropwise via a syringe to the solution which was stirred at ambient temperature for 1 h. After addition of ethyl acetate (5 cm³) the solution was washed with saturated aqueous sodium hydrogen carbonate (5 cm³) and the solvent separated, dried and evaporated. Column chromatography (3:1 light petroleum-ethyl acetate) of the crude product (80 mg) gave a mixture of amines 132 and 133 (58 mg, 71%) as a yellow oil, Rf 0.28.

LTA oxidation of amines 132 and 133

The mixture of amines 132 and 133 (58 mg, 0.20 mmol) obtained previously was dissolved in dichloromethane (1 cm³) at -20°C and HMDS (72 mg, 0.45 mmol) added. LTA (95 mg, 0.21 mmol) was added in small portions over 10 min. and the solution allowed to warm to ambient temperature. Addition of dichloromethane (10 cm³) and
washing with saturated aqueous sodium hydrogen carbonate (5 cm\(^3\)) followed by
drying and evaporation gave the crude product as a yellow oil. Column
chromatography (2:1 light petroleum-ethyl acetate) gave \textit{imine} 134 (18mg, 33\%) as a
colourless oil. \(R_f\) 0.43. (Found: \(M^+\) 281.1529. \(C_{17}H_{19}ON_3\) requires \(M\) 281.1528);
\(v_{\text{max}}/\text{cm}^{-1}\) 1780m, 1675s, 1620s and 1595m; \(\delta_H\) 1.13 (3H, d, \(J\) 6.9, CH\(_3\)CHCH\(_3\)), 1.29
(3H, d, \(J\) 7.2, CHCH\(_3\)), 1.30 (3H, d, \(J\) 6.9, CH\(_3\)CHCH\(_3\)), 2.08 (1H, dd, \(J\) 18.6, 2.5,
CH\(_2\)), 2.75 (1H, dd, \(J\) 18.6, 6.0, CHH), 3.02 (1H, ddd, \(J\) 7.2, 2.5, 1.2, CHMe), 3.31
[1H, h, \(J\) 6.9, CH(CH\(_3\))\(_2\)], 6.55 (1H, dd, \(J\) 5.7, 2.5, CH=CCH\(_2\)), 7.01 (1H, ddd, \(J\) 6.0,
5.7, 2.5, 1.2, C=CHCH\(_2\)), 7.43 [1H, ddd, \(J\) 8.2, 5.1, 2.0, H-6(Q)], 7.71 [2H, m, H-7 and H-8(Q)] and 8.29 [1H, dd, \(J\) 8.2, 1.0, H-5(Q)]; \(m/z(\%)\) 281 (\(M^+\),78), 266 (100), 187 (81) and 173 (73).

Further elution gave \textit{imine} 135 (19mg, 35\%) as a colourless oil, \(R_f\) 0.36. (Found: \(M^+\)
281.1529. \(C_{17}H_{19}ON_3\) requires \(M\) 281.1528); \(v_{\text{max}}/\text{cm}^{-1}\) 1780m, 1675s, 1620s and
1595m; \(\delta_H\) 1.24 (3H, d, \(J\) 6.9, CHCH\(_3\)), 1.28 [6H, d, \(J\) 6.6, CH(CH\(_3\))\(_2\)], 2.55 (1H, dd,
\(J\) 18.1, 2.5, CHH), 3.14 (1H, ddd, \(J\) 6.9, 2.5, 2.5, 1.5, CHMe), 3.23 (1H, d, \(J\) 18.1,
CHH), 3.36 [1H, h, \(J\) 6.6, CH(CH\(_3\))\(_2\)], 5.97 (1H, dd, \(J\) 5.7, 1.5, CH=CCHMe), 6.92
(1H, dd, \(J\) 5.7, 2.5, C=CHCHMe), 7.42 [1H, ddd, \(J\) 8.2, 6.9, 1.2, H-6(Q)], 7.71 [2H, m, H-7 & H-8(Q)] and 8.26 [1H, d, \(J\) 8.2, H-5(Q)]; \(m/z(\%)\) 281 (\(M^+\),71), 266 (100), 188 (53), 187 (96) and 173 (91).

\textbf{Aziridination of 1,3-cyclohexadiene with Q\(^3\)NHOAc}

\begin{center}
\begin{tikzpicture}
  \node (N) [catalyst] {\textit{N}\textsubscript{H}OAc};
  \node (C) [catalyst] at (1,0) {136};
  \node (Q) [catalyst] at (0,0) {Q\(^3\)};
  \draw[->, thick] (N) -- (C) node[midway,above] {43\%} node[midway,below] {HMDS, CH\(_2\)Cl\(_2\)};
  \draw[->, thick] (C) -- (Q) node[midway,right] {Q\(^3\)NHOAc};
\end{tikzpicture}
\end{center}

General aziridination procedure A was followed in this reaction using NAQ\(^3\) (600mg,
2.96 mmol), LTA (1.38g, 3.11 mmol), HMDS (1.19g, 7.40 mmol) and 1,3-
cyclohexadiene (470mg/0.55 cm\(^3\), 5.92 mmol) in dichloromethane (12 cm\(^3\)). Column
chromatography of the crude product (0.68g) using 2:1 light petroleum-ethyl acetate gave aziridine 136 (0.54g, 60%) as a colourless solid, Rf 0.41, mp 93-95°C (from light petroleum-ethyl acetate). (Found: MH+ 282.1606. C17H20ON3 requires M 282.1607; v max/cm⁻¹ 1660s and 1570s; δH 1.32 (3H, d, J 6.6, CH3CHCH3), 1.35 (3H, d, J 6.6, CH3CHCH3), 1.94 (1H, dddd, J 14.0, 6.9, 5.7, 2.5, C=CHCH), 2.35 (1H, ddd, J 18.0, 6.9, 4.7, NCHCHH), 2.50 (1H, ddd, J 18.0, 7.6, 5.7, NCHCHH), 2.83 (1H, ddd, J 14.0, 7.6, 4.4, C=CHCH), 3.20 (1H, dd, J 7.9, 4.7, azir. NCHCH2), 3.62 (1H, d, J 7.9, azir. NCH=C), 3.90 (1H, h, J 6.6, CH(CH3)2), 6.29 (1H, dd, J 8.7, 5.7, C=CHCH2), 6.50 (1H, dd, J 8.7, 4.4, CH=CHCH2), 7.66 [1H, dddd, J 8.1, 6.3, 1.2, H-6(Q)], 7.58 [1H, dd, J 8.1, 1.2, H-8(Q)], 7.64 [1H, dddd, J 8.1, 6.3, 1.2, H-7(Q)] and 8.11 [1H, dd, J 8.1, 1.2, H-5(Q)]; δC 20.4, 23.1 (2 x CH2), 23.4 (2 x CH3), 33.3 [CH(CH3)2], 45.8, 50.8 (2 x C-N), 123.3, 123.6 [HC=CH, CCO(Q)], 128.3, 129.2, 135.5, 135.7 [4 x CH(Q)], 148.4 [CN=C(Q)] and 162.4, 163.7 [CN(Q), CO(Q)]; m/z(%) 282 (MH⁺,100) and 189 (45).

**Reaction of 1,3-cyclohexadiene with Q5NHOAc**

![Chemical structure](image_url)

General aziridination procedure A was followed using NAQ 5 (200mg, 0.87 mmol), LTA (406mg, 0.92 mmol) and 1,3-cyclohexadiene (140mg/0.16 cm³, 1.75 mmol) in dichloromethane (4 cm³). Crystallisation of the crude product (246mg) from ethyl acetate-light petroleum gave aziridine 137 (170mg) as a white solid, mp 103-105°C. (Found: C, 58.6; H, 3.35; N, 13.7%. C15H13ON3F3 requires C, 58.6; H, 3.9; N, 13.7%); v max/cm⁻¹ 1690s, 1610s, 1470m and 1380s; δH 1.43 (1H, dddd, J 13.7, 7.8, 7.0, 1.6, C=CHCH), 1.94 (1H, dd, J 10.7, 7.0, NCHCHH), 2.03 (1H, dddd, J 10.7, 7.8, 4.8, NCHCHH), 2.23 (1H, dddd, J 13.7, 7.8, 4.7, C=CHCH), 3.59 (1H, dd, J 7.5, 4.8, azir.)
NCHCH2), 3.82 (1H, d, J 7.5, azir. NCHC=C), 5.82 (1H, dd, J 9.5, 7.8, NCHC=CH), 5.97 (1H, ddd, J 9.5, 4.7, 2.8, NCHCH=C), 7.41 (1H, ddd, J 8.0, 5.0, 1.0, H-6(Q)), 7.63 [2H, m, H-7 and H-8(Q)] and 8.04 [1H, dd, J 8.0, 1.0, H-5(Q)]; δC 18.6, 21.2 (2 x CH2), 38.5, 44.1 (2 x C-N), 122.1, 123.3 [CCO(Q), HC=CH], 127.2, 128.6, 129.3 [3 x CH(Q)], 133.1, 134.9 [CH(Q), HC=CH], 144.3 [CN=C(Q)], 160.9, 162.3 [CN(Q), CO(Q)] - CF3 not visible; m/z(%) 308 (MH+,100), 230 (24), 215 (46).

Kieselgel chromatography (2:1 light petroleum-ethyl acetate) of the residue after evaporation of the filtrate above gave more aziridine 137 (13mg, total 68%), Rf 0.41.

Further elution gave the dienylamine 142 (13mg, 5%) as a clear colourless oil, Rf 0.33. (Found: MH* 308.1011. C15H13ON3F3 requires M 308.1011); νmax/cm⁻¹ 1695m and 1610m; δH 2.35 (1H, dddd, J 18.0, 6.0, 5.1, 1.9, CHH), 2.42 (1H, ddd, J 18.0, 5.1, 1.0, CHH), 3.93 (1H, ddd, J 6.6, 5.1, 5.1, CHNH), 5.43 (1H, d, J 6.6, NH), 5.83 (1H, dd, J 9.6, 5.1, NCHCH=C), 5.90 (1H, ddd, J 9.4, 5.1, 5.1, C=CHCH2), 6.03 (1H, ddd, J 9.4, 5.0, 1.9, CH=CCCH2), 6.13 (1H, dd, J 9.6, 5.0, CH=CCNH), 7.64 [1H, dd, J 8.2, 4.1, H-6(Q)], 7.86 [2H, m, H-7 and H-8(Q)] and 8.31 [1H, dd, J 8.2, 1.0, H-5(Q)]; δC(75 MHz) 28.3 (CH2), 54.2 (CNH), 122.5 [CCO(Q)], 123.8, 124.0, 126.1, 127.3, 127.6, 129.2, 129.6, 135.5 [4 x CH(Q) & 2 x HC=CH], 145.3 [CN=C(Q)] and 162.4, 168.3 [CN(Q), CO(Q)]; m/z(%) 308 (MH*,44), 307 (M*,42), 230 (100) and 229 (50).

Reaction of 1,3-cyclohexadiene with Q6NHOAc–TTB

![Diagram](image)

General aziridination procedure D was followed using NAQ6 (500mg, 2.01 mmol), LTA (942mg, 2.12 mmol), TTB (1.42g, 4.20 mmol) and 1,3-cyclohexadiene (320mg/0.38 cm³, 4.00 mmol) in dichloromethane (11 cm³). After work up, column
chromatography (8:1 light petroleum-ethyl acetate) gave dienylamine 139 (37mg, 6%) as a colourless oil, Rf 0.17. \([\alpha]_D = +12.9^\circ\) (c=1.0, EtOH); (Found: M+ 325.1791. 

\(C_{16}H_{23}O_2N_2\) requires \(M = 325.1790\); \(n_{\max }/cm^{-1}\) 3500m, 1675s, 1595s and 1470s; \(\delta_H 0.96 [9H, s, (CH_3)_3]\), 2.37 (2H, m, incl. J 6.4, 4.6, 1.4, C=CCH_2), 3.61 (1H, d, J 10.4, CHO), 3.96 (1H, d, J 5.9, CH), 5.08 (1H, d, J 10.4, CH), 5.37 (1H, d, J 5.9, NH), 5.58 (1H, dd, J 9.5, 5.1, C=CHCHNH), 5.92 (1H, ddd, J 9.5, 4.6, 1.2, C=CHCH_2), 6.05 (1H, ddd, J 9.5, 5.0, 1.4, CH=CCH_2), 6.15 (1H, dd, J 9.5, 5.0, CH=CCHNH), 7.48 (1H, ddd, J 8.2, 6.9, 1.0, H-6(Q)), 7.69 [1H, d, J 8.2, H-8(Q)], 7.78 [1H, ddd, J 8.2, 6.9, 1.0, H-7(Q)] and 8.23 [1H, dd, J 8.2, 1.0, H-5(Q)]; \(\delta_C(75\ MHz) 26.3 [(CH_3)_3], 28.3 (CH_2), 38.3 [C(CH_3)_3], 52.0 (C-N), 75.2 (COH), 120.3 [CCO(Q)], 122.9, 123.8, 126.3, 127.1, 127.2, 127.7, 128.2, 134.9 [2 x HC=CH and 4 x CH(Q)], 146.9 [CN=C(Q)] and 160.6, 161.8 [CN(Q), CO(Q)]; \(m/z(\%) 326 (MH^+,52), 248 (48), 233 (100) and 215 (36). Dienylamine 139 could not be separated from a small amount of tert-butoxyaminoquinazolinone 140.99

Further elution gave aziridine 138 (291mg, 54%) as a colourless gum, Rf 0.11, which crystallised from diethyl ether-light petroleum, mp 106-107°C. \([\alpha]_D = +16.9^\circ\) (c=2.5, EtOH); (Found: M+ 325.1790. \(C_{16}H_{23}O_2N_3\) requires \(M = 325.1790\); \(v_{\max }/cm^{-1}\) 3480m, 1660s and 1580s; \(\delta_H 1.02 [9H, s, C(CH_3)_3], 1.65 (1H, ddd, J 13.1, 5.6, 3.2, C=CHH), 2.17 (1H, dd, J 18.8, 4.7, NCHCHH), 2.19 (1H, ddd, J 18.8, 7.6, 2.5, NCHCHH), 2.66 (1H, ddd, J 13.1, 7.6, 4.4, C=CCHH), 2.91 (1H, ddd, J 7.7, 4.7, 1.0, azir. NCHCH_2), 3.57 (1H, d, J 7.7, azir. NCHC=CH), 3.82 (1H, d, J 10.4, CHOH), 5.04 (1H, d, J 10.4, CHOH), 6.03 (1H, ddd, J 9.2, 5.6, 2.5, C=CHCH_2), 6.22 (1H, ddd, J 9.2, 4.4, 3.2, CH=CCH_2), 7.44 [1H, ddd, J 8.2, 6.9, 1.0, H-6(Q)], 7.64 [1H, d, J 8.0, H-8(Q)], 7.70 [1H, ddd, J 8.0, 6.9, 1.2, H-7(Q)] and 8.21 [1H, dd, J 8.2, 1.2, H-5(Q)]; \(\delta_C 18.4, 21.6 (2 x CH_2), 26.3 [C(CH_3)_3], 38.5 [C(CH_3)_3], 45.5, 48.7 (2 x C-N), 75.1 (COH), 120.7, 121.8 [CCO(Q), HC=CH], 126.3, 126.7, 127.0, 127.4, 134.1 [4 x CH(Q), HC=CH], 145.0 [CN=C(Q)] and 158.0, 159.9 [CN(Q), CO(Q)]; \(m/z(\%) 325 (M^+,48), 268 (62), 240 (100), 231 (94) and 215 (80). The NMR spectrum of aziridine 138 before crystallisation showed the presence of another diastereoisomer (138a) with (observable signals) - \(\delta_H 0.99 [9H, s, C(CH_3)_3], 2.45 (1H, dd, J 12.3, 5.5, C=CHH), 3.40 (1H, m, azir. NCHCH_2), 3.41 (1H, m, azir. NCHC=CH), 3.79 (1H, d, J 10.3, CHOH), 5.02 (1H, d, J 10.3, CHOH), 5.80 (1H, ddd, J 8.5, 5.5, 2.3, C=CHCH_2), 6.20
The ratio of aziridine diastereoisomers ranged from 10:1-4:1 in different reactions from comparison of signals at δ 2.66 and 2.45 in the crude reaction product.

Reaction of 1,4-cyclohexadiene with $Q^3$NHOAc

\[
\begin{array}{c}
\text{NHOAc} \\
\text{71} \\
\text{HMDS, CH}_2\text{Cl}_2
\end{array}
\]

General aziridination procedure A was followed in this reaction using NAQ$^3$ (300mg, 1.47 mmol), LTA (687mg, 1.54 mmol), HMDS (474mg, 2.94 mmol) and 1,4-cyclohexadiene (235mg/0.28 cm$^3$, 2.94 mmol) in dichloromethane (6 cm$^3$). After work up the crude product was obtained as a yellow oil. Column chromatography (4:1 light petroleum-ethyl acetate) gave dienylamine 143 (52mg, 13%) as a colourless oil, $R_f$ 0.47. (Found: MH$^+$ 282.1606. C$^{19}$H$^{23}$O$_2$N$_3$ requires $M$ 282.1606); δ$_H$ 1.33 (6H, d, $J$ 6.7, CH$_2$CHCH$_3$), 2.68 (2H, m, incl. $J$ 20.0, 3.2, CH$_2$), 3.80 [1H, h, $J$ 6.7, CH(CH$_3$)$_2$], 4.13 (1H, m, incl. $J$ 5.9, 1.6, CHNH), 5.78 (2H, dd, $J$ 10.7, 1.6, 2 x CH=CCH$_2$), 5.82 (1H, d, $J$ 5.9, NH), 5.98 (2H, dddd, $J$ 10.7, 3.2, 1.5, 1.5, 2 x C=CHCH$_2$), 7.42 [1H, ddd, $J$ 8.2, 6.3, 1.2, H-6(Q)], 7.67 [1H, dd, $J$ 8.2, 1.2, H-8(Q)], 7.72 [1H, ddd, $J$ 8.2, 6.3, 1.0, H-7(Q)] and 8.23 [1H, dd, $J$ 8.2, 1.0, H-5(Q)]; δ$_C$ 27.0 (CH$_2$), 31.2 [(CH$_3$)$_2$], 45.9 [CH(CH$_3$)$_2$], 54.7 (CNH), 120.9 [CCO(Q)], 124.6, 126.5, 127.0, 127.7, 128.5 [3 x CH(Q), 2 x H(C=CH)], 134.5 [CH(Q)], 147.6 [CN=C(Q)] and 162.5, 163.4 [CN(Q), CO(Q)]; $m/z(\%)$ 282 (MH$^+$,36), 204 (100) and 189 (31).

Further elution gave aziridine 144 (113mg, 27%) $R_f$ 0.39, as a colourless solid mp 95-96°C (from light petroleum-ethyl acetate). (Found: C, 72.6; H, 6.8; N, 15.0%.

C$_{17}$H$_{19}$ON$_1$ requires C, 72.6; H, 6.8; N, 14.9%); $\nu_{\max }$/cm$^{-1}$ 1660s and 1570s; δ$_H$ 1.42 (6H, d, $J$ 6.6, 2 x CH$_3$), 2.53 (2H, dd, $J$ 17.1, 2.5, 2 x NCHCHH), 2.88 (2H, dd, $J$ 17.1,
2.2. 2 x NCHCHH), 2.89 (2H, br d, J 7.0, 2 x azir. NCH), 3.62 [1H, h, J 6.6, CH(CH₃)₂], 5.60 (2H, br s, HC≡CH), 7.38 [1H, ddd, J 8.2, 6.3, 1.2, H-6(Q)], 7.63 [1H, dd, J 8.0, 1.2, H-8(Q)], 7.68 [1H, ddd, J 8.0, 6.3, 1.0, H-7(Q)] and 8.17 [1H, dd, J 8.2, 1.0, H-5(Q)]; δ_C 21.6 [(CH₃)₂], 23.4 (2 x CH₂), 31.3 [CH(CH₃)₂], 45.9 (2 x C-N), 121.6 [CCO(Q)], 122.7 (HC≡CH), 126.4, 126.9, 127.7, 133.8 [4 x CH(Q)], 146.5 [CN=C(Q)] and 160.5, 161.5 [CN(Q), CO(Q)]; m/z (%) 281 (M⁺,14), 227 (100), 214 (66) and 203 (56).

**Reaction of 1,4-cyclohexadiene with Q₆NHOAc–TTB**

[Insert reaction diagram]

General aziridination procedure D was followed in this reaction using NAQ⁶ (245mg, 0.98 mmol), LTA (458mg, 1.34 mmol), TTB (696mg, 2.00 mmol) and 1,4-cyclohexadiene (156mg, 1.96 mmol) in dichloromethane (6 cm³). Column chromatography (3:1 light petroleum-ethyl acetate) of the crude product gave dienylamine 146 (86mg, 27%) R_f 0.56, as a colourless solid mp 105-107°C (from ethanol). [α]_D = +135.4° (c=1.5, EtOH); (Found: C, 70.1; H, 7.3; N, 12.8%). C_{19}H_{24}O_{2}N_{3} requires C, 70.1; H 7.1; N, 12.9%); ν_max/cm⁻¹ 3500w, 1670s and 1590s; δ_H 0.99 [9H, s, (CH₃)₃], 2.66 (2H, struct. m, CH₂), 3.63 (1H, d, J 10.4, CHO(H)), 4.16 (1H, ddt, J 5.4, 3.7, 2.2, CHNH), 5.14 (1H, d, J 10.4, CHO(H)), 5.69 (1H, d, J 5.4, NH), 5.79 (1H, ddd, J 9.7, 3.7, 2.0, CH≡CCH₂), 5.84 (1H, ddd, J 9.7, 3.7, 2.0, CH=CCH₂), 5.98 (2H, m. incl. J 9.7, 2.2, 2 x C=CHCH₂), 7.48 [1H, ddd, J 8.2, 6.9, 1.5, H-6(Q)], 7.69 [1H, dd, J 8.2, 1.5, H-8(Q)], 7.78 [1H, ddd, J 8.2, 6.9, 1.0, H-7(Q)] and 8.27 [1H, dd, J 8.2, 1.0, H-5(Q)]; δ_C 25.9 [C(CH₃)₃], 26.6 (CH₂), 37.9 [C(CH₃)₃], 54.4 (CH), 74.7 (C=CH₂), 120.7 [CCO(Q)], 123.7, 124.0, 126.8, 126.9, 127.3, 128.6, [3 x CH(Q), 2
Further elution gave *aziridine* 141 (74mg, 23%) $R_f$ 0.40, as a colourless solid mp 59-60°C (from ethanol). $[\alpha]_D = +72.4^\circ$ (c=1.0, EtOH); (Found: $M^+$ 326.1868. $C_{19}H_{24}O_2N_3$ requires $M$ 326.1869); $\nu \text{max/cm}^{-1}$ 3480 m, 1665 s and 1590 s; $\delta_H$ 1.03 (9H, s, C(CH$_3$)$_3$), 2.52 (2H, m, incl. $J$ 20.1, 12.2, 2 x CHH), 2.80 (1H, dd, $J$ 20.1, 3.7, CHH), 3.00 (1H, dd, $J$ 12.2, 4.4, CHH), 3.02 (1H, dd, $J$ 7.9, 3.7, azir. NCH), 3.15 (1H, dd, $J$ 7.9, 4.4, azir. NCH), 3.80 (1H, d, $J$ 10.0, CHOH), 5.01 (1H, d, $J$ 10.0, CHOH), 5.59 (2H, s, CH=CH), 7.45 (1H, ddd, $J$ 8.2, 6.9, 1.2, H-6(Q)), 7.64 (1H, dd, $J$ 8.2, 1.0, H-8(Q)), 7.71 (1H, ddd, $J$ 8.2, 6.9, 1.0, H-7(Q)) and 8.21 (1H, dd, $J$ 8.2, 1.2, H-5(Q)); $\delta_C$ 23.6 (2 x CH$_2$), 26.5 [C(CH$_3$)$_3$], 38.6 [C(CH$_3$)$_3$], 44.6, 47.0 (2 x C-N), 75.2 (COH), 121.8 [CCO(Q)], 123.5, 126.7, 127.2, 127.3, 134.3 [4 x CH(Q), HC=CH], 145.1 [CN=C(Q)] and 157.7, 160.3 [CN(Q), CO(Q)]; $m/z(\%)$ 326 ($M^+$,60), 268 (24), 233 (100) and 215 (59).

**Reaction of 1,4-cyclohexadiene with nitrene $Q^3N$**

![Reaction of 1,4-cyclohexadiene with nitrene $Q^3N$](image)

General aziridination procedure C was followed using $NAQ^3$ (300mg, 1.47 mmol), LTA (687mg, 1.54 mmol), TEA (1.47g, 14.7 mmol) and 1,4-cyclohexadiene (235mg, 2.94 mmol) in dichloromethane (6 cm$^3$). Column chromatography (4:1 light petroleum-ethyl acetate) of the crude product gave dienylamine 143 (5%) as a colourless oil, $R_f$ 0.44 identical with that isolated previously.

Further elution gave aziridine 144 (23%) as a colourless oil, $R_f$ 0.38 identical with that isolated previously.
Swern oxidation of aziridine 138

DMSO (73mg/0.07 cm³, 0.93 mmol) was added to dichloromethane (1 cm³) pre-cooled to -78°C, followed by dropwise addition of oxalyl chloride (60mg, 0.46 mmol). After stirring for 10 min., aziridine 138 (100mg, 0.31 mmol) was added in a solution of dichloromethane (1 cm³) and the mixture stirred at -78°C for 2 h. Triethylamine (219mg, 2.17 mmol) was added and the solution warmed to ambient temperature. Addition of saturated sodium hydrogen carbonate solution (10 cm³) and extraction with dichloromethane (15 cm³) gave the crude product as a yellow oil after drying and evaporation of the solvent. Column chromatography (3:1 light petroleum-ethyl acetate) gave ketone 147 (51mg, 51%) as a colourless oil, Rf 0.50. (Found: MH⁺ 324.1712. C₁₉H₂₂O₂N₃ requires M 324.1712); δH 1.32 [9H, s, (CH₃)₃], 1.54 (1H, ddd, J 14.0, 7.5, 2.7, NCHCH₂-cis), 2.04 (2H, m, incl. J 7.5, 5.0, 3.5, 2.7, C=CCH₂), 2.34 (1H, ddd, J 14.0, 3.5, 2.1, NCHCH₂-trans), 3.69 (1H, ddd, J 7.8, 4.8, 1.5, azir. NCH=CH), 3.79 (1H, ddd, J 7.8, 2.1, azir. NCHCH₂), 5.88 (1H, dd, J 9.6, 4.8, CH=CH₂), 6.06 (1H, ddd, J 9.6, 5.0, 1.5, C=CHCH₂), 7.48 [1H, ddd, J 8.0, 6.6, 1.1, H-6(Q)], 7.66 [1H, dd, J 8.0, 1.1, H-8(Q)], 7.75 [1H, ddd, J 8.0, 6.6, 1.3, H-7(Q)] and 8.21 [1H, dd, J 8.0, 1.3, H-5(Q)]; δC 18.2 (CH₃)₃, 21.4, 27.1 (2 x CH₂) 40.4 (C-N), 44.9 [C(CH₃)₃], 45.0 (C-N), 122.5, 122.8 [HC=CH, CCO(Q)], 126.7, 127.6, 128.0, 132.9, 134.5 [3 x CH(Q), HC=CH], 146.2 [CN=C(Q)], 153.2, 160.3 [CN(Q), CO(Q)] and 204.9 (C=O); m/z(%) 324 (MH⁺,31), 246 (22), 231 (100) and 215 (44). Further elution gave unreacted aziridine 138 (19mg, 19% recovered), Rf 0.23.
Reduction of ketone 147 with sodium borohydride

Ketone 147 (50mg, 0.16 mmol) was stirred in ethanol (5 cm³) with sodium borohydride (3mg, 0.05 mmol) at ambient temperature for 4 h. Addition of saturated sodium hydrogen carbonate solution (10 cm³) and extraction with ethyl acetate (10 cm³) gave the crude product as a colourless oil after drying and evaporation of the solvent. Column chromatography (3:1 light petroleum-ethyl acetate) gave ketone 147 (14mg, 28% recovered) as a colourless oil, Rf 0.51.

Further elution gave aziridine 138 (18mg, 36%) as a colourless oil, Rf 0.30. (Found: M⁺ 325.1790. C₁₉H₂₁O₂N₃ requires M 325.1790); (mixture of diastereoisomers) major diastereoisomer - δH 1.02 [9H, s, C(CH₃)₃], 1.65 (1H, m, C=CCHH), 2.18 (2H, m, NCHCH₂), 2.66 (1H, ddd, J 13.1, 7.9, 3.2, C=CCHH), 2.91 (1H, ddd, J 7.6, 4.7, 1.0, azir. NCHCH₂), 3.57 (1H, dd, J 7.6, 2.5, azir. NCHC=C), 3.82 (1H, d, J 10.4, CHOH), 5.04 (1H, d, J 10.4, CHOH), 6.03 (1H, dd, J 8.5, 2.5, CH=CCH₂), 6.22 (1H, ddd, J 8.5, 3.2, C=CCH₂), 7.44 [1H, ddd, J 8.2, 6.9, 1.0, H-6(Q)], 7.64 [1H, d, J 8.0, H-8(Q)], 7.70 [1H, ddd, J 8.0, 6.9, 1.2, H-7(Q)] and 8.21 [1H, dd, J 8.2, 1.2, H-5(Q)]; minor diastereoisomer (observable signals) - δH 0.99 [9H, s, (CH₃)₃], 2.45 (1H, dd, J 12.3, 5.5, CHHC=C), 3.40 (1H, m, azir. NCHCH₂), 3.41 (1H, m, azir. NCHC=C), 3.79 (1H, d, J 10.3, CHOH), 5.02 (1H, d, J 10.3, CHOH), 5.80 (1H, m, CH=CCH₂), 6.20 (1H, m, C=CHCH₂). From comparison of signals at δ3.57 and 3.79 aziridine 138 is produced as a 3:2 mixture of diastereoisomers.
Swern oxidation of dienylamine 139

Oxalyl chloride (18mg, 0.14 mmol) was added dropwise to a stirred solution of
dichloromethane (1 cm³) containing DMSO (21mg, 0.28 mmol) at -78°C. After 5 min.
dienylamine 139 (30mg, 0.09 mmol) was added dropwise in a solution of
dichloromethane (1 cm³) and the mixture stirred at -78°C for 4 h. Triethylamine
(56mg, 0.55 mmol) was added and the reaction mixture warmed to ambient
temperature. Addition of saturated sodium hydrogen carbonate solution (10 cm³) and
extraction with dichloromethane (10 cm³) gave the crude product as a yellow oil after
drying and evaporation of the solvent. Column chromatography (7:1 light petroleum-
ethyl acetate) gave ketone 148 (15mg, 50%) as a colourless oil, Rf 0.33. (Found: MH⁺
324.1712. C₁₉H₂₂O₂N₃ requires M 324.1712); νmax/cm⁻¹ 1680s and 1600s; δH 1.29
[9H, s, (CH₃)₃], 2.27 (1H, dddd, J 18.4, 7.8, 2.5, CHH-cis), 2.44 (1H, ddd, J 18.4, 5.0,
5.0, CHH-trans), 3.76 (1H, ddd, J 7.8, 7.8, 5.0, CHNH), 5.50 (1H, d, J 7.8, NH), 5.79
(1H, dd, J 9.7, 5.0, C=CHCHNH), 5.88 (1H, dd, J 9.4, 5.1, CH=CCH₂), 6.01 (1H,
ddd, J 9.4, 5.0, 2.5, 1.1, C=CHCH₂), 6.13 (1H, dd, J 9.7, 5.1, CH=CCHNH), 7.53
[1H, ddd, J 8.2, 6.6, 1.6, H-6(Q)], 7.74 [1H, dd, J 8.0, 1.6, H-8(Q)], 7.79 [1H, ddd, J
8.0, 6.6, 1.1, H-7(Q)] and 8.29 [1H, dd, J 8.2, 1.1, H-5(Q)]; m/z(%) 324 (MH⁺,31),
246 (32), 244 (33), 231 (100) and 215 (29).
Reduction of ketone 148 with sodium borohydride

Ketone 148 (12mg, 0.04 mmol) was stirred in ethanol (2 cm³) with sodium borohydride (1mg, 0.02 mmol) for 2 h. Addition of saturated sodium hydrogen carbonate solution (10 cm³) and extraction with ethyl acetate (10 cm³) gave the crude product as a pale yellow oil after evaporation of the solvent. Column chromatography (7:1 light petroleum-ethyl acetate) gave ketone 148 (2mg, 17% recovered) as a colourless oil, Rf 0.40.

Further elution gave dienylamine 139 (8mg, 67%) as a colourless liquid, Rf 0.31. (Found: MH⁺ 325.1791. C₁₉H₂₂O₂N₃ requires M 325.1791); (mixture of diastereoisomers: one having identical signals to dienylamine 139 obtained during aziridination) observable signals for new diastereoisomer - δH 0.95 [9H, s, (CH₃)₃], 2.23 (1H, ddd, J 16.0, 7.1, 3.0, CHH), 2.29 (1H, ddd, J 16.0, 9.6, 4.8, CHH), 3.56 (1H, d, J 10.4, CHO), 3.76 (1H, dd, J 9.6, 7.1, 2.4, CHNH), 5.06 (1H, d, J 10.4, CHOH), 5.16 (1H, d, J 2.4, NH), 5.93 (2H, m, incl. J 8.9, 5.7, 4.8, 3.0, C=CHCH & C(CH₂)₂), 6.05 (1H, m, incl. J 8.9, CH=CH₂), 6.22 (1H, ddd, J 8.9, 5.7, 3.0, CH=C), 7.51 [1H, ddd, J 8.2, 6.9, 1.0, H-6(Q)], 7.72 [1H, d, J 8.2, H-8(Q)], 7.80 [1H, ddd, J 8.2, 6.9, 1.0, H-7(Q)] and 8.25 [1H, dd, J 8.2, 1.0, H-5(Q)]. From comparison of signals at δ5.37 and 5.16 dienylamine 139 is produced as a 1:1 mixture of diastereoisomers.
Reaction of 9,10-dihydroanthracene with $Q^3\text{NHOAc}$

General aziridination procedure A was followed in this reaction using $\text{NAQ}^3$ (300mg, 1.47 mmol), LTA (687mg, 1.54 mmol), HMDS (474mg, 2.94 mmol) and 9,10-dihydroanthracene (529mg, 2.94 mmol) in dichloromethane (6 cm$^3$). Column chromatography (4:1 light petroleum-ethyl acetate) of the crude product (831mg) gave unreacted 9,10-dihydroanthracene (428mg, 81% recovered), $R_f$ 0.68.

Further elution gave 9-($Q^3$-amino)-9,10-dihydroanthracene 149 (60mg, 12%) as a yellow oil, $R_f$ 0.47. (Found: $M^+$ 382.1914. $C_{25}H_{24}O_3N$ requires $M$ 382.1914); $\nu_{\text{max}}$/cm$^{-1}$ 1680s, 1595s and 1480m; $\delta_{\text{H}}$ 0.66 (3H, d, $J\ 6.9$, $CH_3$), 0.94 (3H, d, $J\ 6.9$, $CH_3$), 2.75 [1H, h, $J\ 6.9$, $CH(CH_3)_2$], 3.97 (1H, d, $J\ 18.2$, $CHH$), 4.39 (1H, d, $J\ 18.2$, $CHH$), 5.42 (1H, d, $J\ 1.9$, $CHNH$), 5.52 (1H, d, $J\ 1.9$, NH), 6.69 [1H, d, $J\ 7.3$, CH(Ar)], 7.01 [1H, dd, $J\ 7.3$, 7.3, CH(Ar)], 7.17-7.41 [5H, m, 5 x CH(Ar)], 7.41 [1H, ddd, $J\ 8.2$, 6.9, 1.2, H-6(Q)], 7.66 [1H, dd, $J\ 8.2$, 1.2, H-8(Q)], 7.74 [1H, ddd, $J\ 8.2$, 6.9, 1.2, H-7(Q)], 7.77-7.81 [1H, m, CH(Ar)] and 8.35 [1H, dd, $J\ 8.2$, 1.2, H-5(Q)]; $\delta_{C}$ 18.8, 22.1 (2 x CH$_3$), 30.7 [CH(CH$_3$)$_2$], 35.7 (CH$_2$), 63.0 (C-N), 121.1 [CCO(Q)], 126.5, 126.8, 127.4 [3 x CH(Q)], 127.6 127.9, 128.1, 128.3, 128.6, 128.8, 129.4, 129.6 [8 x CH(Ar)], 134.5 [CH(Q)], 134.7, 135.0, 138.7, 138.8 [4 x C(Ar)], 147.8 [CN=C(Q)], 162.7, 164.3 [CN(Q), CO(Q)]; $m/z$ (%) 382 ($M^+$,100), 189 (27) and 181 (24).
Reaction of 9,10-dihydroanthracene with $Q^3$NHOAc in the presence of TFA

![Chemical structure](image)

General aziridination procedure E: a solution of $Q^3$NHOAc 71 was prepared using NAD (300mg, 1.47 mmol) and LTA (687mg, 1.54 mmol) in dichloromethane (6 cm$^3$) as in general aziridination procedure A. The solution was stirred at -20°C for 5 min. and filtered to remove insoluble lead di-acetate. With the temperature of the cooling bath at -40°C, 9,10-dihydroanthracene (530mg, 2.94 mmol) was added to the stirred solution followed by TFA (503mg, 4.41 mmol). After 5 min. TEA (1.5g, 14.7 mmol) was added and the reaction mixture allowed to warm to ambient temperature. The reaction was worked up as in procedure A giving the crude product. Column chromatography (4:1 light petroleum-ethyl acetate) gave unreacted 9,10-dihydroanthracene (472mg, 89% recovered), R$_f$ 0.67.

Further elution gave insertion product 149 (11mg, 2%) as a yellow oil, R$_f$ 0.47 identical with that isolated previously. A sample of 2-isopropylquinazolin-4(3H)-one ($Q^3$H) 145 (72mg, 26%) R$_f$ 0.17, was also eluted from the column, mp 230-231°C (lit. mp 230-231°C).
Reaction of 9,10-dihydroanthracene with Q\textsuperscript{6}NHOAc-TTB

\[
\begin{align*}
&\text{O}\textsuperscript{6} \\
&\text{NHOAc} \\
&\text{67} \\
&\text{1)} \text{Ti(OBu)}_{4}, \text{CH}_2\text{Cl}_2 \\
&\text{2)} \text{HNOAc} \rightarrow \text{HNQ}\textsuperscript{6} \\
&\text{10\%} \\
&\text{150}
\end{align*}
\]

General aziridination procedure A was followed in this reaction using NAQ\textsuperscript{6} (100mg, 0.41 mmol), LTA (188mg, 0.43 mmol) and 9,10-dihydroanthracene (110mg, 0.61 mmol) in dichloromethane (3 cm\textsuperscript{3}). After work up the crude product was isolated as a yellow solid (194mg). Column chromatography (4:1 light petroleum-ethyl acetate) gave unreacted 9,10-dihydroanthracene (92mg, 84% recovered), R\textsubscript{f} 0.75. Further elution gave 9-(Q\textsuperscript{6}-amino)-9,10-dihydroanthracene 150 (17mg, 10%) as a yellow oil, R\textsubscript{f} 0.47. [\alpha]D +75.5 (c=1.0, EtOH); (Found: MH\textsuperscript{+} 426.2182. C\textsubscript{27}H\textsubscript{28}O\textsubscript{3} requires M 426.2182); \nu\textsubscript{max}/cm\textsuperscript{-1} 1680s, 1595s and 1480m; \delta\textsubscript{H} 1.71 [9H, s, (CH\textsubscript{3})\textsubscript{3}], 2.58 (1H, d, J 8.5, CHO\textsubscript{H}), 4.05 (1H, d, J 18.5, CHH), 4.18 (1H, d, J 8.5, CHOH), 4.41 (1H, d, J 18.5, CHH), 5.34 (1H, d, J 1.9, CHNH), 5.49 (1H, d, J 1.9, NH), 6.71 [1H, d, J 7.2, CH(Ar)], 7.06 [1H, dd, J 7.6, 7.6, CH(Ar)], 7.30-7.82 [9H, m, 3 x CH(Q) & 6 x CH(Ar)] and 8.28 [1H, dd, J 8.2, 1.0, H-5(Q)]; m/z(%) 426 (M\textsuperscript{+},100).

Attempted reaction of 9-methyl-9,10-dihydroanthracene with Q\textsuperscript{3}NHOAc

\[
\begin{align*}
&\text{Q}\textsuperscript{3} \\
&\text{NHOAc} \\
&\text{71} \\
&\text{HMDS, CH}_2\text{Cl}_2 \\
&\text{Q}\textsuperscript{3} \\
&\text{NH}_2 \\
&\text{187} \\
&\text{Q}\textsuperscript{3} \\
&\text{H} \\
&\text{145}
\end{align*}
\]

General aziridination procedure A was followed in this reaction using NAQ\textsuperscript{3} (50mg, 0.25 mmol), LTA (115mg, 0.26 mmol), HMDS (80mg, 0.50 mmol) and 9-methyl-9,10-dihydroanthracene (96mg, 0.50 mmol) in dichloromethane (2 cm\textsuperscript{3}). Column
chromatography (3:1 light petroleum-ethyl acetate) of the crude product (178mg) gave unreacted 9-methyl-9,10-dihydroanthracene (89mg, 93% recovered) as a white crystalline solid, \( R_f \ 0.76 \).

Further elution gave \( \text{Q}^1 \text{H} \ 145 \) (26mg, 56%) \( R_f \ 0.16 \), identical to that isolated previously, and \( \text{187} \) (15mg, 30%) \( R_f \ 0.10 \).

**Attempted reaction of 9-methyl-9,10-dihydroanthracene with \( \text{Q}^5 \text{NHOAc} \)**

\[
\begin{align*}
\text{Q}^5 \text{NHOAc} & \xrightarrow{\text{HMDS, CH}_2\text{Cl}_2} \text{Q}^5 \text{NH}_2 + \text{HNNQ}^5 \\
\text{52} & \rightarrow \text{110}
\end{align*}
\]

General aziridination procedure A was followed in this reaction using \( \text{NAQ}^5 \) (113mg, 0.49 mmol), LTA (229mg, 0.52 mmol), HMDS (160mg, 0.99 mmol) and 9-methyl-9,10-dihydroanthracene (100mg, 0.52 mmol) in dichloromethane (3 cm\(^3\)). Column chromatography (4:1 light petroleum-ethyl acetate) of the crude product gave unreacted 9-methyl-9,10-dihydroanthracene (81mg, 81% recovered) \( R_f \ 0.68 \).

Further elution gave di(2-trifluoromethyl-3,4-dihydro-4-oxoquinazolin-3-yl)amine (76mg, 34%) \( R_f \ 0.27 \) - identified by a low field \( NH \) signal in its NMR spectrum at \( \delta \sim 10.0 \) - mp 178-179°C (lit. mp 178-179°C).\(^{134} \)
 Attempted reaction of Q₃NHOAc with fluorene

\[
\begin{align*}
Q^3 & \text{NHOAc} \\
71 & \\
\text{HMDS, CH₂Cl₂} & \\
\rightarrow & \\
\text{fluorene} & + \text{Q}^3 \text{H} \\
145 & 
\end{align*}
\]

General aziridination procedure A was followed in this reaction using NAQ³ (300mg, 1.47 mmol), LTA (687mg, 1.55 mmol), HMDS (474mg, 2.94 mmol) and fluorene (488mg, 2.94 mmol) and dichloromethane (6 cm³). After work up, NMR analysis of the crude product (857mg) showed the sample contained unreacted fluorene and Q³H 145. Similarly, no reaction was observed with anthrone, phenanthrene, diphenylmethane or tetraphenylecyclopentadiene.

Reaction of Q³NHOAc with xanthene

\[
\begin{align*}
Q^3 & \text{NHOAc} \\
71 & \\
\text{HMDS, CH₂Cl₂} & \\
\rightarrow & \\
\text{HNQ}^5 & + \text{Q}^3 \text{H} \\
151 & 
\end{align*}
\]

General aziridination procedure A was followed in this reaction using NAQ³ (266mg, 1.31 mmol), LTA (609mg, 1.38 mmol), HMDS (528mg, 3.20 mmol), xanthene (398mg, 2.62 mmol) and dichloromethane (6 cm³). Column chromatography (4:1 light petroleum-ethyl acetate) gave unreacted xanthene, Rf 0.74.

Further elution gave \((Q^3)\)-amine-substituted xanthene 151 (59mg, 13%) as a pale yellow oil, Rf 0.42. (Found: MH⁺ 384.1711. C₃₄H₂₂O₂N₃ requires M 384.1712); \(\nu_{\max }/\text{cm}^{-1}\) 1675 s, 1610 m, 1590 s and 1480 m; \(\delta_H\) 0.61 (3H, d, J 6.8, CH₃CHCH₃), 0.76 (3H, d, J 6.8, CH₃CHCH₃), 2.63 [1H, h, J 6.8, CH(CH₃)₂], 5.29 (1H, d, J 2.0, CHNH), 5.38 (1H, d, J 2.0, NH), 6.44 [1H, d, J 7.5, CH(Ar)], 6.78 [1H, dd, J 7.2, CH(Ar)],
Aziridination of 1,4-pentadiene with Q3NHOAc

General aziridination procedure A was followed in this reaction using NAQ3 (200mg, 0.96 mmol), LTA (459mg, 1.03 mmol), HMDS (318mg, 1.97 mmol) and 1,4-pentadiene (118mg/0.18 cm3, 1.97 mmol) in dichloromethane (4 cm3). Column chromatography (3: 1 light petroleum-ethyl acetate) of the crude product gave aziridine 153 (73mg, 28%) Rf 0.47, as a colourless crystalline solid mp 42-44°C (from light petroleum-ethyl acetate). (Found: M+ 269.1528. C16H19ON3 requires M 269.1528); νmax/cm−1 1670s, 1620m and 1590s; δH 1.39 (3H, d, J 6.6, CH3CHCH3), 1.42 (3H, d, J 6.6, CH3CHCH3), 2.34 (1H, dddd, J 14.4, 6.9, 1.9, 1.2, CHH), 2.46 (1H, dd, J 5.6, 1.9, azir. NCHH), 2.51 (1H, dd, J 7.5, 1.5, azir. NCHH), 2.87 (1H, ddd, J 14.4, 6.9, 1.5, CHH), 2.98 (1H, dddd, J 7.5, 6.9, 5.6, 1.2, azir. NCH), 3.71 [1H, hept, J 6.6, CH(CH3)2], 5.13 (1H, dd, J 10.8, 1.5, C=CHH), 5.18 (1H, ddd, J 16.2, 1.5, C=CHH), 5.91 (1H, dddd, J 16.2, 10.8, 6.9, 1.2, CH=CH2), 7.38 [1H, ddd, J 8.2, 6.6, 1.2, H-6(Q)], 7.61 [1H, dd, J 8.2, 1.2, H-8(Q)], 7.66 [1H, ddd, J 8.2, 6.6, 1.2, H-7(Q)] and 8.17 [1H, dd, J 8.2, 1.2, H-5(Q)]; δC 21.1, 21.8 (2 x CH3), 31.2 [CH(CH3)2], 35.8 (CH3), 40.9 (NCH3), 45.3 (NCH), 117.9 (C=CH2), 121.7 [CCO(Q)], 126.5, 127.1, 127.3, 133.7, 133.9 [4 x CH(Q) and C=CH2], 146.6 [CN=C(Q)] and 160.7, 161.6 [CN(Q), CO(Q)]; m/z(%) 269 (M+,41), 226 (37), 214 (100) and 213 (84).
Aziridination of 1,4-pentadiene with Q₅NHOAc

\[
\begin{align*}
Q^5 & \quad \text{NHOAc} \\
\text{HMDS, CH₂Cl₂} & \quad \rightarrow \\
\text{35%} & \quad \rightarrow \\
52 & \quad 154
\end{align*}
\]

General aziridination procedure A was followed in this reaction using NAQ₅ (225mg, 0.98 mmol), LTA (459mg, 1.03 mmol), HMDS (318mg, 1.97 mmol) and 1,4-pentadiene (118mg/0.18 cm³, 1.97 mmol) in dichloromethane (5 cm³). Column chromatography (3:1 light petroleum-ethyl acetate) of the crude product (156mg) gave aziridine 154 (103mg, 35%) Rf 0.71, as a colourless solid mp 44-45°C (from light petroleum-ethyl acetate). (Found: M⁺ 295.0932. C₁₄H₁₂O₃N₃F₃ requires M 295.0932; νmax/cm⁻¹ 1690s and 1610m; δH 2.18 (1H, dd, J 4.7, 1.5, azir. NCHR), 2.28 (1H, ddd, J 15.0, 6.6, 1.2, CHH), 2.55 (1H, dddd, J 15.0, 6.9, 1.5, 1.5, CHH), 3.41 (1H, dd, J 7.5, 1.2, azir. NCHH), 3.72 (1H, ddd, J 7.5, 6.9, 4.7, azir. NCH), 5.10 (1H, dd, J 9.9, 1.5, C=CHH), 5.15 (1H, dd, J 17.0, 1.5, C=CHH), 5.86 (1H, dddd, J 17.0, 9.9, 6.9, C=CH₂), 7.57 [1H, dddd, J 8.2, 4.0, H-6(Q)], 7.79 [2H, d, J 4.0, H-7 and H-8(Q)] and 8.19 [1H, d, J 8.2, H-5(Q)]; δC 34.8, 36.0 (2 x CH₂), 39.2 (NCH), 117.7 (C=CH₂), 123.4 [CCO(Q)], 126.8, 128.3, 129.4, 133.8, 135.0 [4 x CH(Q), C=CH], 143.8 [CN(Q)], 144.3 [CN=C(Q)] and 161.2 [CO(Q)] - (CF₃ not visible); m/z(%) 296 (M⁺,100) and 214 (62).

Aziridination of allylbenzene with Q³NHOAc

\[
\begin{align*}
Q^3 & \quad \text{NHOAc} \\
\text{HMDS, CH₂Cl₂} & \quad \rightarrow \\
\text{28%} & \quad \rightarrow \\
71 & \quad 156
\end{align*}
\]

General aziridination procedure A was followed in this reaction using NAQ³ (266mg, 1.31 mmol), LTA (609mg, 1.38mmol), HMDS (528mg, 3.28 mmol) and allylbenzene (310mg, 2.62 mmol) in dichloromethane (6 cm³). Column chromatography (3:1 light
petroleum-ethyl acetate) of the crude product (280mg) gave aziridine 156 (117mg, 28%) as a yellow oil, Rf 0.58. (Found: M⁺ 319.1684. C₂₀H₂₁ON₃ requires M 319.1684); ν_max/cm⁻¹ 1670s, 1620m and 1595s; δ_H 1.53 (3H, d, J 6.9, CH₃CHCH₃), 1.58 (3H, d, J 6.9, CH₂CHCH₂), 2.67 (1H, dd, J 6.0, 1.5, azir. NCHH), 2.69 (1H, dd, J 7.8, 1.5, azir. NCHH). 2.96 (1H, dd, J 14.2, 7.0, CHH), 3.33 (1H, dddd, J 7.8, 7.0, 6.0, 4.4, azir. NCH), 3.75 (1H, dd, J 14.2, 4.4, CHH), 3.83 [1H, h, J 6.9, CH(CH₃)₂], 7.47 [5H, struct. m. 5 x CH(Ar)], 7.58 [1H, dddd, J 8.0, 6.6, 1.8, H-6(Q)], 7.79 [1H, dd, J 8.2, 1.8, H-8(Q)], 7.85 [1H, dddd, J 8.2, 6.6, 1.0, H-7(Q)] and 8.37 [1H, dd, J 8.0, 1.0, H-5(Q)]; δ_C 21.2, 21.7 [CH(CH₃)₂], 31.2 [CH(CH₃)₂], 37.9 (CH₂), 41.4 (NCH₂), 46.7 (NCH), 121.7 [CCO(Q)], 126.5, 127.1, 127.4, 128.8, 129.0, 129.5, 134.0 [5 x CH(Ar) and 4 x CH(Q)], 137.7 [C(Ar)], 146.7 [CN=C(Q)] and 160.8, 161.6 [CN(Q), CO(Q)]; m/z(%) 319 (M⁺,100) and 214 (48).

Aziridination of allylbenzene with Q⁵NHOAc

General aziridination procedure A was followed in this reaction using NAQ⁵ (300mg, 1.31 mmol), LTA (609mg, 1.38 mmol), HMDS (528mg, 3.28 mmol) and allylbenzene (310mg, 2.62 mmol) in dichloromethane (6 cm³). Column chromatography (3:1 light petroleum-ethyl acetate) of the crude product (281mg) gave aziridine 157 (154mg, 34%) as a yellow oil, Rf 0.67. (Found: M⁺ 345.1089. C₁₈H₁₄ON₃F₃ requires M 345.1088); ν_max/cm⁻¹ 1690s and 1610m; δ_H 2.14 (1H, dd, J 4.8, 1.2, azir. NCHH), 2.61 (1H, dd, J 14.5, 7.3, CHH), 3.15 (1H, dd, J 14.5, 5.3, CHH), 3.33 (1H, dd, J 7.3, 1.2, azir. NCHH), 3.84 (1H, dddd, J 7.3, 7.3, 5.3, 4.8, azir. NCH), 7.16 [5H, struct. m. 5 x CH(Ar)], 7.47 [1H, dddd, J 7.9, 4.4, H-6(Q)], 7.70 [2H, struct. m. H-7 and H-8(Q)] and 8.09 [1H, d, J 7.8, H-5(Q)]; δ_C 35.1, 37.9 (2 x CH₂), 40.4 (NCH), 123.1 (CCO(Q)), 126.5, 126.6, 128.5, 128.6, 128.9, 134.7 [5 x CH(Ar) and 4 x CH(Q)], 137.6 [C(Ar)], 195
Aziridination of 1,3-cycloheptadiene with $Q^3$NHOAc

The reaction was carried out following general aziridination procedure A using $NAQ^3$ (300mg, 1.48 mmol), LTA (689mg, 1.55 mmol), HMDS (597mg, 3.70 mmol) and 1,3-cycloheptadiene (272mg/0.30 cm$^3$, 2.96 mmol) in dichloromethane (6 cm$^3$). After work up the crude product was obtained as an off-white solid which was crystallised from ethyl acetate-light petroleum giving aziridine 158 (135mg, 31%) as a white crystalline solid, mp 230-231°C. (Found: C, 72.9; H, 7.0; N, 14.2%. $C_{18}H_{22}ON_3$ requires C, 73.1; H, 7.1; N, 14.2%); $\nu_{\text{max}}$/cm$^{-1}$ 1660s and 1585m; $\delta_H$ 1.40 (3H, d, $J$ 6.4, $CH(\text{CH}_3)_2$), 1.42 (3H, d, $J$ 6.4, $CH(\text{CH}_3)$), 1.63-1.84 (2H, struct. m, $CH_2$), 2.06 (1H, m, incl. $J$ 10.7, 4.1, $CHH$), 2.13 (1H, dd, $J$ 10.7, 3.5, $CHH$), 2.35 (1H, struct. m, $CHH$), 2.58 (1H, struct. m, $CHH$), 2.94 (1H, ddd, $J$ 8.0, 4.1, 3.5, azir. NCH$CH_2$), 3.18 (1H, ddd, $J$ 8.0, 4.8, azir. NCH$CH_2$), 3.65 [1H, h, $J$ 6.4, $CH(\text{CH}_3)_2$], 5.95 (1H, ddd, $J$ 11.4, 6.6, 3.2, C--$CH_2$), 6.13 (1H, ddd, $J$ 11.4, 4.8, 2.3, NCH$CH_2$), 7.39 [1H, ddd, $J$ 8.2, 6.8, 1.0, H-6(Q)], 7.62 [1H, dd, $J$ 8.2, 1.0,H-8(Q)], 7.67 [1H, ddd, $J$ 8.2, 6.8, 1.2, H-7(Q)] and 8.18 [1H, dd, $J$ 8.2, 1.2, H-5(Q)]; $\delta_C$ 21.4, 21.5 [$CH(\text{CH}_3)_2$], 23.7, 28.9 (2 x CH$_2$), 31.1 [$CH(\text{CH}_3)_2$], 31.9 (CH$_2$), 50.6, 54.7 (2 x C-N), 121.7 [CCO(Q)], 122.9, 126.4, 126.5, 127.3, 133.8, 138.1 [4 x CH(Q), HC=CH], 146.6 [CN=C(Q)] and 160.5, 161.6 [CN(Q), CO(Q)]; m/z(%) 296 (MH$^+$,100).
Aziridination of 1,3-cycloheptadiene with Q6NHOAc

General aziridination procedure D was followed in this reaction using NAQ6 (200mg, 0.81 mmol), LTA (396mg, 0.89 mmol), TTB (576mg, 1.69 mmol) and 1,3-cycloheptadiene (152mg/0.18 cm³, 2.96 mmol) in dichloromethane (5 cm³). Work up in the normal way gave a light green solid which was crystallised from ethyl acetate-light petroleum giving aziridine 159 (79mg, 29%) as a colourless solid, mp 173-174°C. [Ω]D = +126.9° (c=1.3, EtOH); (Found: MH+ 340.2025. C20H26O2N3 requires MH+ 340.2026); v max/cm⁻¹ 3490m, 1720s and 1580m; δH 1.02 [9H, s, C(CH₃)₃], 1.69-2.09 (4H, struct. m, 2 x CH₂), 2.37 (1H, m, incl. J 15.3, 4.1, NCHCHH), 2.81 (1H, m, incl. J 15.3, NCHCHH), 2.90 (1H, dd, J 8.0, 4.1, azir. NCHCH₂), 3.37 (1H, ddd, J 8.0, 4.8, azir. NCH=C), 3.77 (1H, d, J 10.4, CHOH), 5.08 (1H, d, J 10.4, CHOH), 6.01 (1H, ddd, J 11.9, 6.2, 2.0, C=CHCH₂), 6.10 (1H, ddd, J 11.9, 4.8, 2.5, NCHCH=C), 7.45 [1H, ddd, J 8.0, 6.9, 1.0, H-6(Q)], 7.64 [1H, dd, J 8.2, 1.0, H-8(Q)], 7.71 [1H, ddd, J 8.2, 6.9, 1.0, H-7(Q)] and 8.21 [1H, dd, J 8.0 1.0, H-5(Q)]; δC 23.1 (CH₃), 26.0 [C(CH₃)₃], 28.8, 31.7 (2 x CH₂), 38.4 [C(CH₃)₃], 52.4, 54.4 (2 x C-N), 74.5 (COH), 121.5 [COC(Q)], 121.6, 126.3, 126.7, 126.9, 133.8 [4 x CH(Q), HC=CH], 139.5 (HC=CH), 144.7 [CN=C(Q)] and 157.6, 159.5 [CN(Q), CO(Q)], m/z(%): 340 (MH+,100), 307 (78), 289 (39) and 215 (32).
Aziridination of cycloheptatriene with $Q^3$NHOAc

General aziridination procedure A was followed in this reaction using NAQ$^3$ (300mg, 1.48 mmol), LTA (687mg, 1.55 mmol), HMDS (597mg, 3.69 mmol) and cycloheptatriene (272mg, 0.29 cm$^3$, 2.96 mmol) in dichloromethane (6 cm$^3$) to give the crude product as a yellow oil. Column chromatography (4:1 light petroleum-ethyl acetate) gave aziridine 161 (193mg, 45%) $R_f$ 0.42, as colourless oil which crystallised from ethyl acetate-light petroleum, mp 89-90°C. (Found: MH$^+$ 294.1606. C$_{18}$H$_{20}$O$_3$ requires M 294.1606); $v_{max}$/cm$^{-1}$ 1660s and 1590s; $\delta_H$ 1.42 [6H, d, $J$ 6.6, (CH$_3$)$_2$], 2.84 (1H, dd, $J$ 7.5, 4.8, azir. NCHCH$_2$), 2.97 (1H, m, incl. $J$ 8.0, CHH), 2.99 (1H, m, incl. $J$ 8.0, 3.8, CHH), 3.34 (1H, dd, $J$ 7.5, 4.8, azir. NCHC=C), 3.63 [1H, sept, $J$ 6.6, CH(CH$_3$)$_2$], 5.95 (2H, m, 2 x C=CHCH=C), 6.01 (1H, ddd, $J$ 11.2, 4.8, NCHCH=C), 6.47 (1H, dd, $J$ 11.0, 3.8, C=CHCH$_2$), 7.39 [1H, ddd, $J$ 8.2, 6.6, 1.2, H-6(Q)], 7.63 [1H, dd, $J$ 8.2, 1.2, H-8(Q)], 7.67 [1H, ddd, $J$ 8.2, 6.6, 1.0, H-7(Q)] and 8.17 [1H, dd, $J$ 8.2, 1.0, H-5(Q)]; $\delta_C$ 21.1 [CH(CH$_3$)$_2$], 28.7 (CH$_2$), 30.8 [CH(CH$_3$)$_2$], 48.9, 58.3 (2 x C=N), 121.2 [CCO(Q)], 126.1, 127.0, 127.7, 127.8, 130.6, 130.9 [3 x CH(Q), 2 x HC=CH, 133.5 [CH(Q)], 146.1 [CN=C(Q)] and 160.1, 161.1 [CN(Q), CO(Q)]; $m/z$(%) 294 (MH$^+$,100), 189 (39) and 173 (31).
Reaction of dienylamine 143 with bromine

\[
\begin{align*}
\text{NHQ}^2 & \quad \text{Br}_2, \text{CH}_2\text{Cl}_2 \\ 143 & \quad \text{43\%} \\ \text{NHQ}^3 & \quad \text{163}
\end{align*}
\]

Dienylamine 143 (51 mg, 0.18 mmol) was dissolved in dichloromethane (1 cm³), bromine (29 mg/0.01 cm³, 0.18 mmol) added dropwise and the mixture stirred for 2 h, during which time the bromine colour disappeared. Addition of dichloromethane (10 cm³) and washing with saturated sodium hydrogen carbonate solution (10 cm³), drying and evaporation of the organic solvent gave a yellow oil. Column chromatography (4:1 light petroleum-ethyl acetate) gave unchanged dienylamine 143 (18 mg, 35% recovered) as a colourless oil, Rf 0.46.

Further elution gave epoxide 163 (23 mg, 43%) as a yellow oil, Rf 0.23. (Found: MH⁺ 298.1556. C₁₇H₂₀O₂N₃ requires M 298.1555; νmax/cm⁻¹ 1680s, 1595s and 1470m; δH(400 MHz) 1.36 (3H, d, J 6.6, CH₂CH₃), 1.40 (3H, d, J 6.6, CH₃CHCH₃), 2.42 (1H, ddd, J 19.7, 5.3, 3.0, CHH trans to epoxide), 2.68 (1H, ddd, J 19.7, 6.7, 1.3, CHH cis to epoxide), 3.33 (1H, ddd, J 5.0, 4.1, 2.2, epox. NCCHO), 3.44 (1H, ddd, J 4.1, 3.0, 2.2, 1.3, epox. CHOCH₂), 3.94 [JH, sept, J 6.6, CH(CH₃)₂], 4.00 (1H, dd, J 4.0, 4.4, 2.0, CHNH), 5.56 (1H, ddd, J 10.6, 4.4, 2.2, CH=CHCHNH), 5.66 (1H, dddd, J 10.6, 6.7, 5.3, 2.2, C=CHCH₂), 5.81 (1H, br s, NH), 7.46 [JH, ddd, J 8.2, 6.8, 1.4, H-6(Q)], 7.72 [JH, dd, J 8.2, 1.4, H-8(Q)], 7.76 [JH, ddd, J 8.2, 6.8, 1.4, H-7(Q)] and 8.28 [JH, dd, J 8.2, 1.4, H-5(Q)]; δC(75 MHz) 20.8, 21.8 [CH(CH₃)₂], 25.5 (CH₂), 30.9 [CH(CH₃)₂], 52.0 (C-N), 52.5, 56.1 (2 x C-O), 120.9 [CCO(Q)], 122.4, 125.1, 126.6, 126.9, 127.8, 134.7 [4 x CH(Q), HC=CH], 147.7 [CN=C(Q)] and 162.2, 163.7 [CN(Q), CO(Q)]; m/z(%) 320 (MNa⁺, 100), 298 (MH⁺, 94) and 204 (88).
Bromination of aziridine 144

[Diagram]

Aziridine 144 (50mg, 0.18 mmol) was dissolved in dichloromethane (1 cm³) containing bromine (28mg/0.01 cm³, 0.18 mmol) and the mixture stirred at ambient temperature until the bromine colour had disappeared (~2 h). Addition of further dichloromethane (10 cm³), washing with saturated aqueous sodium hydrogen carbonate (10 cm³) and separation, drying and evaporation of the solvent gave the crude product as a colourless solid. Crystallisation from ethyl acetate-light petroleum gave dibromide 165 (63mg, 81%) as a colourless solid, mp 179-180°C. (Found: MH⁺ 439.9973. C₁₇H₂₉O₃N₃Br₂ requires M 439.9973); δH 1.51 [6H, d, J 6.6, CH(CH₃)₂], 2.68 (1H, ddd, J 14.5, 7.5 6.0, CHH-cis), 2.97 (1H, ddd, J 15.5, 7.3, 6.4, CHH-cis), 3.08 (1H, dd, J 7.5, 6.4, azir. NCH), 3.13 (1H, dd, J 14.5, 4.2, CHH-trans), 3.18 (1H, ddd, J 7.5, 6.0, 1.6, azir. NCH), 3.34 (1H, ddd, J 15.5, 4.1, 1.6, CHH-trans), 3.57 [1H, h, J 6.6, CH(CH₃)₂], 4.37 (1H, ddd, J 12.0, 7.3, 4.1, CHBr), 4.45 (1H, ddd, J 12.0, 7.5, 4.2, CHBr), 7.48 [1H, ddd, J 8.2, 6.6, 1.5, H-6(Q)], 7.70 [1H, dd, J 8.2, 1.5, H-8(Q)], 7.76 [1H, ddd, J 8.2, 6.6, 1.0, H-7(Q)] and 8.23 [1H, dd, J 8.2, 1.0, H-5(Q)]; δc 21.1, 21.3 [CH(CH₃)₂], 31.3 (CH₂), 31.7 [CH(CH₃)₂], 32.2 (CH₂), 44.1, 44.9 (2 x C-N), 48.2, 49.5 (2 x CHBr), 121.6 [CCO(Q)], 126.4, 126.7, 127.5, 134.1 [4 x CH(Q)], 146.5 [CN=C(Q)] and 160.7, 161.0 [CN(Q), CO(Q)]; m/z(%) 443 (MH⁺,48), 441 (MH⁺,100), 439 (MH⁺,52) and 281 (53).
Bromination of dienylamine 143 in dichloromethane saturated with hydrogen sulphide gas

Dienylamine 143 (51 mg, 0.18 mmol) was dissolved in dichloromethane (1 cm³) previously saturated with hydrogen sulphide gas. Bromine (29 mg/0.01 cm³, 0.18 mmol) was added dropwise and the mixture stirred for 2 h until the bromine colour was discharged. Addition of dichloromethane (10 cm³), washing the dichloromethane solution with saturated aqueous sodium hydrogen carbonate (10 cm³) then drying and evaporation gave a yellow solid. Column chromatography (4:1 light petroleum-ethyl acetate) gave unchanged dienylamine 143 (17 mg, 34% recovered) as a colourless oil, R f 0.46.

Further elution gave bromohydrin 167 (13 mg, 19%) as a yellow oil, R f 0.23. (Found: MH + 378.1753. C 17 H 21 O 2 N 3 Br requires M 378.1752); ν max/cm -1 1660 s, 1615 m and 1590 s; δ H 1.36 [6H, d, J 6.9, (CH₃)₂], 2.70 (1H, dddd, J 18.8, 5.7, 3.6, 1.5, CHH-cis to OH), 3.01 (1H, dddd, J 18.8, 5.7, 5.0, 2.1, CHH-trans to OH), 3.44 [1H, hept, J 6.8, CH(CH₃)₂], 3.83 (1H, ddd, J 5.7, 3.6, 3.6, CHBr), 3.94 (1H, ddd, J 4.9, 3.6, 1.1, CHNH), 4.41 (1H, q, J 5.7, CHOH), 5.09 (1H, br s, COH), 5.59 (1H, dddd, J 9.8, 4.9, 2.1, 1.5, CH=CH₂), 5.81 (1H, dddd, J 9.8, 5.0, 3.6, 1.1, C=CHCH₂), 5.84 (1H, br s, NH), 7.31 [1H, ddd, J 8.0, 6.9, 1.2, H-6(Q)], 7.58 [1H, dd, J 8.2, 1.2, H-8(Q)], 7.63 [1H, ddd, J 8.2, 6.9, 1.0, H-7(Q)] and 8.10 [1H, dd, J 8.0, 1.0, H-5(Q)]; m/z(%) 378 (MH + .100), 251 (63) and 203 (24).

Further elution gave quinazolin-4-thione 168 (8 mg, 11%) as a yellow oil, R f 0.19. (Found: MH + 394.0589. C 17 H 21 ON₂ BrS requires M 394.0588); δ H 1.37 [6H, d, J 6.8,
(CH₃)₂], 2.69 (1H, dddd, J 19.0, 5.6, 3.7, 1.6, CHH), 3.02 (1H, dddd, J 19.0, 5.6, 4.4, 2.5, CHH), 3.08 [1H, hept, J 6.8, CH(CH₃)₂], 4.08 (1H, m, incl. J 5.3, 4.0, CHNH), 4.53 (1H, ddd, J 7.3, 5.6, 5.6, CHOH), 4.85 (1H, dd, J 7.3, 4.0, CHBr), 5.19 (1H, br s, COH), 5.65 (1H, dddd, J 9.9, 5.3, 2.5, 1.6, CH=CHCH₂), 5.88 (1H, dddd, J 9.9, 4.4, 3.7, 1.1, C=CHCH₂), 7.21 [1H, dddd, J 8.0, 7.2, 1.6, H-6(Q)], 7.42 [1H, dddd, J 8.0, 7.2, 1.1, H-7(Q)], 7.85 [1H, dd, J 8.0, 1.6, H-8(Q)], 9.45 [1H, d, J 8.0, H-5(Q)] and 12.59 (1H, br s, NH): m/z(%) 394 (MH⁺, 20), 380 (23), 378 (24), 362 (100), 360 (94), 329 (21), 307 (89) and 289 (81).
Experimental relating to Chapter 4
Ring-opening of aziridine 138 with 4-chlorothiophenol

Aziridine 138 (100mg, 0.3 mmol; 4:1 diastereoisomer ratio) was dissolved in dichloromethane (2 cm³) containing 4-chlorothiophenol (89 mg, 0.61 mmol) and heated at 90°C in a sealed Young’s tube for 2 h. After cooling, saturated sodium hydrogen carbonate solution (10 cm³) was added and the mixture extracted with dichloromethane (10 cm³) giving a light brown solid after drying and evaporation of the solvent. Column chromatography (6:1 light petroleum-ethyl acetate) gave 4-chlorothiophenol followed by the ring-opened aziridine which was rechromatographed using Kieselgel (8:1 light petroleum-ethyl acetate) to give allylsulphide 172 (14mg, 10%) Rf 0.21, as a colourless crystalline solid, mp 91-93°C (from ethanol). [α]D +25.3° (c=1.0, EtOH); (Found: MH+ 470.1669. C25H29O2N3ClS requires M 470.1669); νmax/cm⁻¹ 1695m, 1680s, 1670m and 1595s; δh(300 MHz) 0.85 [9H, s, (CH₃)₃], 1.78 (1H, dd, J 13.0, 5.2, C=CCHH), 2.02 (1H, dd, J 16.6, 5.2, NHCHCHH), 2.14 (1H, ddd, J 13.0, 5.8, 4.4, C=CCHH), 2.25 (1H, ddd, J 16.6, 5.8, 2.6, NHCHCHH), 3.38 (2H, m, CHNH and CHSAr), 3.53 (1H, d, J 10.1, CHOH), 4.98 (1H, d, J 10.1, CHOH), 5.16 (1H, br s, NH), 5.81 (1H, dd, J 9.9, 1.8, CH=CCH₂), 5.99 (1H, d, J 9.9, 4.4, C=CHCH₂), 6.55 (2H, d, J 8.4, 2 x CH(Ar)), 6.86 [2H, d, J 8.4, 2 x CH(Ar)], 7.46 [1H, ddd, J 8.1, 6.9, 1.1, H-6(Q)], 7.70 [1H, dd, J 8.1, 1.1, H-8(Q)], 7.76 [1H, ddd, J 8.1, 6.9, 1.1, H-7(Q)] and 7.99 [1H, dd, J 8.1, 1.1, H-5(Q)]; m/z(%) 470 (MH⁺,100), 231 (71), 222 (98).
Further elution gave *allylsulphide* 173 (59mg, 42%) as a colourless oil, Rf 0.18. (Found: MH+ 470.1669. C25H29O2N3S requires M 470.1669); νmax/cm−1 1690m, 1675s, 1665m and 1590s; δH(300 MHz) 0.89 [9H, s, (CH3)3], 1.59 (1H, dd, J 6.8, 5.7, NHCHCHH), 1.65 (1H, dd, J 5.7, 2.5, NHCHCHH), 2.04 (1H, ddd, J 11.9, 6.8, 5.7, CHCHSAr), 2.18 (1H, ddd, J 11.9, 5.7, 3.5, CHSAr), 3.53 (1H, d, J 9.9, CHO), 3.71 (1H, m, incl. J 5.5, CHNH), 3.78 (1H, d, J 3.5, CHSAr), 4.96 (1H, d, J 9.9, CHOH), 5.38 (1H, d, J 5.5, NH), 5.53 (1H, m, incl. J 9.5, CH=CH), 5.91 (1H, dd, J 9.5, 2.5, C=CH), 7.28 [2H, d, J 8.4, 2 x CH(Ar)], 7.33 [2H, d, J 8.4, 2 x CH(Ar)], 7.43 [1H, ddd, J 8.1, 6.9, 1.0, H-6(Q)], 7.63 [1H, dd, J 8.1, 1.0, H-8(Q)], 7.71 [1H, ddd, J 8.1, 6.9, 1.1, H-7(Q)] and 8.18 [1H, dd, J 8.1, 1.1, H-5(Q)]; m/z(%) 470 (MH+,100), 307 (87) and 231 (54).

Further elution gave *aziridine* 138 (27mg, 27% recovered) as a colourless paste, Rf 0.18.

The reaction above was repeated using a sample of *aziridine* 138 (100mg, 0.30 mmol) consisting of only the major diastereoisomer giving *sulphides* 172 (7mg, 5%) and 173 (28mg, 20%) as single diastereoisomers.

**Oxidation of sulphide 172**

![Diagram](image) Allylsulphide 172 (20mg, 42.5 μmol) was stirred in glacial acetic acid (10 cm³) containing hydrogen peroxide (1.4mg/5 μl, 42.5 μmol) for 2 h. Addition of ethyl acetate (10 cm³) and washing with saturated sodium hydrogen carbonate solution (10 cm³) gave the crude product as a colourless oil after drying and evaporation of the solvent. Column chromatography (2:1 light petroleum-ethyl acetate) gave unreacted *sulphide* 172 (17mg, 85% recovered) as a colourless crystalline solid, Rf 0.21.
Oxidation of sulphide 173

Allylsulphide 173 (40mg, 85.1 μmol - derived from a 5:1 mixture of diastereoisomers of aziridine 138) was stirred in glacial acetic acid (10 cm³) containing hydrogen peroxide (2.8mg/10 μl, 82.1 μmol) for 2h. Addition of ethyl acetate (10 cm³) and washing with saturated sodium hydrogen carbonate solution (10 cm³) gave the crude product as a colourless oil after drying and evaporation of the solvent. Column chromatography (4:1 light petroleum-ethyl acetate) gave sulphoxide 174 (25mg, 62%) as a colourless oil, R<sub>f</sub> 0.40.

Sulphoxide 174 (25mg, 51.4 μmol) was heated at reflux in carbon tetrachloride (1 cm³) under nitrogen for 2 h. On cooling, addition of ethyl acetate (10 cm³) to the reaction mixture and washing with saturated sodium hydrogen carbonate solution (10 cm³) gave the crude product as a colourless oil after drying and evaporation of the solvent. Column chromatography (4:1 light petroleum-ethyl acetate) gave dienylamine 139 (15mg, 90%) R<sub>f</sub> 0.35, as a colourless oil whose NMR spectrum showed the presence of a 3:1 ratio of diastereoisomers, from comparison of this compound previously isolated and in particular the signals at δ5.37 and 5.16.
Formation of dienylamine 139 from the major diastereoisomer of aziridine 138

The reaction above was repeated using allylsulphide 173 (20mg, 42.5 μmol) obtained from ring-opening of the pure major diastereoisomer of aziridine 138 with 4-chlorothiophenol. Stirring in acetic acid (1 cm³) with hydrogen peroxide (1.4mg/5 μl, 42.5 μmol) for 2 h gave the corresponding sulphoxide 174 (8mg, 38%, 1.6 μmol) after work up. Heating under reflux in carbon tetrachloride (1 cm³) for 2 h, work up as described above and column chromatography (4:1 light petroleum-ethyl acetate) gave dienylamine 139 (4mg, 88%) R₇ 0.35, as a colourless oil whose NMR spectrum showed the presence of a single diastereoisomer, identical with that isolated as the by-product in reaction of 1,3-cyclohexadiene with Q₆NHOAc (see Chapter 3).

Ring-opening of aziridine 144 with 4-chlorothiophenol

Aziridine 144 (96mg, 0.34mmol) was heated at 90°C in neat 4-chlorothiophenol (98mg, 0.68mmol) for 2 h. After cooling, the reaction mixture was dissolved in dichloromethane (10 cm³) and washed with saturated sodium hydrogen carbonate solution (15 cm³). Separation, drying and evaporation of the solvent followed by column chromatography (4:1 light petroleum-ethyl acetate) of the resultant solid gave 4-chlorothiophenol (52mg, 51% recovered) as a colourless solid, R₇ 0.80.
Further elution gave arylsulphide 169 (58mg, 40%) as a colourless oil, Rf 0.40. (Found: MH+ 426.1407. C25H25ON3S requires M 426.1406); νmax/cm⁻¹ 1695s, 1680s, 1670m and 1595s; δH 1.21 (3H, d, J 6.9, CH₃CHCH₃), 1.35 (3H, d, J 6.9, CH₃CHCH₃), 2.07 (2H, br s, CH₂), 2.20 (1H, ddd, J 18.0, 5.5, 2.4, CHH), 2.63 (1H, dd, J 18.0, 3.5, 1.8, CHH), 3.37 (1H, br s, CHSAr), 3.70 [1H, hept, J 6.9, CH(CH₃)₂], 3.82 (1H, br s, CHNH), 5.60 (2H, br s, H=CH), 6.20 (1H, br s, NH), 7.30 [2H, d, J 7.8, 2 x CH(Ar)], 7.44 [1H, ddd, J 8.2, 6.9, 1.2, H-6(Q)], 7.5-7.6 [2H, m, 2 x CH(Ar)], 7.67 [1H, dd, J 8.2, 1.2, H-8(Q)], 7.73 [1H, ddd, J 8.2, 6.9, 1.0, H-7(Q)] and 8.22 [1H, dd, J 8.2, 1.0, H-5(Q)]; m/z(%) 426 (MH⁺, 45), 223 (100) and 204 (38).

Further elution gave unreacted aziridine 144 (25mg, 26% recovered), Rf 0.23.

Ring-opening of aziridine 141 with 4-chlorothiophenol

Aziridine 141 (87mg, 0.27mmol) was heated at 90°C in neat 4-chlorothiophenol (77mg, 0.53 mmol) for 2 h. After cooling, the reaction mixture was dissolved in dichloromethane (10 cm³) and washed with saturated sodium hydrogen carbonate solution (15 cm³). Separation, drying and evaporation of the solvent followed by column chromatography (4:1 light petroleum-ethyl acetate) of the resultant solid gave 4-chlorothiophenol (52mg, 51% recovered) as a colourless solid, Rf 0.80. Further elution gave aziridine 141 (80mg, 92% recovered) as a colourless crystalline solid, Rf 0.23.
The reaction was repeated but heated under reflux at 90°C in a sealed Young’s tube for 24 h. On cooling, an NMR spectrum of the crude product showed the bulk of aziridine 141 was unchanged; being isolated by column chromatography (6:1 light petroleum-ethyl acetate) in 90% yield.

**Ring-opening of aziridine 144 with thiophenolate**

Aziridine 144 (60mg, 0.20 mmol) was dissolved in acetonitrile (1 cm³) containing 4-chlorothiophenol (28mg, 0.20 mmol) and sodium hydroxide (4mg, 0.11 mmol) and heated at 90°C in a sealed Young’s tube for 30 min. During this period the solution turned cloudy. On cooling, saturated sodium hydrogen carbonate solution (10 cm³) was added and the mixture extracted with ethyl acetate (2 x 10 cm³) giving the crude product as a light brown solid. Column chromatography (6:1 light petroleum-ethyl acetate) gave a mixture of products. Subsequent Kieselgel chromatography gave 4-chlorothiophenol, Rf 0.70, arylsulphide 169 (38mg, 45%) Rf 0.43, as a colourless oil, identical with that isolated previously and aziridine 144 (20mg, 33% recovered) as a crystalline solid, Rf 0.31.

**Ring-opening of aziridine 141 with thiophenolate**

Aziridine 141 (108mg, 0.33 mmol) was dissolved in acetonitrile (1 cm³) containing 4-chlorothiophenol (48mg, 0.33 mmol) and sodium hydroxide (10mg, 0.25 mmol), and
heated at 90°C in a sealed Young’s tube for 1 h. During this period the solution turned cloudy. After cooling, saturated sodium hydrogen carbonate solution (10 cm³) was added and the mixture extracted with ethyl acetate (2 x 10 cm³) giving the crude product as a light brown solid after drying and evaporation of the solvent. Column chromatography (6:1 light petroleum-ethyl acetate) gave a mixture of the ring-opened product and excess 4-chlorothiophenol. Re-chromatography using Kieselgel (8:1 light petroleum-ethyl acetate) gave 4-chlorothiophenol (Rf 0.68). Further elution gave arylsulphide 170 (71 mg, 46%) as a colourless oil, Rf 0.31. (Found: MH⁺ 470.1669. C₂₅H₂₉O₂N₃ClS requires M 470.1669); v max/cm⁻¹ 3400w, 1695s, 1680s, 1670m and 1595s; δH(300 MHz) 0.92 [9H, s, (CH₃)₃], 2.05 (2H, m, incl. J 12.0, 6.0, NHCHCH₂), 2.09 (1H, ddd, J 18.0, 15.8, 2.0, CHHCHSAr), 2.61 (1H, dd, J 18.0, 5.5, CHHCHSAr), 3.35 (1H, ddd, J 15.8, 9.0, 5.5, CHSAr), 3.58 (1H, d, J 10.1, CHO), 3.67 (1H, ddd, J 9.0, 6.0, 2.3, CHNH), 5.19 (1H, d, J 10.1, CHO), 5.53 (1H, dd, J 9.9, 1.8, CH=C), 5.60 (1H, dd, J 9.9, 2.0, C=CH), 6.11 (1H, d, J 2.3, NH), 7.32 [2H, d, J 8.4, 2 x CH(Ar)], 7.50 [1H, ddd, J 8.1, 6.9, 1.1, H-6(Q)], 7.57 [2H, d, J 8.4, 2 x CH(Ar)], 7.70 [1H, d, J 8.2, H-8(Q)], 7.79 [1H, ddd, J 8.2, 6.9, 1.1, H-7(Q)] and 8.28 [1H, dd, J 8.1, 1.1, H-5(Q)]; m/z(%) 470 (MH⁺, 100) and 307 (87).

**Oxidation of sulphide 170**

\[
\begin{align*}
\text{ArS} & \xrightleftharpoons[H₂O₂, AcOH]{} \text{NHQ₈}^+ \\
170 & \xrightarrow{\text{CCl₄, heat}} \text{NHQ₈}^+ \\
\end{align*}
\]

Arylsulphide 170 (102 mg, 0.22 mmol) was stirred in glacial acetic acid (10 cm³) containing hydrogen peroxide (7 mg/23 µl, 0.22 mmol) for 2 h. Addition of ethyl acetate (10 cm³) and washing with saturated sodium hydrogen carbonate solution (10 cm³) gave the crude product as a colourless oil after separation, drying and
evaporation of the solvent. Column chromatography (6:1 light petroleum-ethyl acetate) gave the corresponding sulphoxide (49mg, 46%) as a colourless oil, R_f 0.41. The sulphoxide was heated at reflux in carbon tetrachloride (1 cm^3) under nitrogen for 2 h. After cooling, dichloromethane (10 cm^3) was added, the solution washed with saturated sodium hydrogen carbonate solution (10 cm^3), dried and evaporated to give the crude product as a colourless oil. Column chromatography (3:1 light petroleum-ethyl acetate) gave dienylamine 139 (21mg, 64%) as a colourless oil, R_f 0.51, whose NMR spectrum showed the presence of a 1:1 mixture of diastereoisomers by comparison with that obtained previously.

**Ring-opening of aziridine 138 with thiophenolate**

Aziridine 138 (100mg, 0.31 mmol) (dr 4:1) was dissolved in acetonitrile (1 cm^3) containing 4-chlorothiophenol (89mg, 0.62 mmol) and sodium hydroxide (6mg, 0.16 mmol) and heated at 90°C in a sealed Young’s tube for 1 h. During this period the solution turned cloudy. After cooling, saturated sodium hydrogen carbonate solution (10 cm^3) was added and the mixture extracted with ethyl acetate (2 x 10 cm^3) giving the crude product as a light brown solid. Column chromatography (6:1 light petroleum-ethyl acetate) gave a mixture of the ring-opened product and excess 4-chlorothiophenol. Re-chromatography using Kieselgel (7:1 light petroleum-ethyl acetate) gave 4-chlorothiophenol (R_f 0.73). Further elution gave sulphide 172 (59mg, 41%) as a colourless solid, R_f 0.20, identical with that isolated previously.
Separate signals for the expected minor diastereoisomer ring-opened product were not observed.

**Oxidation of dienylamine 139 with LTA**

Dienylamine 139 (30mg, 92.3 μmol) was dissolved in dichloromethane (1 cm³) at -20°C and powdered LTA (43mg, 96.9 μmol) added in small portions over 10 min. After warming to room temperature, additional dichloromethane (10 cm³) was added and the solution washed with saturated aqueous sodium hydrogen carbonate (10 cm³). Separation, drying and evaporation of the solvent gave the crude product (22mg) which was chromatographed (3:1 light petroleum-ethyl acetate) to give unchanged dienylamine 139 (3mg, 10%) as a colourless oil, Rf 0.40.

Further elution gave aziridine 176 (10mg, 30%) as a yellow oil, Rf 0.26. [α]D +12.1 (c=1.0, EtOH); (Found: MH⁺ 384.1923. C₂₁H₂₆O₄N₃ requires M 384.1923); νmax/cm⁻¹ 1735s, 1680s and 1600s; δH(400 MHz) 2.38 (1H, dddd, J 20.0, 6.9, 4.5, 2.1, CHH-cis). 2.84 (1H, dddd, J 20.0, 4.2, 3.3, 1.5, CHH-trans), 3.56 (1H, d, J 10.4, CHOCH), 3.77 (1H, dddd, J 7.7, 6.4, 3.3, 1.0, azir. NCHCOAc), 4.35 (1H, ddd, J 7.7, 4.5, 1.5, azir. NCHCH₂). 5.52 (1H, d, J 10.4. CHOCH), 5.57 (1H, ddd, J 10.0, 4.0, 2.1, CH=CHCH₂), 5.63 (1H, ddd, J 6.4, 4.0, 2.2, CHOAc), 5.74 (1H, dddd, J 10.0, 6.9, 4.2, 2.2, C=CHCH₂). 7.50 [1H, ddd, J 8.0, 6.9, 1.2, H-6(Q)], 7.70 [1H, dd, J 8.0, 1.2, H-8(Q)]. 7.78 [1H, ddd, J 8.0, 6.9, 1.0, H-7(Q)] and 8.27 [1H, dd, J 8.0, 1.0, H-5(Q)]; m/z(%) 384 (MH⁺,100).
Aziridination of cyclohexene with Q^3NHOAc

General aziridination procedure A was followed using NAQ^3 (500mg, 2.61 mmol), LTA (1.14g, 2.63 mmol), HMDS (794mg, 4.92 mmol) and cyclohexene (404mg, 4.92 mmol) in dichloromethane (10 cm^3). Work up in the normal way gave the crude product as a light brown crystalline solid which was chromatographed (2:1 light petroleum-ethyl acetate) to give aziridine 178 (221mg, 30%) R_f 0.64, as a pale yellow crystalline solid, mp 210-211°C (from ethyl acetate-light petroleum). (Found: MH^+ 284.1763. C_{17}H_{22}ON_{3} requires M 284.1762); ν_{max}/cm^{-1} 1665s and 1590s; δ_H 1.20-1.36 (2H, m, CH₂), 1.38 [6H, d, J 6.6, (CH₃)₂], 1.42-1.57 (2H, m, CH₂), 1.88-2.02 (2H, m, NCHCH₂), 2.18 (2H, m, incl. J 14.2, 7.1, NCHCH₂), 2.71 (2H, dd, J 7.1, 3.7, 2 x azir. NCH), 3.54 [1H, h, J 6.6, CH(CH₃)₂], 7.34 [1H, ddd, J 8.0, 6.2, 1.8, H-6(Q)], 7.57 [1H, dd, J 8.0, 1.8, H-8(Q)], 7.63 [1H, ddd, J 8.0, 6.2, 1.2, H-7(Q)] and 8.13 [1H, dd, J 8.0, 1.2, H-5(Q)]; δ_C 20.5 (2 x CH₂), 21.3 (2 x CH₃), 23.2 (2 x CH₂), 31.4 [CH(CH₃)₂], 47.2 (2 x NCH), 121.7 [CO(Q)], 126.3, 126.4, 127.3, 133.7 [4 x CH(Q)], 146.5 [CN=C(Q)] and 160.6, 161.0 [CN(Q), CO(Q)]; m/z(%) 284 (MH^+,100) and 189 (27).

Further elution gave 2-isopropylquinazolin-4(3H)-one 145 (246mg, 49%) R_f 0.51, as a colourless solid identical to that isolated previously.

Aziridination of cyclohexene with Q^3NHOAc in the presence of TFA

General aziridination procedure E was followed using NAQ^3 (300mg, 1.51 mmol), LTA (1.14g, 1.55 mmol), cyclohexene (404mg, 4.92 mmol) and TFA (502mg/0.33 cm^3, 4.41 mmol) in dichloromethane (6 cm^3). Work up in the normal way gave the
crude product as a light brown crystalline solid which was chromatographed (2:1 light petroleum-ethyl acetate) to give aziridine 178 (382mg, 80%) Rₚ 0.64, as a pale yellow crystalline solid, mp 210-211°C (from ethyl acetate-light petroleum) identical with that isolated above.

**Ring-opening of aziridine 178 with 4-chlorothiophenol**

Aziridine 178 (70mg, 0.25 mmol) was heated in a sealed Young’s tube with 4-chlorothiophenol (35mg, 0.25 mmol) in dichloromethane (2 cm³) at 90°C for 24 h. On cooling, dichloromethane (10 cm³) was added and the reaction mixture washed with saturated sodium hydrogen carbonate solution (10 cm³). Separation of the organic layer, drying and evaporation gave unchanged aziridine 178 (57mg, 81% recovered) after column chromatography (2:1 light petroleum-ethyl acetate), Rₚ 0.64.

**Ring-opening of aziridine 178 with thiophenolate**

Aziridine 178 (50mg, 0.18 mmol) was heated in a sealed Young’s tube with 4-chlorothiophenol (26mg, 0.18 mmol) and sodium hydroxide (5mg, 0.11 mmol) in acetonitrile (1 cm³) at 90°C for 1 h. After cooling, ethyl acetate (10 cm³) was added
and the reaction mixture washed with saturated sodium hydrogen carbonate solution (10 cm³). The organic layer was dried and evaporated and column chromatography (4:1 light petroleum-ethyl acetate) of the crude product gave 4-chlorothiophenol (13mg, 50% recovered) as a white solid, R_f 0.75.

Further elution gave arylsulphide 179 (43mg, 56%) as a colourless oil, R_f 0.56.

(Found: M_H^+ 428.1563. C_{23}H_{27}O_N_Cl requires M 428.1563); \delta_H 1.18-1.29 (4H, m, 2x CH_2), 1.36 [6H, d, J 6.9, (CH_3)_2], 1.68 (3H, m, CH_2 and CHH), 2.10 (1H, br s, CHH), 2.96 (1H, br s, CHSAr), 3.30 (1H, br s, CHNH), 3.89 [1H, h, J 6.9, CH(CH_3)_2], 6.45 (1H, br s, NH), 7.31 [2H, br s, 2 x CH(Ar)], 7.43 [1H, ddd, J 8.0, 6.9, 1.8, H-6(Q)], 7.59 [2H, br s, 2 x CH(Ar)], 7.67 [1H, dd, J 8.2, 1.8, H-8(Q)], 7.73 [1H, ddd, J 8.2, 6.9, 1.3, H-7(Q)] and 8.25 [1H, d, J 8.0, H-5(Q)]; m/z(%) 428 (MH^+,82), 226 (50), 225 (90) and 224 (100).

**Oxidation of sulphide 179**

![Diagram](image)

Arylsulphide 179 (43mg, 0.10 mmol) was stirred with hydrogen peroxide (3mg/ 10 μl 30% solution, 0.10 mmol) in acetic acid (1 cm³) for 2 h. Washing with saturated sodium hydrogen carbonate solution (10 cm³) and extraction with ethyl acetate (10 cm³) gave the crude product as a pale yellow oil. Column chromatography (4:1 light petroleum-ethyl acetate) gave unchanged arylsulphide 179 (38mg, 88% recovered) as a colourless oil, R_f 0.66.
Ring-opening of aziridine 178 with the phenylselenide anion

Diphenyl diselenide (31 mg, 0.10 mmol) was added to a stirred solution of sodium borohydride (8 mg, 0.20 mmol) in aqueous sodium hydroxide (2 M, 400 µl) and ethanol (400 µl) and the solution was heated under reflux for 30 min in a nitrogen atmosphere. After cooling, aziridine 178 (50 mg, 0.18 mmol) dissolved in THF (1 cm³) was added dropwise to the stirred solution containing the selenide anion. Stirring continued for a further 30 min at ambient temperature. Diethyl ether (10 cm³) was added and the solution washed with saturated sodium hydrogen carbonate solution (10 cm³), dried and evaporated to give the crude product as a pale yellow oil. Column chromatography (5:1 light petroleum-ethyl acetate) gave phenylselenide 180 (33 mg, 43 %) as a colourless oil, Rf 0.50. (Found: MH⁺ 442.1397. C₂₃H₂₈ON₃Se requires M 442.1397); δH 1.26 (4H, m, incl. J 13.1, 2.3, 2 x CH₂), 1.36 [6H, d, J 6.9, (CH₃)₂], 1.52 (1H, dd, J 13.1, 1.8, CHH), 1.63 (3H, m, CHH and CH₂), 3.11 (1H, br s, CHSePh), 3.34 (1H, br s, CHNH), 3.88 [1H, h, J 6.9, CH(CH₃)₂], 6.44 (1H, br s, NH), 7.29 [3H, m, 3 x CH(Ar)], 7.42 [1H, ddd, J 8.0, 6.1, 1.8, H-6(Q)], 7.58–7.81 [4H, m, H-7(Q), H-8(Q) and 2 x CH(Ar)] and 8.25 [1H, d, J 8.0, H-5(Q)]; m/z(%) 442 (MH⁺, 44), 440 (27), 284 (46), 239 (100), 224 (73), 237 (51) 236 (49) and 189 (64).
Oxidation of phenylselenide 180

Selenide 180 (30mg, 67.7 µmol) was dissolved in acetic acid (1 cm³) containing hydrogen peroxide (2mg/8 µl 30% solution, 68.2 µmol) and the solution stirred at ambient temperature for 90 min. Addition of ethyl acetate (10 cm³) and washing with saturated sodium hydrogen carbonate solution (10 cm³) followed by separation, drying and evaporation of the solvent gave selenoxide 181 (20mg, 65%) as a colourless solid (from light petroleum-ethyl acetate). (Found: MH⁺ 458.1347. C₂₃H₂₈O₂N₃Se requires M 458.1346); δH 1.28 (4H, m, 2 x CH₂), 1.36 [6H, d, J 6.9, (CH₃)₂], 1.68 (3H, m, CHH and CH₂), 1.91 (1H, m, CHH), 2.79 (1H, br s, CHSePh), 3.28 (1H, br s, CHNH), 3.88 [1H, h, J 6.9, CH(CH₃)₂], 6.39 (1H, br s, NH), 7.44 [1H, ddd, J 8.0, 6.9, 1.0, H-6(Q)], 7.60-7.84 [7H, m, 5 x CH(Ar), H-7 and H-8(Q)] and 8.25 [1H, dd, J 8.0, 1.0, H-5(Q)]; m/z(%) 458 (MH⁺,28), 329 (21) and 284 (100).

Formation of allylamine 182

Selenoxide 181 (20mg, 43.6 µmol) was heated in carbon tetrachloride (1 cm³) at 80°C for 2 h. After cooling, ethyl acetate (10 cm³) was added and the solution washed with saturated sodium hydrogen carbonate solution (10 cm³), dried and evaporated to give the crude product as a pale yellow oil. Column chromatography (5:1 light petroleum-ethyl acetate) gave diphenyl selenoxide, Rf 0.73, as a yellow oil.
Further elution gave allylamine 182 (8mg, 65%) as a colourless oil, Rf 0.46. (Found: MH\textsuperscript{+} 284.1762. C\textsubscript{17}H\textsubscript{22}ON\textsubscript{3} requires M 284.1763); \nu\textsubscript{max}/cm\textsuperscript{-1} 1675s, 1615m, 1595s and 1570m; \delta\textsubscript{H} 1.31 [6H, d, J 6.6, (CH\textsubscript{3})\textsubscript{2}]; 1.63 (4H, m, incl. J 5.8, 3.5, 2 x CH\textsubscript{2}), 1.85 (1H, ddd, J 7.5, 2.8, 1.6, CHH), 2.05 (2H, m, incl. J 5.8, 2.8, CH\textsubscript{2}), 2.07 (1H, dd, J 2.8, 2.8, CHH), 3.70 (1H, br s, CHNH), 3.82 [1H, h, J 6.6, CH(CH\textsubscript{3})\textsubscript{2}], 5.55 (1H, br s, NH), 5.63 (1H, m, incl. J 10.1, 3.5, C=CHCH\textsubscript{2}), 5.92 (1H, ddd, J 10.1, 5.1, 1.6, C=CH\textsubscript{2}), 7.42 [1H, ddd, J 8.0, 6.4, 1.8, H-6(Q)], 7.67 [1H, dd, J 8.2, 1.8, H-8(Q)], 7.73 [1H, ddd, J 8.2, 6.4, 1.0, H-7(Q)] and 8.23 [1H, ddd, J 8.0, 1.0, H-5(Q)]; \delta\textsubscript{C}(75 MHz) 19.6 (CH\textsubscript{2}), 21.3 (2 x CH\textsubscript{3}), 25.7, 27.8 (2 x CH\textsubscript{2}), 30.9 [CH(CH\textsubscript{3})\textsubscript{2}], 55.5 (C-N), 121.0 [CCO(Q)], 126.1, 126.3, 126.8, 127.7, 132.0, 134.4 [3 x CH(Q), HC=CH], 147.8 [CN=C(Q)] and 162.6, 163.4 [CN(Q), CO(Q)]; m/z(%) 284 (MH\textsuperscript{+},100) and 204 (28).

Aziridination of 1-methylcyclohexene with Q\textsuperscript{2}NHOAc

[Diagram]

General aziridination procedure A was followed using NAQ\textsuperscript{2} (500mg, 2.64 mmol), LTA (1.23g, 2.77 mmol), HMDS (1.28g, 5.28 mmol) and 1-methylcyclohexene (510mg, 5.28 mmol) in dichloromethane (10 cm\textsuperscript{3}). After work up in the normal way, the crude product was isolated as a pale yellow semi-solid. Trituration (ethyl acetate-light petroleum) gave a pure sample of 2-ethylquinazolin-4(3H)-one. Column chromatography (4:1 light petroleum-ethyl acetate) gave aziridine 183 (225mg, 30%) as a yellow oil, Rf 0.31. (Found: MH\textsuperscript{+} 284.1763. C\textsubscript{17}H\textsubscript{22}ON\textsubscript{3} requires M 284.1763); \nu\textsubscript{max}/cm\textsuperscript{-1} 1670s, 1580s and 1460m; \delta\textsubscript{H} 1.13 (3H, s, CH\textsubscript{3}), 1.34 (2H, struct. m, CH\textsubscript{2}), 1.41 (3H, t, J 7.4, CH\textsubscript{3}CH\textsubscript{2}), 1.50 (1H, dd, J 13.3, 7.8, CHH), 1.59 (2H, struct. m, CH\textsubscript{2}), 2.04 (1H, ddd, J 13.7, 8.7, 5.9, CHH), 2.20 (1H, dd, J 13.7, 6.9, CHH), 2.34
(1H, ddd, J 13.3, 7.3, 6.2, CHH), 2.81 [1H, dq, J 8.5, 7.4, CHHCH₃(Q)], 2.93 (1H, br s, NCH), 3.03 [1H, dq, J 8.5, 7.4, CHHCH₃(Q)], 7.38 [1H, ddd, J 8.0, 6.3, 1.1, H-6(Q)], 7.62 [1H, dd, J 8.0, 1.1, H-8(Q)], 7.66 [1H, dd, J 8.0, 6.3, 1.0, H-7(Q)] and 8.17 [1H, dd, J 8.0, 1.0, H-5(Q)]; \(\delta\)C 10.9 (CH₃), 20.2 (CH₂), 20.4 (CH₃), 20.9, 23.7, 28.5, 30.2 (4 x CH₂), 50.2, 51.1 (NCH, NCMe), 121.8 [CCO(Q)], 126.3, 126.4, 127.1, 133.7 [4 x CH(Q)], 146.4 [CN=C(Q)] and 159.1, 161.1 [CN(Q), CO(Q)]; m/z(%) 284 (MH⁺,100), 200 (25), 174 (40) and 110 (43).

**Ring-opening of aziridine 183 with phenylselenide anion**

Diphenyl diselenide (31 mg, 0.10 mmol) was added to a stirred solution of sodium borohydride (8 mg, 0.20 mmol) in aqueous sodium hydroxide (2 M, 400 µL) and ethanol (400 µL), the solution was then heated under reflux for 30 min in a nitrogen atmosphere. After cooling, aziridine 183 (50 mg, 0.18 mmol) dissolved in THF (1 cm³) was added dropwise to the stirred solution containing the selenide anion which was stirred for a further 30 min at ambient temperature. Addition of diethyl ether (10 cm³) and washing with saturated sodium hydrogen carbonate solution (10 cm³) and brine (10 cm³) followed by separation, drying and evaporation of the solvent gave the crude product as a pale yellow oil. Column chromatography (5:1 light petroleum-ethyl acetate) gave *phenylselenide* 184 (20 mg, 26 %) as a colourless oil, \(R_f\) 0.45. (Found: MH⁺ 442.1397. C₂₃H₂₈ON₃Se requires \(M\) 442.1397); \(\delta\)H 1.24-1.33 (6H, struct. m, 2 x CH₂ and 2 x CHH), 1.36 (3H, d, J 7.3, CH₃), 1.51-1.60 (2H, struct. m, 2 x CHH), 1.58 (3H, s, CH₃), 2.91 (1H, m, CH₂CHH), 3.22 (1H, dd, J 15.4, 7.5, CHSePh), 3.61 (1H, m, CH₂CHH), 6.39 (1H, br s, NH), 7.37 [1H, s, CH(Ar)], 7.40 [2H, s, 2 x CH(Ar)], 7.44 [1H, ddd, J 8.2, 6.9, 1.3, H-6(Q)], 7.66 [1H, dd, J 8.2, 1.3, H-8(Q)], 7.73 [1H,
dd. J 8.2, 6.9, 1.2, H-7(Q)], 7.91 [2H, br s, 2 x CH(Ar)] and 8.28 [1H, dd, J 8.2, 1.2, H-5(Q)]; m/z(%) 442 (MH⁺,100), 284 (63), 253 (41) and 190 (44).

Formation of allylamine 720

Selenide 184 (18mg, 41.0 μmol) was stirred in glacial acetic acid (1 cm³) containing hydrogen peroxide (1.4mg/5 μl 30% solution, 45.0 μmol) at ambient temperature for 2 h. Addition of ethyl acetate (10 cm³) and washing with saturated sodium hydrogen carbonate solution (10 cm³), separation, drying and evaporation of the solvent, gave the crude product as a pale yellow oil. Column chromatography (5:1 light petroleum-ethyl acetate) gave diphenyl selenoxide, Rf 0.70, as a yellow oil. Further elution gave allylamine 185 (4mg, 33%) as a colourless oil, Rf 0.42. (Found: MH⁺ 284.1763. C₁₇H₂₂ON₃ requires M 284.1763); ν_max/cm⁻¹ 1670s, 1595s and 1470s; δH 1.35 (3H, t, J 7.5, CH₃CH₂), 1.53 (3H, br s, CH₃), 1.71 (3H, struct. m, CH₂ and CHH), 2.16 (1H, ddd, J 13.0, 7.8, 5.2, CHHC=C), 2.49 (1H, ddd, J 13.0, 8.4, 5.0, CHHC=C), 3.01 (2H, m, CH₃CH₂), 3.60 (1H, br s, HHCCNMe), 4.75 (1H, br s, CH=C), 4.78 (1H, br s, C=CH), 5.61 (1H, br s, NH), 7.43 [1H, ddd, J 8.0, 6.9, 1.3, H-6(Q)], 7.66 [1H, dd, J 8.2, 1.3, H-8(Q)], 7.73 [1H, ddd, J 8.2, 6.9, 1.2, H-7(Q)] and 8.22 [1H, dd, J 8.0, 1.2, H-5(Q)]; m/z(%) 284 (MH⁺,100), 190 (58) and 175 (49).
Experimental relating to Chapter 5
**Reaction of Q₃NHOAc with 1,4-cyclohexadiene in the presence of TFA**

![Reaction Scheme](attachment:image.png)

General aziridination procedure A was followed for the preparation of 71 using NAQ³ (300mg, 1.47 mmol) and LTA (687mg, 1.54 mmol) in dichloromethane (4 cm³). After stirring at -20°C for 10 min, the insoluble lead diacetate was filtered off and the solution of 3-acetoxyaminoquinazolinone added dropwise to a solution of TFA (502mg, 4.41 mmol) and 1,4-cyclohexadiene (235mg, 2.94 mmol) in dichloromethane (2 cm³) at -40°C. The reaction mixture was allowed to warm to ambient temperature before work up in the normal way. Column chromatography (7:1 light petroleum-ethyl acetate) of the crude product (280 mg) gave trifluoroacetate 186 (180mg, 31%) Rₐ 0.37, as a colourless solid, mp 131-133°C (from light petroleum-ethyl acetate).

(Found: C, 57.9; H, 5.1; N, 10.7%. C₁₉H₂₁O₃N₃F₃ requires C, 57.7; H, 5.1; N, 10.6%);

v_{max}/cm⁻¹ 1790m, 1730s, 1675s, 1600s and 1180s; δ_H 1.23 [6H, d, J 6.9, CH(CH₃)₂], 2.25 (3H, m, incl. J 18.0, 8.0, CH₂ and CHH), 2.78 (1H, dd, J 18.0, 4.0, CHH), 3.69 [2H, m, CHNH and CH(CH₃)₂], 5.26 (1H, dd, J 8.0, 8.0, CHOCOCF₃), 5.59 (2H, s, H₂=CH), 5.78 (1H, d, J 8.0, NH), 7.43 [1H, ddd, J 8.0, 6.9, 1.2, H-6(Q)], 7.63 [1H, dd, J 8.0, 1.2, H-8(Q)], 7.74 [1H, ddd, J 8.0, 6.9, 1.0, H-7(Q)] and 8.22 [1H, dd, J 8.0, 1.0, H-5(Q)]; m/z(%) 396 (M⁺,100), 189 (36), 188 (21) and 173 (26).

Further elution gave 2-isopropylquinazolin-4(H)-one 145 (22mg, 8%) Rₐ 0.19, as a colourless solid identical to that isolated previously.¹⁵⁰

The reaction above was repeated using general aziridination procedure E. Column chromatography of the crude product (5:1 light petroleum-ethyl acetate) gave dienylamine 143 (18mg, 5%) Rₐ 0.62, as a colourless oil identical with that isolated previously.
Further elution gave aziridine 144 (248mg, 60%) \( R_f 0.49 \), also a colourless oil identical with that isolated previously, and 2-isopropylquinazolin-4(3H)-one 145 (31mg, 11%) as a colourless solid, \( R_f 0.36 \).

**Dienylamine 143 stability in the presence of TFA**

\[
\begin{align*}
\text{HNQ}^3 & \\
\text{143} & \\
\text{TFA, CH}_2\text{Cl}_2, 1 \text{ h} & \\
68\% & \\
\text{NH}_2 & \\
\text{187} & \\
\end{align*}
\]

Dienylamine 143 (50mg, 0.18 mmol) was stirred in dichloromethane (1 cm\(^3\)) with TFA (2 drops) for 1 h. Addition of dichloromethane (10 cm\(^3\)) and washing with saturated sodium hydrogen carbonate solution (10 cm\(^3\)) followed by separation, drying and evaporation of the solvent gave the crude product as a colourless solid. Column chromatography (4:1 light petroleum-ethyl acetate) gave NAQ\(^3\) 187 (21mg, 68%) \( R_f 0.21 \), as a white solid identical with an authentic sample.

**Aziridination of 1,4-cyclohexadiene with Q\(^3\)NHOAc in acetonitrile**

\[
\begin{align*}
\text{Q}^3 & \\
\text{NHOAc} & \\
\text{71} & \\
\text{HMDS, CH}_2\text{CN} & \\
\text{143} & \\
\text{HNQ}^3 & \\
\text{144} & \\
\end{align*}
\]

General aziridination procedure A was followed using NAQ\(^3\) (200mg, 0.98 mmol), LTA (458mg, 1.04 mmol), HMDS (397mg, 2.46 mmol) and 1,4-cyclohexadiene (158mg/0.18 cm\(^3\), 1.97 mmol) in acetonitrile (4 cm\(^3\)). After work up the crude product was obtained as a yellow oil. Column chromatography (3:1 light petroleum-ethyl acetate) gave dienylamine 143 (24mg, 9%) as a clear colourless oil, \( R_f 0.65 \). Further
elution gave aziridine 144 (82mg, 30%) as a colourless oil, Rf 0.53 and 2-isopropylquinazolin-4(3H)-one 145 (11mg, 5%) as a colourless solid, R 0.21.

Aziridination of 1,3-cyclohexadiene with Q\(^3\)NHOAc in acetonitrile

![Diagram](attachment:diagram.png)

General aziridination procedure A was followed using NAQ\(^3\) (200mg, 0.98 mmol), LTA (458mg, 1.04 mmol), HMDS (397mg, 2.46 mmol) and 1,3-cyclohexadiene (158mg/0.18 cm\(^3\), 1.97 mmol) in acetonitrile (4 cm\(^3\)). After work up the crude product was obtained as a yellow oil. Column chromatography (2:1 light petroleum-ethyl acetate) gave alcohol 188 (74mg, 27%) as a colourless oil, Rf 0.88. (Found: MH\(^+\) 300.1712. \(C_{17}H_{25}O_2N_3\) requires \(M 300.1712\); \(\nu_{\text{max}}/\text{cm}^{-1}\) 3420m, 3300m, 1660s, 1615m and 1590s; \(\delta_H\) 1.34 (3H, d, J 6.9, \(CH_3CHCH_3\)), 1.41 (3H, d, J 6.9, \(CH_3CHCH_3\)), 1.81 (1H, ddd, J 12.2, 6.3, 2.0, C=CH), 1.93 (1H, ddd, J 12.2, 7.0, 4.4, C=CH), 2.11 (1H, m, incl. J 14.2, 6.3, NHCH), 2.30 (1H, ddd, J 14.2, 7.0, 5.3, NHCH), 2.85 (1H, ddd, J 6.9, 6.9, 3.3, CHNH), 3.64 [1H, h, J 6.9, \(CH(CH_3)_2\)], 3.96 (1H, br s, CHOH), 4.83 (1H, br s, OH), 5.81 (1H, dddd, J 11.9, 5.4, 3.3, 1.9, \(CH=CH_2\)), 5.88 (1H, ddd, J 11.9, 4.4, 2.0, C=CH), 5.93 (1H, d, J 6.9, NH), 7.46 [1H, ddd, J 8.0, 6.6, 1.3, H-6(Q)], 7.69 [1H, dd, J 8.0, 1.3, H-8(Q)], 7.76 [1H, ddd, J 8.0, 6.6, 1.0, H-7(Q)] and 8.23 [1H, dd, J 8.0, 1.0, H-5(Q)]; \(\delta_C(\text{CDCl}_3\), 62.9 MHz) 20.5 (CH(CH(CH)CH)), 21.6 (CH\(_2\)), 21.8 (CH(CHCH(CH))), 26.0 (CH\(_2\)), 30.8 [CH(CH(CH)CH)), 45.0 (C-N), 62.6 (C-OH), 119.8 [CCO(Q)], 126.5, 126.6, 127.4, 131.3, 134.5 [4 x CH(Q), HC=CH], 147.2 [CN=CC(Q)] and 162.5, 163.4 [CN(Q), CO(Q)]; \(m/z(\%)\) 300 (MH\(^+\),100), 282 (39), 204 (22), 189 (75) and 188 (50).

Further elution gave aziridine 136 (43mg, 15%) Rf 0.57, as a colourless oil identical with that isolated previously and 2-isopropylquinazolin-4(3H)-one 145 (3mg, 2%) Rf 0.22, as a colourless solid.\(^{150}\)
Aziridination of 1,4-cyclohexadiene with Q\(^6\)NHOAc 67 in acetonitrile

General aziridination procedure followed using NAQ\(^6\) (245mg, 0.98 mmol), LTA (458mg, 1.34 mmol), TTB (696mg, 2.00 mmol) and 1,4-cyclohexadiene (156mg, 1.96 mmol) in acetonitrile (6 cm\(^3\)). After work up in the normal way, column chromatography (2:1 light petroleum-ethyl acetate) gave dienylamine 146 (59mg, 20%) R\(_f\) 0.66, as a colourless solid identical with that isolated previously. Further elution gave aziridine 141 (27mg, 10%) as a colourless solid, R\(_f\) 0.50.

Aziridination of 1,3-cyclohexadiene with Q\(^6\)NHOAc in acetonitrile

General aziridination procedure D was followed using NAQ\(^6\) (500mg, 2.01 mmol), LTA (942mg, 2.12 mmol), TTB (1.42g, 4.20 mmol) and 1,3-cyclohexadiene (320mg/0.38 cm\(^3\), 4.00 mmol) in dichloromethane (11 cm\(^3\)). After work up, column chromatography (6:1 light petroleum-ethyl acetate) gave dienylamine 139 (19mg, 7%) as a colourless oil, R\(_f\) 0.26. Further elution gave aziridine 138 (101mg, 38%) as a single diastereoisomer, R\(_f\) 0.21. The third fraction eluted was alcohol 189 (72mg, 26%) as a mixture of diastereoisomers, R\(_f\) 0.16. Kieselgel chromatography (6:1 light petroleum-ethyl acetate) gave the major alcohol diastereoisomer 189a (33mg, 12%) as
a colourless oil, Rf 0.19. [α]D +91.0° (c=2.0, EtOH); (Found: MH+ 344.1975. C19H26O3N3 requires M 344.1975); υ_{max}/cm⁻¹ 3460s, 1660s, 1590s and 1470s; δ_θ(400 MHz) 1.05 [9H, s, (CH₃)₃], 1.65 (1H, dddd, J 12.6, 9.8, 6.0, 3.0, CHHCN), 1.76 (1H, s, OH), 1.84 (1H, dddd, J 12.6, 10.7, 7.6, 5.1, CHHCN), 2.04 (1H, m, incl. J 13.5, 10.7, 6.0, C=CCHH₂), 2.24 (1H, dddd, J 13.5, 9.8, 5.1, 3.5, C=CCHH), 3.18 (1H, dddd, J 7.6, 7.6, 3.0, 3.0, CHNH), 3.62 (1H, br s, OH), 4.17 [1H, m, incl. J 3.0, CH(OH)CN], 5.16 (1H, br s, CHOH), 5.82 (1H, dddd, J 10.0, 1.8, 1.8, HC=CH₂), 5.85 (1H, dddd, J 10.0, 3.5, 1.2, C=CH₂), 5.90 (1H, d, J 7.6, NH), 7.50 [1H, dddd, J 8.2, 7.1, 1.2, H-6(Q)], 7.72 [1H, dddd, J 8.2, 1.2, H-8(Q)], 7.72 [1H, dddd, J 8.2, 7.1, 1.0, H-7(Q)] and 8.27 [1H, dddd, J 8.2, 1.0, H-5(Q)]; m/z(%) 344 (MH⁺, 100) and 233 (42).

Further elution gave the minor alcohol diastereoisomer 189b (17mg, 6%) as a colourless oil, Rf 0.14. [α]D +113.3° (c=1.2, EtOH); (Found: MH+ 344.1975. C19H26O3N3 requires M 344.1975); υ_{max}/cm⁻¹ 3420m, 1660s, 1595s and 1470m; δ_θ(400 MHz) 1.05 [9H, s, (CH₃)₃], 1.80 (1H, dddd, J 12.5, 9.0, 6.3, 3.2, CHHCN), 1.92 (1H, dddd, J 12.5, 10.0, 6.1, CHHCN), 2.19 (1H, dddd, J 18.0, 6.3, 5.4, 2.6, C=CCHH), 2.31 (1H, m, incl. J 18.0, 9.0, 6.1, 4.8, C=CH₂), 2.96 (1H, dddd, J 10.0, 10.0, 3.2, CHNH), 3.60 (1H, d, J 10.5, Bu'CHOH), 3.93 [1H, m, incl. J 4.4, 3.2, CH(OH)CN], 4.63 [1H, d, J 4.4, CH(OH)CN], 5.03 (1H, d, J 10.5, Bu'CHOH), 5.79 (1H, dddd, J 9.9, 5.4, 2.6, 1.3, CH=CH₂), 5.84 (1H, d, J 10.0, NH), 5.90 (1H, dddd, J 9.9, 4.8, 2.6, C=CH₂), 7.55 [1H, dddd, J 8.2, 7.1, 1.2, H-6(Q)], 7.74 [1H, dddd, J 8.0, 1.2, H-8(Q)], 7.83 [1H, dddd, J 8.0, 7.1, 1.2, H-7(Q)] and 8.30 [1H, dddd, J 8.2, 1.2, H-5(Q)]; δ_C(75 MHz) 22.2, 26.2 (2 x CH₂), 26.3 [(CH₃)₃], 38.5 (CHNH), 62.6 (COH), 75.0 (CHOH), 120.5 [CCO(Q)], 126.5, 127.2, 127.6, 127.7, 131.6, 135.4 [4 x CH(Q), HC=CH], 146.3 [CN=C(Q)] and 158.8, 163.5 [CO(Q), CN(Q)]; m/z(%) 344 (MH⁺, 100) and 233 (30).

Diennylamine 139 could not be separated from a small amount of tert-butoxyaminoquinazolinone 140.99
Ring-opening of aziridine 138 with TFA

Aziridine 138 (20mg, 61.5 μmol) was stirred at -20°C in dichloromethane (1 cm³) containing TFA (2 drops) for 1 h. After warming to ambient, addition of dichloromethane (10 cm³) and washing with saturated sodium hydrogen carbonate solution (10 cm³) followed by separation, drying and evaporation of the solvent gave the crude product. Column chromatography (1:1 light petroleum-ethyl acetate) gave a mixture of unidentified compounds (18mg) Rf 0.27. Further elution gave 2-isopropylquinazolin-4(3H)-one 145 (2mg, 17 %) as a colourless solid, Rf 0.22.

The unidentified mixed fraction above was stirred in ethanol (2 cm³) saturated with sodium carbonate for 3 h. Addition of water (5 cm³) and extraction with ethyl acetate (10 cm³) followed by separation, drying and evaporation of the solvent gave the crude product. Column chromatography gave alcohol 190 (10mg, 47%) as a colourless oil, Rf 0.37. (Found: MH⁺ 344.1974. C₁₉H₂₆O₃N₃ requires M 344.1974); δH 0.99 [9H, s, C(CH₃)₃], 1.26 (1H, s, OH), 1.79 [2H, m, incl. J 5.5, NHCHCH₂], 1.89 [2H, m, incl. J 11.6, 5.5, CH(OH)CH₂], 3.62 [1H, d, J 10.3, CHOH(Q)], 3.75 [1H, m, incl. J 5.6, CHNH], 4.19 (1H, br s, CHOH), 5.13 [1H, d, J 10.3, CHOH(Q)], 5.54 (1H, d, J 5.6, NH), 5.63 (1H, dd, J 9.0, 2.8, HC=CH), 5.97 (1H, ddd, J 9.0, 2.8, 1.9, HC=CH), 7.50 [1H, ddd, J 8.0, 6.9, 1.2, H-6(Q)], 7.70 [1H, dd, J 8.0, 1.2, H-8(Q)], 7.78 [1H, ddd, J 8.0, 6.9, 1.0, H-7(Q)] and 8.27 [1H, dd, J 8.0, 1.0, H-5(Q)]; m/z(%) 344 (MH⁺,100), 259 (25) and 176 (20).
Ring-opening of aziridine 136 in acetonitrile-water-acetic acid

Aziridine 136 (240mg, 0.85 mmol) was stirred in acetonitrile (1 cm³) containing water (0.25 cm³) at ambient temperature for 2 h. Addition of ethyl acetate (10 cm³) and washing with saturated sodium hydrogen carbonate solution (10 cm³) followed by separation, drying and evaporation of the solvent gave the crude product (238mg) whose NMR spectrum showed no ring opening had occurred. Column chromatography (2:1 light petroleum-ethyl acetate) gave aziridine 136 (205mg, 85%) as a colourless solid, Rf 0.39.

The reaction above was repeated using aziridine 136 (200mg, 0.71 mmol) but glacial acetic acid (2 drops) was added to the acetonitrile(1 cm³) /water (0.25 cm³) mix and the solution stirred for 2 h. Column chromatography (2:1 light petroleum-ethyl acetate) of the crude product (180mg) gave alcohol 188 (82mg, 38%) Rf 0.69, as a colourless oil identical with that isolated previously. Further elution gave unchanged aziridine 136 (96mg, 48%) as a colourless solid, Rf 0.40.
Aziridine 138 (220mg, 0.68 mmol) was stirred in acetonitrile (4 cm³) containing water (1 cm³) and toluene p-sulphonic acid (5-10 crystals) at ambient temperature for 2 h. Addition of ethyl acetate (10 cm³) and washing with saturated sodium hydrogen carbonate solution (10 cm³) followed by separation, drying and evaporation of the solvent, and column chromatography (7:1 light petroleum-ethyl acetate) of the residue gave diazaoxepine 191 (53mg, 24%) as a colourless oil, Rf 0.38. [α]D +151.5° (c=1.0, EtOH); (Found: MH⁺ 326.1869. C₁₉H₂₄O₂N₃ requires M 326.1868); νmax/cm⁻¹ 1660s, 1600s, 1520m and 1470s; δH 1.30 [9H, s, (CH₃)₃], 1.92-2.37 (4H, m, 2 x CH₂), 3.23 (1H, struct. m, CHNH), 4.53 (1H, br s, HCO), 4.81 (1H, s, Bu'CHO), 5.78 (1H, m, incl. J 10.3, CH=CCH₂), 6.06 (1H, d, J 10.3, 3.9, 2.0, C=CHCH₂), 6.60 (1H, br s, NH), 7.48 [1H, d, J 8.2, 6.8, 1.0, H-6(Q)], 7.71 [1H, d, J 8.2, 1.0, H-8(Q)], 7.75 [1H, d, J 8.2, 6.8, 1.2, H-7(Q)] and 8.25 [1H, d, J 8.2, 1.2, H-5(Q)]; δC 20.8, 26.3 (2 x CH₂), 27.2 [(CH₃)₃], 34.9 [C(CH₃)₃], 56.2 (C-N), 74.4, 76.9 (2 x CHO), 120.4 [CCO(Q)], 126.6, 126.9, 127.2, 128.6, 132.4, 134.2 [4 x CH(Q), HC=CH], 146.7 [CN=C(Q)] and 154.1, 160.6 [CN(Q), CO(Q)]; m/z(%) 326 (MH⁺,100), 246 (30) and 215 (48).

Further elution gave the major alcohol diastereoisomer 189a (35mg, 15%) Rf 0.27, and the minor diastereoisomer 189b (34mg, 14%) Rf 0.14, both as colourless oils identical with those isolated previously.

The reaction was repeated and column chromatography was carried out using base-washed (2% TEA) silica. This gave diazaoxepine 191 (54mg, 24%) Rf 0.38, major
alcohol diastereoisomer 189a (114mg, 49%) R\textsubscript{f} 0.27, and minor alcohol diastereoisomer 189b (31mg, 13%) R\textsubscript{f} 0.14, all as colourless oils.

Ring-opening of aziridine 138 in hydrogen sulphide-saturated acetonitrile

Aziridine 138 (dr 4:1, 50mg, 0.15 mmol) was dissolved in acetonitrile (1 cm\textsuperscript{3}) previously saturated with hydrogen sulphide gas, toluene p-sulphonic acid (5-6 crystals) added and the mixture stirred at ambient temperature for 3 h. Addition of ethyl acetate (10 cm\textsuperscript{3}) and washing with saturated sodium hydrogen carbonate solution (10 cm\textsuperscript{3}) followed by separation, drying and evaporation of the solvent gave the crude product as a yellow oil. Column chromatography (4:1 light petroleum-ethyl acetate) gave a 3:1 mixture of alcohols 189a and 189b (21 mg, 40%) as a colourless oil, R\textsubscript{f} 0.42.

Further elution gave quinazolin-4-thione 193 (7mg, 13%) as a yellow oil, R\textsubscript{f} 0.13. (Found: MH\textsuperscript{+} 360.1746. C\textsubscript{19}H\textsubscript{26}O\textsubscript{2}N\textsubscript{3}S requires M 360.1746); v\textsubscript{max}/cm\textsuperscript{-1} 1680s, 1615s, 1595s and 1470m; \delta H 0.99 [9H, s, (CH\textsubscript{3})\textsubscript{3}], 1.68 (COH), 1.86 (1H, ddd, J 9.4, 5.5, 2.9, CHHCN), 1.93 (1H, dd, J 8.0, 5.5, C=CCHH), 2.04 (1H, dd, J 9.4, 6.2, CHHCN), 2.16 (1H, dd, J 8.0, 6.2, C=CCHH), 3.36 (1H, dddd, J 6.2, 6.2, 2.9, 2.9, CHNH), 3.55 (1H, dd, J 9.4, 6.2, Bu'CHOH), 4.17 (1H, struct. m, CHO), 5.59 (1H, d, J 10.3, Bu'CHOH), 5.85 (2H, br s, HC=CH), 7.19 (1H, d, J 6.2, NH), 7.53 (1H, ddd, J 8.2, 6.6, 1.2, H-6(Q)), 7.73 (1H, dd, J 8.0, 1.2, H-8(Q)), 7.79 (1H, ddd, J 8.0, 6.6, 1.2, H-
7(\text{Q})\) and 8.69 [1H, dd, J 8.2, 1.2, H-5(\text{Q})]; \text{m/z(\%)} 360 (\text{MH}^+80), 307 (100), 289 (72) and 249 (51).

Cyclisation of alcohol 188 with 1,1'-carbonyldiimidazole

Alcohol 188 (60mg, 0.20 mmol) was heated under reflux in THF (1 cm\textsuperscript{3}) with sodium hydride (5mg, 0.22 mmol) and 1,1'-carbonyldiimidazole (45mg, 0.30 mmol) under nitrogen for 3 h. After cooling, addition of ethyl acetate (10 cm\textsuperscript{3}) and washing with saturated sodium hydrogen carbonate solution (10 cm\textsuperscript{3}) followed by separation, drying and evaporation of the solvent gave the crude product as a colourless solid. Column chromatography (5:1 light petroleum-ethyl acetate) gave unchanged alcohol 188 (21mg, 35\%) as a colourless oil, R\textsubscript{f} 0.49.

Further elution gave oxazolidinone 194 (35mg, 53\%) as a colourless solid (R\textsubscript{f} 0.33), mp 148-149\textdegree\text{C} (from ethanol). (Found: MH\textsuperscript{+} 326.1505. C\textsubscript{18}H\textsubscript{20}O\textsubscript{3}N\textsubscript{3} requires M 326.1504); \nu\text{max/cm}^{-1} 1770s, 1680s and 1600s; \delta\textsubscript{H} 1.34 (3H, d, J 6.6, CH\textsubscript{3}CH\textsubscript{3}), 1.40 (3H, d, J 6.6, CH\textsubscript{2}CH\textsubscript{2}CH\textsubscript{2}), 1.86 (2H, m, incl. J 12.8, 4.3, CHCH\textsubscript{2}), 2.11 (1H, m, incl. J 17.8, CHHC=C), 2.30 (1H, m, incl. J 17.8, 3.9, C=CCH\textsubscript{3}), 3.43 [1H, h, J 6.6, CH(CH\textsubscript{3})\textsubscript{3}], 4.67 (1H, ddd, J 8.5, 4.3, 4.3, NCH), 5.29 (1H, m, incl. J 8.5, 2.6, HCO), 5.91 (1H, m, incl. J 10.2, 2.6, CH=CCH\textsubscript{2}), 6.22 (1H, ddd, J 10.2, 3.9, 3.9, C=CHCH\textsubscript{3}), 7.45 [1H, ddd, J 8.0, 6.8, 1.4, H-6(\text{Q})], 7.70 [1H, dd, J 8.2, 1.4, H-8(\text{Q})], 7.77 [1H, ddd, J 8.2, 6.8, 1.1, H-7(\text{Q})] and 8.22 [1H, dd, J 8.0, 1.1, H-5(\text{Q})]; \delta\textsubscript{C} 20.2 (CH\textsubscript{2}), 21.0 (CH\textsubscript{3}), 22.8 (CH\textsubscript{2}), 22.9 (CH\textsubscript{3}), 30.6 [CH(CH\textsubscript{3})\textsubscript{3}], 54.4 (NCHCH\textsubscript{2}), 71.1 (C=CHCO), 121.4 [CCO(\text{Q})], 123.2, 127.1, 127.3, 127.9, 133.3, 135.4 [4 x CH(\text{Q}), HC=CH], 147.4 [CN=C(\text{Q})], 157.6 (C=O) and 159.9, 163.4 [CN(\text{Q}), CO(\text{Q})]; \text{m/z(\%)} 326 (\text{MH}^+66), 307 (100) and 289 (50).
Cyclisation of major alcohol diastereoisomer 189a with 1,1’-carbonyldiimidazole

Alcohol 189a (37mg, 0.11 mmol) was heated under reflux in THF (1 cm³) with sodium hydride (3mg, 0.12 mmol) and 1,1’-carbonyldiimidazole (22mg, 0.14 mmol) under nitrogen for 3 h. After cooling, addition of ethyl acetate (10 cm³) and washing with saturated sodium hydrogen carbonate solution (10 cm³) followed by separation, drying and evaporation of the solvent gave the crude product as a colourless solid. Column chromatography (5:1 light petroleum-ethyl acetate) gave unchanged alcohol 189a (16mg, 43%) as a colourless oil, Rf 0.18.

Further elution gave oxazolidinone 195a (20mg, 49%) as a colourless oil, Rf 0.10. [α]D +39.5° (c=1.0, EtOH); (Found: MH⁺ 370.1766. C₂₀H₂₄O₄N₃ requires M 370.1767); νmax/cm⁻¹ 1790m, 1705m and 1605m; δH 0.99 [9H, s, (CH₃)₃], 1.71 (1H, m, incl. J 13.9, 4.6, CHHCN), 1.81 (1H, m, incl. J 13.9, CHHCN), 2.02 (1H, dd, J 15.4, 4.0, C=CCHH), 2.19 (1H, dd, J 15.4, 4.6, C=CCHH), 3.32 (1H, d, J 10.8, CHOΗ), 4.12 (1H, ddd, J 6.7, 4.6, 4.6, NCH), 4.43 (1H, d, J 10.8, CHOΗ), 4.92 (1H, ddd, J 6.7, 3.1, 1.5, HCO), 5.93 (1H, dd, J 9.9, 3.1, CH=CCH₂), 6.23 (1H, ddd, J 9.9, 4.0, 1.5, C=CHCH₂), 7.45 [1H, ddd, J 8.0, 6.9, 1.0, H-6(Q)], 7.62 [1H, dd, J 8.0, 1.0, H-8(Q)], 7.73 [1H, ddd, J 8.0, 6.9, 1.0, H-7(Q)] and 8.21 [1H, dd, J 8.0, 1.0, H-5(Q)]; m/z(%) 370 (MH⁺,100), 344 (22), 307 (25), 215 (28).
Cyclisation of minor alcohol diastereoisomer 189b with 1,1'-carbonyldiimidazole

Alcohol 189b (23mg, 67 µmol) was heated under reflux in THF (1 cm³) with sodium hydride (2mg, 73 µmol) and 1,1'-carbonyldiimidazole (16mg, 0.10 mmol) under nitrogen for 3 h. After cooling, addition of ethyl acetate (10 cm³) and washing with saturated sodium hydrogen carbonate solution (10 cm³) followed by separation, drying and evaporation of the solvent gave the crude product as a colourless solid. Column chromatography (3:1 light petroleum-ethyl acetate) gave alcohol 189b (11mg, 48%) as a colourless oil, Rf 0.24.

Further elution gave oxazolidinone 195b (11mg, 44%) as a colourless oil, Rf 0.19. (Found: MH⁺ 370.1766. C₂₀H₂₄O₄N₃ requires M 370.1767); νmax/cm⁻¹ 1790m, 1695m and 1605m; δH 1.06 [9H, s, (CH₃)₃], 1.94 (2H, m, incl. J 15.9, 9.8, 6.2, 3.9, CH₂CN), 2.19 (1H, m, incl. J 18.0, 9.5, 4.1, C=CCHH), 2.44 (1H, ddd, J 18.0, 6.2, 2.7, C=CCHH), 2.95 (1H, d, J 11.2, CHOH), 4.54 (1H, ddd, J 8.4, 3.9, NCH), 4.71 (1H, d, J 11.2, CHOH), 5.27 (1H, ddd, J 8.4, 4.6, 1.6, HCO), 5.90 (1H, ddd, J 10.3, 4.6, 2.7, CH=CH₂), 6.22 (1H, ddd, J 10.3, 4.1, 1.6, C=CHCH₂), 7.52 [1H, ddd, J 8.2, 6.8, 1.1, H-6(Q)], 7.70 [1H, dd, J 8.2, 1.1, H-8(Q)], 7.82 [1H, ddd, J 8.2, 6.8, 1.1, H-7(Q)] and 8.27 [1H, dd, J 8.2, 1.1, H-5(Q)]; δC (75 MHz) 20.3, 21.9 (2 x CH₂), 26.3 [(CH₃)₃], 37.2 [C(CH₃)₃], 70.9 74.7 (2 x CH), 121.7 [CCO(Q)], 122.8, 127.7, 127.9, 128.0, 133.2, 135.7 [4 x CH(Q), HC=CH], 146.2 [CN=C(Q)], 157.2 [OC(O)N] and 159.0, 159.6 [CN(Q), CO(Q)]; m/z(%) 370 (MH⁺,100).
Attempted Q°-N bond cleavage of oxazolidinone 195a with aluminium amalgam

Oxazolidinone 195a (20mg, 53.9 μmol) was dissolved in THF (1 cm³) and freshly prepared aluminium amalgam³⁸ (0.5g) added. After stirring for 1 h the reaction mixture was dissolved in ethyl acetate (5 cm³) and washed with saturated sodium carbonate solution (5 cm³), the solvent separated, dried and evaporated to give the crude product as a colourless oil (17mg, 85% recovered). NMR and mass spectrometry analysis showed that the product was unchanged oxazolidinone 195a.

Q°-N bond cleavage of oxazolidinone 195a with samarium(II) iodide

A two-necked round-bottom flask fitted with a 3-way tap and a septum cap was flame dried, flushed with argon and oxazolidinone 195a (17mg, 45.9 μmol) dissolved in THF (1 cm³) was added via a syringe followed by tert-butanol (0.5 cm³) in THF (0.5 cm³). Samarium(II) iodide (0.1M solution in THF) was then added dropwise until the dark blue colour of samarium(II) persisted (~1 cm³).³⁹ Addition of ethyl acetate (5 cm³) and washing with saturated sodium carbonate solution (5 cm³) followed by separation, drying and evaporation of the solvent gave the crude product as a yellow semi-solid. Column chromatography (6:1 light petroleum-ethyl acetate) gave a mixture of products. Subsequent Kieselgel chromatography (9:1 ethyl acetate-methanol) gave aminooquinazolin-4(3H)-one 197 (8mg, 75%) as a colourless crystalline solid, Rf 0.71. δH 1.07 [9H, s, (CH₃)₃], 3.10 (1H, br s, CHO), 4.36 (1H, s, CH)
Further elution gave oxazolidinone 196a (4mg, 62%) as a colourless solid, mp 85-86°C (from light petroleum-ethyl acetate). [α]D -10.6° (c=0.5, EtOH); (Found: MH+ 140.0711. C7H9O2N requires M 140.0712); νmax/cm⁻¹ 3220m and 1740m; δH 1.70 (1H, ddd, J 13.1, 6.4, 3.6, C=CH2), 1.85 (1H, dd, J 9.7, 9.7, 6.4, 3.4, NCH2), 1.99 (1H, ddd, J 9.7, 4.8, 3.4, NCH2), 2.24 (1H, dddd, J 13.1, 9.7, 4.8, 2.5, C=CH2), 3.98 (1H, ddd, J 7.8, 3.4, 3.4, NCH), 4.91 (1H, m, incl. J 7.8, 3.4, HCO), 5.13 (1H, br s, NH), 5.83 (1H, ddd, J 10.3, 3.4, 2.5, CH=CH2) and 6.16 (1H, ddd, J 10.3, 3.6, 1.5, C=CH2); m/z(%) 162 (MNa+,100) and 140 (MH+,67).

Q6-N bond cleavage of oxazolidinone 195b with samarium(II) iodide

The procedure above was carried out using oxazolidinone 195b (11mg, 29.7 μmol), and tert-butanol (0.5 cm³) in THF (1 cm³). Samarium(II) iodide (0.1M solution in THF) was added dropwise until the dark blue colour of samarium(II) metal persisted (~0.8 cm³).139 After work up column chromatography (6:1 light petroleum-ethyl acetate) of the yellow residue gave a mixture of products. Subsequent Kieselgel chromatography (9:1 ethyl acetate-methanol) gave aminoquinazolin-4(3H)-one 197 (5mg, 72%) Rf 0.71, as a colourless crystalline solid identical to that isolated previously.

Further elution gave oxazolidinone 196b (2.5mg, 60%) as a colourless solid, mp 87-88°C (from light petroleum-ethyl acetate). [α]D +13.2° (c=0.5, EtOH); (Found: MH+ 140.0711. C7H9O2N requires M 140.0712); νmax/cm⁻¹ 3220m and 1740m; δH 1.68 (1H, ddd, J 13.9, 6.6, 4.3, C=CH2), 1.86 (1H, dddd, J 9.8, 9.8, 6.6, 3.6, NCH2), 2.00
(1H, ddd, J 9.8, 5.3, 3.6, NCH2CHH), 2.24 (1H, dddd, J 13.9, 9.8, 5.3, 2.2, C=C=CHH),
3.97 (1H, ddd, J 7.5, 3.6, 3.6, NCH), 4.90 (1H, m, incl. J 7.5, 3.6, HCO), 5.07 (1H, br
s, NH), 5.83 (1H, ddd, J 10.2, 3.6, 2.2, CH=CH2) and 6.14 (1H, ddd, J 10.2, 4.3, 1.2,
C=CHCH2); m/z (%) 162 (MNa+,100) and 140 (MH+,67).
Experimental relating to Chapter 6
Ring-opening of aziridine 202 with hydriodic acid

Ring-opening procedure A: aziridine 202 (93mg, 0.44 mmol) was stirred in dichloromethane (2 cm³) with hydriodic acid (2 drops) for 1 min. Addition of further dichloromethane (5 cm³), washing the dichloromethane solution with saturated aqueous sodium hydrogen carbonate (10 cm³), drying and evaporation of the solvent gave the crude product as a colourless oil after. Column chromatography (3:1 light petroleum-ethyl acetate) gave iodide 205 (54mg, 36%) as a colourless oil, Rf 0.29. (Found: M⁺ 341.0025. C₁₂H₁₂ON₃I requires M 341.0025); νmax/cm⁻¹ 3240m, 1665s, 1600s, 1245m and 780m; δH 1.96 (1H, ddd, J 14.1, 6.9, 6.6, CHHCHN), 2.31 [1H, ddd, J 14.1, 7.6, 6.9, CHHCHN], 3.02 [2H, m, incl. J 13.8, 6.9, CH₂(Q)], 3.27 (1H, s, CHI), 3.29 (1H, s, CHI), 3.50 (1H, ddd, J 7.6, 6.6, 2.2, CHNH), 7.31 (1H, d, J 2.2, NH), 7.48 [1H, ddd, J 8.2, 6.9, 1.2, H-5(Q)], 7.67 [1H, dd, J 8.0, 1.2, H-8(Q)], 7.75 [1H, ddd, J 8.0, 6.9, 1.0, H-7(Q)] and 8.27 [1H, dd, J 8.2, 1.0, H-5(Q)]; m/z(%) 341 (M⁺,23), 200 (100) and 185 (22).

Further elution gave iodide 206 (53mg, 35%) as a colourless oil, Rf 0.15. (Found: M⁺ 341.0025. C₁₂H₁₂ON₃I requires M 341.0025); νmax/cm⁻¹ 3260m, 1665s, 1600s and 1500s; δH(400 MHz, 233K) (mixture of N-N bond rotamers) major rotamer - 2.19 (1H, dd, J 13.0, 7.4, CHHCHI), 2.81-3.06 [3H, m, CH₂(Q) and CHNH], 3.39 (1H, m, incl. J 13.0, CHHCHI), 3.95 (1H, ddd, J 13.8, 5.8, 5.8, CHNH), 4.39 (1H, ddd, J 13.8, 7.4, 4.0, 4.0, CHI), 6.86 (1H, d, J 5.8, NH), 7.55 [1H, dd, J 8.0, 6.9, H-6(Q)], 7.67 [1H, d, J 8.0, H-8(Q)], 7.82 [1H, ddd, J 8.0, 6.9, 1.2, H-7(Q)] and 8.27 [1H, dd, J
8.0, 1.2, H-5(Q)]; minor rotamer (observable signals) - δH 2.03 (1H, m, incl. J 13.0, CHHCHI), 2.56 [1H, dd, J 17.0, 4.4, CHH(Q)], 2.81-3.06 [2H, m, CHHCHI and CHH(Q)], 3.84 (2H, dd, J 13.8, 5.8, CH2NH), 4.85 (1H, m, CHI) and 7.07 (1H, d, J 5.8, NH); m/z(%) 341 (M+,77), 214 (48), 200 (100) and 185 (61). From comparison of the NH signals at δ6.86 and 7.07 show a 3:2 ratio of rotamers is present in solution.

Aziridination of isobutene with Q3NHOAc

\[
\begin{array}{c}
\text{Q}^3 \text{NHOAc} \\
\text{71} \\
\text{HMDS, CH}_2\text{Cl}_2 \\
\text{70\%} \\
\text{208}
\end{array}
\]

General aziridination procedure A was followed using NAQ3 (900mg, 4.44 mmol), LTA (2.06g, 4.65 mmol) and HMDS (1.79g, 4.65 mmol) in dichloromethane (4 cm³). After separation from lead-diacetate, the flask was removed from the cooling bath and isobutene gas bubbled through the solution for one minute. On warming to room temperature the mixture was worked up in the usual way. 2-Isopropylquinazolin-4(3H)-one 145 was removed from the crude product by trituration with ethyl acetate-light petroleum and aziridine 208 obtained as a yellow oil after evaporation of the solvent. Crystallisation gave aziridine 208 (798mg, 70%) as a colourless solid, mp 72-73°C (from ethyl acetate-light petroleum). (Found: M⁺ 257.1528. C₁₅H₁₉O₃N requires M 257.1528); δH 1.12 (3H, s, CH₃), 1.32 (3H, d, J 6.6, CH₂CHCH₃), 1.46 (3H, d, J 6.6, CH₂CHCH₃), 1.49 (3H, s, CH₃), 2.62 (1H, br s, azir. CHH), 2.74 (1H, d, J 3.2, azir. CHH), 3.41 [1H, h, J 6.9, CH(CH₃)₂], 7.38 [1H, ddd, J 8.2, 5.0, 1.0, H-6(Q)], 7.60-7.68 [2H, m, H-7 and H-8(Q)] and 8.17 [1H, d, J 8.2, H-5(Q)]; δC 19.3, 20.1 [CH(CH₃)₂], 21.3, 23.8 (2 x CH₃), 46.6 [CH(CH₃)₂], 47.6 (CH₂), 121.8 [CCO(Q)], 126.3, 126.4, 127.4, 133.7 [4 x CH(Q)], 146.5 [CN=C(Q)] and 160.8, 162.0 [CN(Q), CO(Q)]; m/z(%) 257 (MH⁺,15), 189 (66), 173 (96) and 130 (100).
Ring-opening of aziridine 208 with hydriodic acid

\[
\begin{align*}
\text{208} & \quad \text{HI, CH}_2\text{Cl}_2
\end{align*}
\]

Ring-opening procedure A was followed using aziridine 208 (100mg, 0.39 mmol) and hydriodic acid (1 drop) in dichloromethane (1 cm\textsuperscript{3}). After stirring for 0.75 h the reaction mixture was worked up giving a yellow oil after evaporation of the solvent. Column chromatography (3:1 light petroleum-ethyl acetate) gave iodide 209 as a clear oil (80mg, 53%), R\textsubscript{f} 0.71. (Found: M\textsuperscript{+} 385.0652. C\textsubscript{15}H\textsubscript{20}ON\textsubscript{3}I requires M 385.0651); \nu\textsubscript{max}/cm\textsuperscript{-1} 1705s and 1610s; \delta\textsubscript{H} 1.11 (3H, br s, CH\textsubscript{3}), 1.21 [6H, br s, CH(CH\textsubscript{3})\textsubscript{2}], 1.31 (3H, br s, CH\textsubscript{3}), 3.28 (1H, br s, CHHI), 3.39 (1H, br s, CHHT), 3.77 [1H, h, J 6.9, CH(CH\textsubscript{3})\textsubscript{2}], 5.62 (1H, s, NH), 7.33 [1H, ddd, J 8.2, 6.9, 1.5, H-6(Q)], 7.58 [1H, dd, J 8.2, 1.5, H-8(Q)], 7.63 [1H, ddd, J 8.2, 6.9, 1.0, H-7(Q)] and 8.11 [1H, dd, J 8.2, 1.0, H-5(Q)]; m/z(%) 385 (MH\textsuperscript{+}, 63), 258 (33), 244 (74), 216 (26), 203 (30) and 189 (100).

\[
\begin{align*}
\text{209} & \quad \text{211}
\end{align*}
\]

On setting aside (6 months), iodide 209 was converted into alcohol 211, a colourless oil. (Found: M\textsuperscript{+} 276.1712. C\textsubscript{15}H\textsubscript{22}O\textsubscript{2}N\textsubscript{3} requires M 276.1712); \nu\textsubscript{max}/cm\textsuperscript{-1} 3450m, 1655s, 1590s and 1470m; \delta\textsubscript{H} 0.89 (3H, s, CH\textsubscript{3}), 1.18 (3H, d, J 6.9, CH\textsubscript{3}CHCH\textsubscript{3}), 1.30 (3H, s, CH\textsubscript{3}), 1.40 (3H, d, J 6.9, CH\textsubscript{3}CHCH\textsubscript{3}), 3.08 (1H, dd, J 12.3, 10.0, CHH), 3.18 (1H, dd, J 12.3, 5.2, CHH), 3.99 [1H, h, J 6.9, CH(CH\textsubscript{3})\textsubscript{2}], 4.62 (1H, dd, J 10.0, 5.2, OH), 5.60 (1H, s, NH), 7.45 [1H, ddd, J 8.2, 6.8, 1.6, H-6(Q)], 7.69 [1H, dd, J 8.2, 1.6, H-8(Q)], 7.76 [1H, ddd, J 8.2, 6.8, 1.6, H-7(Q)] and 8.21 [1H, dd, J 8.2, 1.6, H-5(Q)]; \delta\textsubscript{C} 19.0, 20.9, 22.2, 24.3 (4 x CH\textsubscript{3}), 30.9 [CH(CH\textsubscript{3})\textsubscript{2}], 60.5 (CN), 67.0 (CH\textsubscript{2}), 119.9 [CCO(Q)], 126.4, 126.6, 127.3, 134.6 [4 x CH(Q)], 147.1 [CN=C(Q)] and 164.6, 164.7 [CN(Q), CO(Q)]; m/z(%) 276 (MH\textsuperscript{+}, 100), 244 (69) and 204 (72).
Ring-opening of aziridine 208 with sodium iodide and acetic acid

Ring-opening procedure B: aziridine 208 (50mg, 0.19 mmol) was dissolved in acetonitrile (1 cm$^3$) and sodium iodide (86mg, 0.58 mmol) added, followed by glacial acetic acid (2μl, 0.19 mmol) and the solution stirred at ambient temperature for 30 min. Addition of ethyl acetate (20 cm$^3$), washing of the solution with saturated aqueous sodium hydrogen carbonate (15 cm$^3$) followed by drying and evaporation of the solvent gave the crude product. Column chromatography (4:1 light petroleum-ethyl acetate) gave iodide 209 $R_f$ 0.61, identical with that isolated above (56mg, 75%). Further elution gave iodide 210 (6mg, 8%) $R_f$ 0.54, as a colourless oil. (Found: $M^+$ 385.0652. C$_{15}$H$_{26}$ON$_3$I requires $M$ 385.0651); δ$_H$ 1.41 [6H, d, J 6.6, (CH$_3$)$_2$], 1.79 (6H, s, 2 x CH$_3$), 3.23 (2H, m, CH$_2$), 3.69 [1H, h, J 6.9, CH(CH$_3$)$_2$], 5.89 (1H, t, J 7.8, NH), 7.33 [1H, ddd, J 8.2, 6.9, 1.5, H-6(Q)], 7.58 [1H, dd, J 8.2, 1.5, H-8(Q)], 7.63 [1H, ddd, J 8.2, 6.9, 1.0, H-7(Q)] and 8.11 [1H, dd, J 8.2, 1.0, H-5(Q)]; $m/z$% 385 (MH$^+$,64), 258 (36), 244 (69), 216 (30), 203 (39) and 189 (100).

Ring-opening of aziridine 208 in the presence of samarium(III) chloride

Ring-opening procedure C: aziridine 208 (50mg, 0.19 mmol) and samarium(III) chloride (50mg, 0.19 mmol) were dissolved in acetonitrile (1 cm$^3$). After stirring for 5 min., sodium iodide (86mg, 0.58 mmol) was added followed after 5 min. by acetic acid (2μl, 0.19 mmol) and the solution then stirred for 30 min. Addition of ethyl acetate (20 cm$^3$), washing of the solution with saturated aqueous sodium hydrogen carbonate (15 cm$^3$), drying and evaporation of the solvent gave the crude product. Column chromatography (4:1 light petroleum-ethyl acetate) gave iodide 209 identical with that isolated above (31mg, 42%).
Further elution gave iodide 210 (30mg, 40%) as a colourless oil identical with that isolated above.

**Ring-opening of aziridine 208 with acetic acid**

\[
\begin{array}{c}
\text{O} \\
\text{N} \\
\text{N} \\
\text{O} \\
\text{AcOH, 1 h} \\
\end{array} \Rightarrow \begin{array}{c}
\text{HNQ}^3 \\
\text{OAc} \\
\text{HNQ}^3 \\
\text{OH} \\
\end{array}
\]

Ring-opening procedure D: aziridine 208 (100mg, 0.39 mmol) was stirred in glacial acetic acid (1 cm\(^3\)) for 1 h. Addition of ethyl acetate (20 cm\(^3\)), washing the solution with saturated aqueous sodium hydrogen carbonate (15 cm\(^3\)) followed by drying and evaporation of the organic solvent gave the crude product as a yellow oil. Column chromatography (3:1 light petroleum-ethyl acetate) separated two compounds in 4:1 ratio. *Acetate 212* was the faster running fraction (R\(_f\) 0.69), was isolated as a clear oil (87mg, 69%). (Found: M\(^+\) 317.1738. C\(_{17}\)H\(_{23}\)O\(_3\)N\(_3\) requires M\(^+\) 317.1738); \(\nu_{\text{max}}/\text{cm}^{-1}\) 1740s, 1695s and 1610s; \(\delta_H\) 1.36 [6H, d, J 6.6, CH(CH\(_3\))\(_2\)], 1.62 (6H, s, 2 x CH\(_3\)), 2.01 (3H, s, OCOCH\(_3\)), 3.20 (2H, br s, CH\(_2\)), 3.62 (1H, h, J 6.6, CH(CH\(_3\))\(_2\)), 5.84 (1H, t, J 7.8, NH), 7.43 [1H, ddd, J 8.2, 6.3, 1.5, H-6(Q)], 7.66-7.77 [2H, m, H-7 and H-8(Q)] and 8.22 [1H, dd, J 8.2, 1.0, H-5(Q)]; \(\delta_C\) 22.3, 24.3 (4 x CH\(_3\)), 30.6 (COCH\(_3\)), 40.0 [CH(CH\(_3\))\(_2\)], 59.4 (CH\(_2\)), 80.4 (COCH\(_3\)), 120.6 [CCO(Q)], 126.2, 126.4, 127.5, 134.2 [4 x CH(Q)], 147.3 [CN=C(Q)], 161.8, 162.8 [CN(Q), CO(Q)]; \(m/z\) (%) 317 (M\(^+\),5), 216 (70), 189 (91) and 173 (100).

Further elution with the same solvent gave *alcohol 213* (18mg, 17%) as a colourless oil. (Found: M\(^+\) 276.1711. C\(_{15}\)H\(_{22}\)O\(_2\)N\(_3\) requires \(M\) 276.1712); \(\nu_{\text{max}}/\text{cm}^{-1}\) 3450w, 1700s and 1610s; \(\delta_H\) 1.37 [6H, s, HOC(CH\(_3\))\(_2\)], 1.38 [6H, d, J 6.9, CH(CH\(_3\))\(_2\)], 2.37 (1H, s, OH), 3.00 (2H, br s, CH\(_2\)), 3.63 (1H, h, J 6.9, CH(CH\(_3\))\(_2\)), 5.88 (1H, t, J 7.3, NH), 7.43 [1H, ddd, J 8.2, 6.9, 1.5, H-6(Q)], 7.65-7.77 [2H, m, H-7 and H-8(Q)] and 8.21 [1H, dd, J 8.2, 1.0, H-5(Q)]; \(\delta_C\) 20.5 [CH(CH\(_3\))\(_2\)], 30.8 [HOC(CH\(_3\))\(_2\)], 40.0
[CH(CH₃)₂], 61.6 (CH₂), 70.0 (COH), 120.6 [CCO(Q)], 126.2, 126.3, 127.5, 134.2 [4 x CH(Q)], 147.3 [CN=C(Q)] and 162.0, 162.5 [C=N(Q),C=O(Q)]; m/z(%) 276 (M⁺,3), 216 (42), 188 (70) and 173 (100).

Synthesis of NAQ 218

Formation of N-acylanthranilate 217

5-Methylenehexanoic acid 216 was prepared by alkylation of dimethyl malonate with methallyl chloride followed by decarboxylation and then hydrolysis according to a literature procedure. Following the method of K. Woodthorpe, acid 216 (2.05g, 18 mmol) was added to a solution of sodium metal (410mg, 20 mmol) in methanol (50 cm³) and stirred for 30 min., evaporation of the solvent gave the sodium salt as a white solid (1.53g, 11 mmol) which was suspended in diethyl ether (50 cm³) containing dry pyridine (4 drops), cooled in ice and treated dropwise with oxalyl chloride (9.8 cm³, 113 mmol) with stirring. After 30 min. the solvent was evaporated, the residual acid chloride dissolved in diethyl ether (50 cm³), added briskly dropwise to a stirred solution of diethyl ether (50 cm³) containing methyl anthranilate (5.12g, 34mmol) and the mixture then heated under reflux for 3 h. After cooling the solution was filtered, the filter cake washed with diethyl ether and the filtrate extracted with hydrochloric acid (2M, 2 x 50 cm³) and washed with water (2 x 50 cm³) giving anthranilate 217 (1.22g, 30%) as a yellow oil after evaporation of the solvent. (Found: MH⁺ 248.1286. C₁₄H₁₈O₃N requires M 248.1286); νmax/cm⁻¹ 1690s, 1610s, 1590s and 1525s; δH 1.83 (3H, s, CH₃), 2.46 (2H, m, incl. J 8.8, 6.6, CH₂), 2.60 (2H, m, incl. J
8.8, 6.6, 1.9, CH₂), 3.93 (3H, s, CO₂CH₃), 4.76 (2H, br s, C=CH₂), 7.07 [1H, ddd, J 8.2, 7.0, 1.0, H-5(Ar)], 7.54 [1H, ddd, J 8.5, 7.0, 1.5, H-4(Ar)], 8.02 [1H, dd, J 8.2, 1.5, H-6(Ar)], 8.72 [1H, dd, J 8.5, 1.0, H-3(Ar)] and 11.00 (1H, br s, NH); δC 22.9 (CH₃), 33.4, 37.2 (2 x CH₂), 40.0 (C=CH₂), 52.7 (CO₂CH₃), 110.9 (C=CH₂), 115.2 [CCO(Q)], 120.8, 122.8, 131.2, 135.1 [4 x CH(Ar)], 144.5 [CN=C(Q)] and 169.2, 171.9 (2 x C=O); m/z(%) 248 (MH⁺,100), 154 (50), 152 (52) and 151 (48).

Cyclisation of N-acylanthranilate 217 to 3-aminoquinazolinone 218

```
\[ \text{NHN} \]
\[ \text{CO}_2\text{Me} \]
\[ \text{217} \]
\[ \text{N} \]
\[ \text{218} \]
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Anthranilate ester 217 (1.22g, 4.90 mmol) was dissolved in methanol (50 cm³) containing hydrazine hydrate (1.23g, 24.60 mmol) and the solution heated under reflux for 3 h. Washing with water followed by drying and evaporation of the solvent gave a yellow solid. Column chromatography (2:1 light petroleum-ethyl acetate) gave 3-aminoquinazolinone 218 (Rf 0.81) as a pale yellow solid (511mg, 46%), mp 100-101°C (from ethanol). (Found: M⁺ 229.1215. C₁₃H₁₅ON₃ requires M 229.1215; νmax/cm⁻¹ 3330m, 1670s, 1595s and 1470s; δH 1.83 (3H, s, CH₃), 2.56 (2H, m, incl. J 8.2, 7.5, 5.4, CCH₂), 3.19 (2H, m, incl. J 8.2, 7.5, 5.4, CH₂), 4.78 (2H, br s, C=CH₂), 4.85 (2H, s, NH₂), 7.45 [1H, ddd, J 8.2, 6.9, 1.0, H-6(Q)], 7.67 [1H, dd, J 8.2, 1.0, H-8(Q)], 7.74 [1H, ddd, J 8.2, 6.9, 1.0, H-7(Q)] and 8.24 [1H, dd, J 8.2, 1.0, H-5(Q)]; δC 23.0 (CH₃), 33.3, 35.2 (2 x CH₂), 111.3 (C=CH₂), 120.4 [CCO(Q)], 126.7, 126.9, 127.6, 134.6 [4 x CH(Q)], 144.9 (C=CH₂), 147.4 [CN=C(Q)] and 158.2, 162.3 [CN(Q), CO(Q)]; m/z(%) 229 (MH⁺,100), 214 (61), 198 (62), 197 (61) and 175 (64).
Intramolecular aziridination of 3-aminoquinazolinone 218

3-Aminoquinazolinone 218 (156mg, 0.68 mmol) and LTA (360mg, 0.82 mmol) were added alternately and continuously in very small portions (~5mg) to stirred dichloromethane (6 cm³) at -10°C over 10 min. after which the solution was allowed to warm to ambient temperature. Addition of further dichloromethane (15 cm³), washing of the dichloromethane solution with saturated aqueous sodium hydrogen carbonate (20 cm³), drying and evaporation of the solvent gave a colourless solid. Crystallisation gave aziridine 207 as a colourless solid (104mg, 66%) mp 164-166°C (from light petroleum-ethyl acetate). (Found: M⁺ 227.1059. C₁₃H₁₃ON₃ requires M 227.1059); νmax/cm⁻¹ 1680s, 1605s, 1570m, 1470s and 1365s; δH 1.49 (3H, s, CH₃), 1.71 (1H, ddd, J 13.7, 10.1, 6.4, NCC'H), 2.06 (1H, d, J 2.3, azir. CHH), 2.43 (1H, ddd, J 13.7, 3.9, 3.9, NCCH'H), 2.83 (1H, d, J 2.3, azir. CHH), 2.96 (1H, dd, J 10.1, 3.9, CH'H-Q), 2.99 (1H, dd, J 6.4, 3.9, CH'H-Q), 7.45 [1H, ddd, J 8.2, 6.9, 1.0, H-6(Q)], 7.67 [1H, dd, J 8.2, 1.0, H-8(Q)], 7.74 [1H, ddd, J 8.2, 6.9, 1.0, H-7(Q)] and 8.24 [1H, dd, J 8.2, 1.0, H-5(Q)]; δC 23.9 (CH₃), 28.2, 28.5 (2 x CH₂), 44.2 (C-N), 51.1 (N-CH₂), 121.9 [CCO(Q)], 126.6, 126.9, 127.0, 134.1 [4 x CH(Q)], 146.5 [CN=C(Q)] and 153.6, 159.6 [CN(Q), CO(Q)]; m/z (%) 227 (MH⁺,31), 200 (28) and 199 (100).
Ring-opening of aziridine 207 with hydriodic acid

Ring-opening procedure A was followed using aziridine 207 (70mg, 0.31 mmol) dissolved in dichloromethane (2 cm³) and two drops of hydriodic acid. After stirring for 1 min. the reaction mixture was worked up in the normal way, giving the crude product as a colourless oil. Column chromatography (3:1 light petroleum-ethyl acetate) gave iodide 219 (85mg, 78%) as a colourless solid which crystallised from light petroleum: ethyl acetate, mp. 149-150°C. (Found: C, 44.3; H, 4.1; N, 11.5%. C₁₅H₁₅ON₃I requires C, 44.0; H, 4.0; N, 11.8%); νmax/cm⁻¹ 1665s and 1610s; δH 1.42 (3H, s, CH₃), 2.09 (2H, ddd, J 14.2, 7.0, 6.5, CH₂), 2.99 [2H, dd, J 7.0, 6.5, CH₂(Q)], 3.30 (1H, d, J 10.3, CHHI), 3.32 (1H, d, J 10.3, CHHI), 6.86 (1H, s, NH), 7.48 [1H, ddd, J 8.2, 6.8, 1.2, H-6(Q)], 7.68 [1H, dd, J 8.2, 1.2, H-8(Q)], 7.75 [1H, ddd, J 8.2, 6.8, 1.0, H-7(Q)] and 8.28 [1H, dd, J 8.2, 1.0, H-5(Q)]; δC 17.0 (CH₂), 28.7 (CH₃), 28.9 (CH₂), 33.7 (CH₂I), 56.7 (CN), 120.0 [CCO(Q)], 126.7, 126.8, 127.5, 134.3 [4 x CH(Q)], 147.0 [CN=C(Q)] and 152.8, 158.2 [CN(Q), CO(Q)]; m/z(%) 356 (MH⁺,100), 330 (22) and 307 (42).
Ring-opening of aziridine 226 with hydriodic acid

Ring-opening procedure A was followed using aziridine 226 (100mg, 0.35 mmol) dissolved in acetonitrile (1 cm³) with hydriodic acid (2 drops). After stirring for 45 min. the reaction was worked up to give the crude product as a dark red oil. Column chromatography (3:1 light petroleum-ethyl acetate) gave a 3:2 mixture of regioisomers 227 and 228 as a yellow oil (88mg, 61%) Rf 0.45, from comparison of NMR signals at δ 5.91 and 5.92 respectively. (Found: MH⁺ 416.0472. C₁₇H₁₉O₃N₃I requires M 416.0472); ν max/cm⁻¹ 1740s, 1680s and 1600s; for iodide 227 - δH 1.34 (3H, d, J 7.0, CH₃CHCH₃), 1.37 (3H, d, J 7.0, CH₂CHCH₃), 3.47 (1H, br s, CHH), 3.59 (1H, br s, CHH), 3.62 [1H, h, J 7.0, CH(CH₃)₂], 3.79 (3H, s, CO₂CH₃), 4.54 (1H, dd, J 7.8, 6.2, CHI), 5.91 (1H, t, J 7.2, NH), 7.43 [1H, ddd, J 8.2, 6.6, 1.5, H-6(Q)], 7.64-7.78 [2H, m, H-7 and H-8(Q)] and 8.21 [1H, dd, J 8.2, 1.0, H-5(Q)]; δC 15.0 (CHI), 30.6 (2 x CH₃), 39.2 [CH(CH₃)₂], 53.2 (CO₂CH₃), 55.5 (CH₂), 120.3 [CCO(Q)], 126.3, 126.4, 127.5, 134.4 [4 x CH(Q)], 147.1 [CN=C(Q)], 162.1, 169.5 [CN(Q), CO(Q)] and 172.2 (CO₂CH₃); for iodide 228 (observable signals) - δH 1.32 (3H, d, J 6.9, CH₃CHCH₃), 1.38 (3H, d, J 6.9, CH₃CHCH₃), 3.40 (1H, m, CHH), 3.59 (1H, m, CHH), 3.62 [1H, h, J 6.9, CH(CH₃)₂], 3.82 (3H, s, CO₂CH₃), 4.10 (1H, dd, J 7.2, 4.7, CHNH), 5.92 (1H, d, J 7.2, NH), 7.41 [1H, ddd, J 8.2, 6.6, 1.5, H-6(Q)] and 8.15 [1H, d, J 8.2, H-5(Q)]; m/z(%) 416 (MH⁺,100), 307 (28), 289 (25), 288 (43), 189 (22) and 173 (23).
Ring-opening of aziridine 226 with sodium iodide/glacial acetic acid

1) NaI (3 eq.), CH₃CN, 2) AcOH (1 eq.), 20 min → 70%

Ring-opening procedure B was followed using aziridine 226 (100mg, 0.35 mmol), sodium iodide (156mg, 1.05 mmol) and glacial acetic acid (20mg/20 µl, 0.35 mmol) in acetonitrile (1 cm³). After stirring for 20 min. work up gave the crude product as a dark red oil. Column chromatography (3:1 light petroleum-ethyl acetate) gave a mixture of iodide 227 (79mg, 55%) and ester 229 (15mg, 15%) as a yellow oil, Rf 0.47. For ester 229 - δH 1.34 (3H, d, J 6.9, CH₃CHCH₃), 1.38 (3H, d, J 6.9, CH₃CHCH₃), 2.61 (2H, t, J 7.0, CH₂CO₂Me), 3.29 (2H, m, NHCH₂), 3.60 [1H, h, J 6.9, CH(CH₃)₂], 3.72 (3H, S, CO₂CH₃), 5.80 (1H, t, J 7.0, NH), 7.42 [1H, ddd, J 8.2, 6.6, 1.2, H-6(Q)], 7.58 [1H, dd, J 8.0, 1.2, H-8(Q)], 7.70 [1H, ddd, J 8.0, 6.6, 1.2, H-7(Q)] and 8.25 [1H, dd, J 8.2, 1.2, H-5(Q)].

The reaction above was repeated but the mixture stirred at ambient temperature for 2 h. After work up column chromatography (3:1 light petroleum-ethyl acetate) gave a mixture of iodide 227 (69mg, 48%) and ester 229 (20mg, 20%) as a yellow oil, Rf 0.47.

Stability of iodide 227 to conditions in the previous experiment

1) NaI (3 eq.), CH₃CN, 2) AcOH (10 eq.), 2 h → no reaction

Ring-opening procedure B was followed using iodide 227 (50mg, 0.12 mmol), sodium iodide (54mg, 0.36 mmol) and glacial acetic acid (7mg/7 µl, 0.12 mmol) in acetonitrile.
After stirring for 2 h., work up gave the crude product as a dark red oil. Column chromatography (3:1 light petroleum-ethyl acetate) gave iodide 227 (48mg, 97% recovered) as a yellow oil, $R_f$ 0.47.

**Ring-opening of aziridine 226 using excess glacial acetic acid**

Ring-opening procedure B was followed using aziridine 226 (100mg, 0.35 mmol), sodium iodide (156mg, 1.05 mmol) and glacial acetic acid (200mg/0.20 cm³, 0.35 mmol) in acetonitrile (1 cm³). After stirring for 20 min. work up gave the crude product as a dark red oil. Column chromatography (3:1 light petroleum-ethyl acetate) gave a mixture of iodide 227 (76mg, 53%) and ester 229 (19mg, 19%) as a yellow oil, $R_f$ 0.47.

**Ring-opening of aziridine 226 in the presence of samarium(III) chloride**

Ring-opening procedure C was followed using aziridine 226 (100mg, 0.35 mmol), samarium(III) chloride (89mg, 0.35 mmol), sodium iodide (156mg, 1.05 mmol) and glacial acetic acid (20mg/20 μl, 0.35 mmol) in acetonitrile (1 cm³) and the mixture was stirred for 20 min. Work up gave the crude product as a dark red oil. Column chromatography (3:1 light petroleum-ethyl acetate) gave a mixture of iodide 227 (85mg, 59%) and ester 229 (17mg, 17%) as a yellow oil, $R_f$ 0.47.
Ring-opening of aziridine 115 with hydriodic acid

\[
\begin{align*}
\text{HI, CH}_3\text{CN} & \quad \text{30 min} \\
\text{Ring-opening procedure A was followed using aziridine 115 (100mg, 0.32 mmol) and hydriodic acid (2 drops) in acetonitrile (1 cm}^3\text{). After stirring for 30 min., work up gave the crude product as a dark red oil. Column chromatography (3:1 light petroleum-ethyl acetate) gave a 1:1 mixture of regioisomers 230 and 231 as a yellow oil (110mg, 78\%) R_f 0.49, from comparison of NMR signals at } & \\
\delta & \text{ 5.76 and 6.15 respectively. A sample of iodide 230 (30mg) was separated from the mixture by Kieselgel chromatography (5:1 light petroleum-ethyl acetate). (Found: MH}^+ \text{ 441.9875. C}_{13}\text{H}_{12}\text{O}_{3}\text{N}_{3}\text{IF}_3 \text{ requires } M \text{ 441.9874); } \\
\delta & \text{H 3.45 (2H, m, CH}_2\text{), 3.82 (3H, s, CO}_2\text{CH}_3\text{), 4.62 (1H, dd, } J & \text{ 8.8, 5.6, CHI)}\text{, 5.76 (1H, t, } J & \text{ 6.9, NH)}\text{, 7.63 [1H, ddd, } J & \text{ 8.2, 4.8, 1.0, H-6(Q)}\text{], 7.85 [2H, m, H-7 and H-8(Q)] and 8.30 [1H, dd, } J & \text{ 8.2, 1.0, H-5(Q)}\text{]; } \\
\delta & \text{C} 14.7 \text{(CHI), 53.2 (CO}_2\text{CH}_3\text{), 55.4 (CH}_2\text{), 115.6 (CF}_3\text{), 122.0 [CCO(Q)], 126.9, 128.9, 129.4, 135.3 [4 x CH(Q)], 144.9 [CN=Q(Q)] and 161.6, 170.9 [CO/CN(Q) and CO}_2\text{CH}_3\text{] - [CO/CN(Q) missing]; for iodide 232 (observable signals)- } \\
\delta & \text{H 3.48 (2H, d, } J & \text{ 6.3, CH}_2\text{), 3.86 (3H, s, CO}_2\text{CH}_3\text{), 3.98 (1H, dt, } J & \text{ 6.3, 6.3, CHNH)}\text{, 6.15 (1H, d, } J & \text{ 6.3, NH)}\text{, 7.63 [1H, dd, } J & \text{ 8.2, 4.0, H-6(Q)] and 8.27 [1H, dd, } J & \text{ 8.2, 1.0, H-5(Q)}\text{] (for NMR spectrum of pure iodide 232, see below); } \\
\text{m/z} & \text{(%)} 442 (M}^+,100), 314 (37), 282 (27), 230 (23), 229 (32) and 215 (23). 
\end{align*}
\]
Ring-opening of aziridine 115 with sodium iodide/glacial acetic acid

Ring-opening procedure B was followed using aziridine 115 (100 mg, 0.32 mmol), sodium iodide (143 mg, 0.96 mmol) and glacial acetic acid (23 mg/22 μl, 0.32 mmol) in acetonitrile (1 cm³). After stirring for 2 min., work up gave the crude product as a dark yellow oil. Column chromatography (3:1 light petroleum-ethyl acetate) gave a 6:1 mixture of iodides 230 and 231 as a yellow oil (96 mg, 68%) Rf 0.50, from comparison of NH signals at δ 5.76 and 6.15 in the NMR spectrum of the mixture.

Ring-opening of aziridine 115 with sodium iodide/glacial acetic acid: stability of products to the reaction conditions

As in the previous experiment, ring-opening procedure B was followed using aziridine 115 (100 mg, 0.32 mmol), sodium iodide (143 mg, 0.96 mmol) and glacial acetic acid (23 mg/22 μl, 0.32 mmol) in acetonitrile (1 cm³). After stirring for 1 h., work up gave the crude product as a dark yellow oil. Column chromatography (3:1 light petroleum-ethyl acetate) gave a 5:1 mixture of iodides 230 and 231 as a yellow oil (72 mg, 51%) Rf 0.50, from comparison of the same NMR signals above.

Further elution gave NAQ⁵ (15 mg, 21%) as a white solid, Rf 0.34 and ester 232 (17 mg, 17%) as a colourless oil, Rf 0.28. (Found: MH⁺ 316.0908. C₁₃H₁₃O₃N₃F₃ requires M 316.0909); δH 2.81 (2H, t, J 5.8, CH₂CO₂Me), 3.47 (2H, m, NHCHO₂), 3.82 (3H, s, CO₂CH₃), 5.94 (1H, t, J 7.2, NH), 7.63 [1H, dd, J 8.2, 4.0, H-6(Q)], 7.83-7.93
[2H, m, H-7 and H-8(Q)] and 8.27 [1H, dd, J 8.2, 1.0, H-5(Q)]; m/z(%) 316 (M+,100), 230 (47) and 215 (41).

Stability of iodide 230 to reaction conditions in the previous experiment

Ring opening procedure B was followed using iodide 230 (60mg, 0.13 mmol), sodium iodide (58mg, 0.39 mmol) and glacial acetic acid (7mg/8μl, 0.13 mmol) in acetonitrile (1 cm³). After stirring for 2h., work up gave the crude product as a dark red oil. Column chromatography (3:1 light petroleum-ethyl acetate) gave iodide 230 (46mg, 93% recovered) as a yellow oil, Rf 0.47.

Ring-opening of aziridine 115 with iodide in the presence of samarium(III) chloride

Ring-opening procedure C was followed using aziridine 115 (100mg, 0.32 mmol), samarium(III) chloride (82mg, 0.32 mmol), sodium iodide (143mg, 0.96 mmol) and glacial acetic acid (23mg/22 μl, 0.32 mmol) in acetonitrile (1 cm³). After stirring for 2 min., work up gave the crude product as a dark red oil. Column chromatography (3:1 light petroleum-ethyl acetate) gave iodide 231 (55mg, 39%) as a yellow oil, Rf 0.51. (Found: MH⁺ 441.9875. C₁₃H₁₂O₃N₃IF₃ requires M 441.98744); ν_MAX/cm⁻¹ 1690s, 1645s and 1610s; δ_H 3.48 (2H, d, J 6.2, CH₂), 3.86 (3H, s, CO₂CH₃), 3.98 (1H, dt, J 6.3, 6.3, CHNH), 6.15 (1H, d, J 6.3, NH), 7.63 [1H, dd, J 8.2, 4.0, H-6(Q)], 7.83 [2H,
m, H-7 and H-8(Q)] and 8.27 [1H, dd, J 8.2, 1.0, H-5(Q)]; δC 33.1 (CH₂), 46.9
(CO₂CH₃), 52.3 (C-N), 120.4 (CF₃), 122.6 [CCO(Q)], 127.2, 129.2, 129.6, 135.5 [4 x
CH(Q)], 145.4 [CN=C(Q)], 161.7, 163.0 [CO(Q), CN(Q)] and 172.5 (C=O ester);
m/z(%) 442 (M⁺, 100), 314 (31), 282 (29), 230 (23), 229 (52) and 215 (33).

Further elution gave NAQ⁵ 110 (19mg, 25%) as a white solid, Rf 0.34 and ester 232
(26mg, 26%) as a colourless oil Rf 0.28, identical with that isolated previously.

**Ring-opening of aziridine 233 with hydriodic acid**

Ring-opening procedure A was followed using aziridine 233 (100mg, 0.30 mmol) in
acetonitrile (1 cm³) with hydriodic acid (2 drops). After stirring for 30 min., work up
gave the crude product as a dark red oil. Column chromatography (3:1 light
petroleum-ethyl acetate) gave a 1:1 mixture of iodide regioisomers 234 and 235 as a
yellow oil (48mg, 38%) Rf 0.43, from comparison of NMR signals at δ 5.83 and 6.08
respectively. Pure iodide 235 was obtained by Kieselgel chromatography. (Found:
MH⁺ 430.06283. C₁₇H₁₉O₃N₃I requires M 430.06286); δH 1.25 (3H, s, CH₃), 1.35 [3H,
d, J 6.9, CH(CH₃)₂]; 1.38 [3H, d, J 6.9, CH(CH₃)₂], 3.35 (1H, d, J 10.2, CHH), 3.48
(1H, d, J 10.2, CHH), 3.62 [1H, h, J 6.9, CH(CH₃)₂], 3.75 (3H, s, CO₂CH₃), 5.83
(1H, s, NH), 7.30 [1H, ddd, J 8.0, 6.6, 1.2, H-6(Q)], 7.54 [1H, dd, J 8.0, 1.2, H-8(Q)],
7.61 [1H, ddd, J 8.0, 6.6, 1.2, H-7(Q)] and 8.08 [1H, dd, J 8.0, 1.2, H-5(Q)]; δC 11.7,
14.6, 30.6 (3 x CH₃), 28.4 (CH₂), 53.8 (CO₂CH₃), 64.4 [CH(CH₃)₂], 73.9 (C), 120.7
[CCO(Q)], 126.7, 127.0, 127.5, 134.7 [4 x CH(Q)], 147.5 [CN=C(Q)], 161.1, 163.3
[CN(Q), CO(Q)] and 172.0 (CO₂CH₃); for iodide 234 (observable signals in NMR
spectrum of the crude product) - δH 2.04 (3H,s, CH₃), 6.08 (1H, t, J 7.6, NH); m/z(%) 430 (MH⁺,100), 321 (33), 303 (21), 302 (49), 189 (23) and 173 (22).

Further elution gave aziridine 233 (55mg, 55% recovered) as a yellow oil, Rf 0.27.
Ring-opening of aziridine 233 with sodium iodide/glacial acetic acid

Ring-opening procedure C was followed using aziridine 233 (100mg, 0.30 mmol), sodium iodide (135mg, 0.90 mmol) and glacial acetic acid (18mg/18 μl, 0.30 mmol) in acetonitrile (1 cm³). After stirring for 4 h., work up gave the crude product as a dark yellow oil. Column chromatography (3:1 light petroleum-ethyl acetate) gave an unseparated 2:3 mixture of iodides 234 and 235 as a yellow oil (63mg, 49%) R_f 0.48, from comparison of the same NMR signals above.

Further elution gave aziridine 233 as a yellow oil (35mg, 35% recovered) R_f 0.27.

Ring-opening of aziridine 233 by iodide in the presence of samarium(III) chloride

Ring-opening procedure C was followed using aziridine 233 (100mg, 0.30 mmol), samarium(III) chloride (77mg, 0.30 mmol), sodium iodide (135mg, 0.90 mmol) and glacial acetic acid (18mg/19 μl, 0.30 mmol) in acetonitrile (1 cm³). The mixture was stirred for 25 min. and work up gave the crude product as a dark red oil. Column chromatography (3:1 light petroleum-ethyl acetate) gave iodide 234 (48mg, 37%) R_f 0.51, as a yellow oil identical with that isolated previously.

Further elution gave aziridine 233 as a yellow oil (39mg, 39%) R_f 0.28.
Ring-opening of aziridine 233 with iodide in the presence of excess glacial acetic acid

Ring-opening procedure B as followed using aziridine 233 (100mg, 0.30 mmol), sodium iodide (135mg, 0.90 mmol) and glacial acetic acid (180mg/0.18 cm³, 3.00 mmol) in acetonitrile (1 cm³). After stirring for 4 h., work up gave the crude product as a dark yellow oil. Column chromatography (3:1 light petroleum-ethyl acetate) gave a 2:3 mixture of iodides 234 and 235 as a yellow oil (59mg, 46%) Rf 0.48, from comparison of the same signals in the NMR spectrum referred to previously.

Further elution gave aziridine 233 as a yellow oil (32mg, 32% recovered) Rf 0.27.

Stability of iodides 234 and 235 to sodium iodide/acetic acid

Ring-opening procedure B was followed using a 2:3 mixture of iodide regioisomers 234 and 235 (59mg, 0.14 mmol), sodium iodide (61mg, 0.40 mmol) and glacial acetic acid (7mg/8µl, 0.17 mmol) in acetonitrile (1 cm³). After stirring for 2 h., work up gave the crude product as a dark red oil. Column chromatography (3:1 light petroleum-ethyl acetate) gave a 2:3 mixture of iodides 234 and 235 (55mg, 94% recovered) as a yellow oil, Rf 0.47.
Ring-opening of aziridine 116 with hydriodic acid

Ring-opening procedure A was followed using aziridine 116 (66mg, 0.30 mmol) in acetonitrile (1 cm³) with hydriodic acid (2 drops). The reaction was stirred for 30 min. and work up gave the crude product as a dark red oil. Column chromatography (3:1 light petroleum-ethyl acetate) gave a 1:1 mixture of iodide regioisomers 236 and 237 (78mg, 57%) as a yellow oil, Rf 0.47.
Further elution gave aziridine 116 (20mg, 31% recovered) as a yellow oil, Rf 0.27.

Ring-opening of aziridine 116 with sodium iodide/glacial acetic acid

Ring-opening procedure B was followed using aziridine 116 (93mg, 0.28 mmol), sodium iodide (127mg, 0.85 mmol) and glacial acetic acid (16mg/17 μl, 0.28 mmol) in acetonitrile (1 cm³). After stirring for 20 min., work up gave the crude product as a dark yellow oil. Column chromatography (3:1 light petroleum-ethyl acetate) gave a 1:1 mixture of iodides 236 and 237 (63mg, 45%) as a yellow oil, Rf 0.48.
Further elution gave aziridine 116 (34mg, 35% recovered) as a yellow oil, Rf 0.24.
Stability of iodides 236 and 237 to the previous reaction conditions

Ring-opening procedure B was followed using a 1:1 mixture of iodide regioisomers 236 and 237 (63mg, 0.14 mmol), sodium iodide (62mg, 0.41 mmol) and glacial acetic acid (8mg/8µl, 0.14 mmol) in acetonitrile (1 cm³). After stirring for 2 h., work up gave the crude product as a dark red oil. Column chromatography (3:1 light petroleum-ethyl acetate) gave a 1:1 mixture of iodides 236 and 237 (55mg, 87% recovered) as a yellow oil, Rf 0.48.

Ring-opening of aziridine 116 with iodide in the presence of samarium(III) chloride

Ring-opening procedure C was followed using aziridine 116 (54mg, 0.17 mmol), samarium(III) chloride (44mg, 0.17 mmol), sodium iodide (75mg, 0.50 mmol) and glacial acetic acid (10mg/10 µl, 0.17 mmol) in acetonitrile (1 cm³). After stirring for 25 min., work up gave the crude product as a dark red oil. Column chromatography (3:1 light petroleum-ethyl acetate) gave a 1:3 mixture of iodides 236 and 237 as a yellow oil (53mg, 68%) Rf 0.51, from comparison of NH signals at δ5.78 and 5.88 in the NMR spectrum respectively. Kieselgel chromatography (5:1 light petroleum-ethyl acetate) gave a sample of iodide 236 as a pale yellow oil. (Found: MH⁺ 456.0032. C₁₄H₁₄O₃N₃IF₃ requires M 456.0033); v₅max/cm⁻¹ 1735s, 1700s and 1610m; δ₁H 1.44 (3H, s, CCH₃), 3.22 (1H, dd, J 12.0, 7.5, CHH), 3.48 (1H, dd, J 12.0, 7.0, CHH), 3.97 (3H, s, CO₂CH₃), 5.78 (1H, dd, J 7.5, 7.0, NH), 7.58 [1H, ddd, J 8.2, 5.0, 1.0, H-
Further elution gave a pure sample of iodide \(237\) as a pale yellow oil. (Found: MH\(^+\) 456.0032. \(\text{C}_{14}\text{H}_{14}\text{O}_3\text{N}_3\text{IF}_3\) requires \(M\) 456.0033); \(\nu_{\text{max}}/\text{cm}^{-1}\) 1735s, 1700s and 1610m; \(\delta_\text{H}\) 1.25 (3H, s, CCH\(_3\)), 3.34 (1H, d, \(J\) 10.0, CHH), 3.52 (1H, d, \(J\) 10.0, CHH), 3.93 (3H, s, \(\text{CO}_2\text{CH}_3\)), 5.88 (1H, s, NH), 7.63 [1H, ddd, \(J\) 8.2, 5.0, 1.2, H-6(Q)], 7.84-7.88 [2H, m, H-7 and H-8(Q)] and 8.28 [1H, dd, \(J\) 8.2, 1.0, H-5(Q)]; \(\delta_\text{C}\) 22.4 (CH\(_3\)), 53.6 (\(\text{CO}_2\text{CH}_3\)), 57.1 (CH\(_2\)), 73.9 (C), 122.0 [\(\text{CCO}(Q)\)], 127.3, 129.2, 129.7, 135.6 [4 \(\text{CH}(Q)\)], 144.9 [\(\text{CN}=\text{C}(Q)\)], 148.3 (CF\(_3\)), 161.5 [\(\text{CN}(Q)/\text{CO}(Q)\)] and 170.3 [\(\text{CO}_2\text{CH}_3\) - \(\text{CN}(Q)/\text{CO}(Q)\) missing]; \(m/z\)% 456 (M\(^+\),34), 328 (21), 308 (23), 307 (100) and 289 (53).

### Aziridination of \(\alpha\)-methylene-\(\gamma\)-butyrolactone with \(Q^3\text{NHOAc}\)

![Diagram](image)

General aziridination procedure \(A\) was followed using \(\text{NAQ}^3\) (200mg, 0.98 mmol). LTA (458mg, 1.03 mmol), \(\alpha\)-methylene-\(\gamma\)-butyrolactone (193mg/0.17 cm\(^3\), 1.97 mmol) and HMDS (395mg, 2.45 mmol) in dichloromethane (2 cm\(^3\)). Column chromatography (1:1 light petroleum-ethyl acetate) of the crude product (290mg) gave \(\alpha\)-methylene-\(\gamma\)-butyrolactone (154mg, 78% recovered) as a yellow oil, R 0.23. Further elution gave aziridine \(238\) as a colourless solid (97mg, 33%) R\(_f\) 0.14, mp 126-127\(^\circ\)C (from ethanol). (Found: \(M^+\) 299.12696. \(\text{C}_{16}\text{H}_{17}\text{O}_3\text{N}_3\) requires \(M\) 299.12699); \(\nu_{\text{max}}/\text{cm}^{-1}\) 2980m, 1770m and 1660m; \(\delta_\text{H}\) 1.34 (3H, d, \(J\) 6.6, CH\(_3\)CH\(_3\)H), 1.49 (3H, d, \(J\) 6.6, CH\(_3\)CH\(_3\)H), 2.60 (1H, ddd, \(J\) 16.9, 9.4, 3.9, OCH\(_3\)), 2.88 (1H, ddd, \(J\) 13.9, 8.3, 3.9, NCC\(_3\)H\(_3\)), 2.97 (1H, br s, azir. NCH\(_3\)), 3.08 (1H, br s, azir. NCH\(_3\)), 3.49
Aziridination of α-methylene-γ-butyrolactone with Q5NHOAc

General aziridination procedure A aziridination was followed using NAQ5 (225mg, 0.98 mmol), LTA (458mg, 1.03 mmol) and α-methylene-γ-butyrolactone (193mg/0.17 cm3, 1.97 mmol) in dichloromethane (2 cm3). Crystallisation of the crude product (287mg) from ethanol gave aziridine 239 (105mg, 33%) as a colourless solid, mp 133-135°C. (Found: C, 51.7; H, 3.0; N 13.1%. C16H17O3N3 requires C, 51.7; H, 3.0; N, 12.9%); νmax/cm−1 2960s, 1765s and 1660s; δH 2.60 (1H, ddd, J 16.3, 9.0, 4.3, OCHH), 2.95 (1H, ddd, J 13.7, 8.8, 4.3, NCCCH), 3.13 (1H, d, J 2.2, azir. NCHH), 3.32 (1H, br s, azir. NCHH), 4.56 (1H, dd, J 13.7, 9.0, NCCCH), 4.96 (1H, dd, J 16.3, 8.8, OCHH), 7.62 (1H, ddd, J 8.2, 4.1, H-6(Q)), 7.70-7.90 [2H, m, H-7 and H-8(Q)] and 8.22 (1H, dd, J 8.2, 1.0, H-5(Q)); δC 28.6 (OCH2CH2), 47.4 (NCH2), 48.3 (NCCO), 66.5 (OCH2), 120.6 [CCO(Q)], 122.3 (CF3), 127.1, 128.8, 129.9, 135.1 [4 x CH(Q)], 144.0 [CN=C(Q)], 160.1 [CN/CO(Q)] and 172.1 (lactone C=O) - [CN/CO(Q) missing]; m/z(%) 325 (M+, 100), 215 (33), 214 (30) and 171 (72).
Ring-opening of aziridine 238 with sodium iodide/acetic acid

Ring-opening procedure B was followed using aziridine 238 (90mg, 0.29 mmol), sodium iodide (136mg, 0.90 mmol) and glacial acetic acid (17mg/18μl, 0.29 mmol) in acetonitrile (1 cm³). After stirring for 20 min. the reaction was worked up to give the crude product as a yellow oil. Column chromatography (2:1 light petroleum-ethyl acetate) gave iodide 240 (47mg, 38%) as a yellow oil, Rf 0.35. (Found: M⁺ 428.04711. C₁₆H₁₉O₃N₃I requires M⁺ 428.04710; νmax/cm⁻¹ 1770s and 1660s; δH 1.22 (3H, d, J 6.8, CH₃CHCH₃), 1.25 (3H, d, J 6.8, CH₂CHCH₂), 2.24 (1H, ddd, J 14.0, 6.9, NCCCH), 2.56 (1H, ddd, J 14.0, 8.4, NCCCHH), 3.43 (1H, d, J 11.9, CH₂I), 3.62 [1H, h, J 6.8, CH(CH₃)₂], 4.27 (2H, m, OCH₂), 5.81 (1H, s, NH), 7.37 [1H, ddd, J 8.2, 6.9, 1.0, H-6(Q)], 7.57-7.72 [2H, m, H-7 and H-8(Q)] and 8.12 [1H, dd, J 8.2, 1.0, H-5(Q)]; δC 9.5 (CH₃I), 20.7, 21.3 (2 x CH₃), 31.1 [CH(CH₃)₂], 33.0 (CCH₂), 65.2 (NCCO), 65.5 (OCH₂), 120.4 [CCO(Q)], 126.9, 127.0, 127.7, 135.3 [4 x CH(Q)], 147.2 [CN=C(Q)] and 162.3, 164.0 [CN(Q), CO(Q)] - lactone C=O missing; m/z(%) 428 (M⁺,100).

Further elution gave aziridine 238 (43mg, 48% recovered) as a white crystalline solid, R 0.29.

Ring-opening of aziridine 238 with iodide in the presence of samarium(III) chloride

Ring-opening procedure C was followed using aziridine 238 (145mg, 0.48 mmol), samarium(III) chloride (123mg, 0.48 mmol), sodium iodide (136mg, 0.90 mmol) and glacial acetic acid (17mg/18μl, 0.29 mmol) in acetonitrile (1 cm³). After stirring for 20 min. the reaction was worked up to give the crude product as a yellow oil. Column
chromatography (2:1 light petroleum-ethyl acetate) gave iodide 240 (92mg, 45%) Rf 0.36, as a yellow oil identical to that isolated previously.

Further elution gave aziridine 238 (57mg, 39% recovered) as a white crystalline solid, R 0.27.

Ring-opening of aziridine 239 with sodium iodide/acetic acid

Ring-opening procedure B was followed using aziridine 239 (100mg, 0.31 mmol), sodium iodide (136mg, 0.92 mmol) and glacial acetic acid (19mg/19μl, 0.31 mmol) in acetonitrile (1 cm³). After stirring for 20 min. the reaction was worked up to give the crude product as a yellow oil. Crystallisation from ethanol gave iodide 241 (47mg, 38%) as a colourless crystalline solid, mp 181-183°C. (Found: M+ 452.97972. C₁₄H₁₁O₃N₃I₃ requires M 452.97971); νmax/cm⁻¹ 1780s and 1710s; δH 2.10 (1H, ddd, J 15.4, 9.5, 6.3, OCHH), 2.39 (1H, ddd, J 14.4, 9.1, 6.3, NCCHH), 3.46 (2H, s, NCH₂), 4.16 (1H, ddd, J 14.4, 9.5, 5.3, NCCCHH), 4.30 (1H, ddd, J 15.4, 9.1, 6.3, OCHH), 5.65 (1H, s, NH), 7.59 [1H, ddd, J 8.2, 5.3, 2.8, H-6(Q)], 7.77-7.88 [2H, m, H-7 and H-8(Q)] and 8.23 [1H, d, J 8.2, H-5(Q)]; δC 10.1 (CH₂), 32.8 (OCH₂CH₂), 64.8 (NCCO), 66.3 (OCH₂), 121.1 [CCO(Q)], 122.9 (CF₃), 127.0, 128.4, 129.8, 134.7 [4 × CH(Q)], 144.3 [CN=C(Q)], 160.8 [CN/CO(Q)] and 171.8 (lactone C=O) - [CN/CO(Q) missing]; m/z(%) 453 (M⁺,6), 340 (29), 229 (100), 228 (82), 215 (29), 214 (34), 213 (36) and 200 (31).

Evaporation of the crystallisation liquor gave aziridine 239 (41mg, 41%) as a colourless oil.
Ring-opening of aziridine 239 with iodide in the presence of samarium(III) chloride

Ring-opening procedure C was followed using aziridine 239 (100mg, 0.31 mmol), samarium(III) chloride (78mg, 0.31 mmol), sodium iodide (137mg, 0.92 mmol) and glacial acetic acid (19mg/20μl, 0.29 mmol) in acetonitrile (1 cm³). After stirring for 20 min. the reaction was worked up giving the crude product as a yellow oil. Crystallisation from ethanol gave iodide 241 (85mg, 62%) as a colourless crystalline solid mp 181-183°C, identical with that isolated previously. Evaporation of the crystallisation liquor gave aziridine 239 (27mg, 27%) as a colourless oil.

Aziridination of tert-butyl methacrylate with Q5NHOAc

General aziridination procedure A was followed in this reaction using NAQ5 110 (100mg, 0.42 mmol), LTA (200mg, 0.44 mmol) and tert-butyl methacrylate (100mg, 0.69 mmol) (prepared by literature procedure) in dichloromethane (2 cm³). After stirring for 3 h. work up in the normal way gave the crude product as a yellow oil. Column chromatography (4:1 light petroleum-ethyl acetate) gave aziridine 242 (87mg, 56%) as a colourless oil, Rf 0.57. (Found: MH⁺ 370.1379. C₁₇H₁₉O₃N₃F₃ requires M 370.1379); νmax/cm⁻¹ 2990m, 1725s, 1690s, 1605s and 1465s; (3:1 mixture of N-invertomers) major invertomer - δH(300 MHz) 1.17 [9H, s, (CH₃)₃], 1.62 (3H, s, CH₃), 2.75 (1H, d, J 2.0, azir. NCHH), 3.37 (1H, br s, azir. NCHH), 7.49 [1H, ddd, J 8.0, 5.3, 2.5, H-6(Q)], 7.72 [2H, m, H-7 and H-8(Q)] and 8.11 [1H, d, J 8.0, H-5(Q)]; δC 19.2 (CH₃), 27.8 [C(CH₃)₃], 42.7 (CH₂), 48.1 [C(CH₃)₃], 82.9 (C), 120.6 [CCO(Q)], 122.7 (CF₃), 126.9, 128.7, 129.4, 134.7 [4 x CH(Q)], 144.1 [CN=C(Q)], 159.9 [CN(Q)/CO(Q)] and 167.3 (OCOBu¹) - [CN(Q)/CO(Q) missing]; minor
invertomer (observable signals) - δ<sub>H</sub>(300 MHz) 1.34 (3H, s, CH₃), 1.41 [9H, s, (CH₃)₃], 3.06 (1H, d, J 2.0, azir. NCHH), 4.38 (1H, br s, azir. NCHH) and 8.12 [1H, d, J 8.0, H-5(Q)]; δ<sub>C</sub> 13.2 (CH₃), 28.1 [C(CH₃)₃], 47.1 [C(CH₃)₃], 49.0, (CH₂), 82.5 (C), 116.3 [CCO(Q)], 123.4 (CF₃), 127.2 [CH(Q)], 127.8 [CN=C(Q)], 128.9, 129.7 [2 x CH(Q)], 130.3 [CN(Q)], 135.1 [CH(Q)], 169.0 [OCOBu¹] - [CO(Q) missing]; m/z(%) 370 (MH⁺,53), 314 (100), 215 (46).

Ring-opening of aziridine 242 with iodide in the presence of samarium(III) chloride

Ring-opening procedure C was followed using aziridine 242 (55mg, 0.15 mmol), samarium(III) chloride (39mg, 0.15 mmol), sodium iodide (67mg, 0.45 mmol) and glacial acetic acid (10mg/10 μl, 0.15 mmol) in acetonitrile (1 cm<sup>3</sup>). After stirring for 5 min., work up gave the crude product as a dark red oil. Column chromatography (3:1 light petroleum-ethyl acetate) gave a 1:2 mixture of iodides 243 and 244 as a yellow oil (59mg, 79%) R<sub>t</sub> 0.51, from comparison of NMR signals at δ 5.95 and 5.86 respectively. (Found: MH⁺ 498.0503. C<sub>17</sub>H<sub>20</sub>O<sub>3</sub>N<sub>3</sub>I requires M 498.0502); for iodide 244 - δ<sub>H</sub> 1.25 (3H, s, CCH₃), 1.62 [9H, s, (CH₃)₃], 3.37 (1H, d, J 10.0, CHH), 3.53 (1H, d, J 10.0, CHH), 5.86 (1H, s, NH), 7.63 [1H, d, J 8.2, 5.0, 1.0, H-6(Q)], 7.83-7.88 [2H, m, H-7 and H-8(Q)] and 8.28 [1H, dd, J 8.2, 1.0, H-5(Q)]; for iodide 243 (observable signals) - δ<sub>H</sub> 1.15 [9H, s, (CH₃)₃], 2.22 (3H, s, CCH₃), 5.95 (1H, t, J 6.7, NH) and 8.32 [1H, dd, J 8.2, 1.0, H-5(Q)]; m/z(%) 498 (MH⁺,38), 370 (100), 314 (51) and 215 (53).
Appendix
1.1 VT NMR spectra following aziridination of naphthalene with $Q^3\text{NHOAc}$ 71 from 253K (bottom) to ambient (top) at 5K intervals.
1.2 NMR spectrum of dienylamine 139

1.3 NMR spectrum of aziridine 176
1.4 NMR spectrum of alcohol 189a

1.5 NMR spectrum of alcohol 189b
Appendix 2

2.1 Crystal structure data for aziridine 130
Table 1. Crystal data and structure refinement for 130

| Identification code | 9839 |
| Empirical formula   | C₁₈H₂₁N₃O₂ |
| Formula weight      | 311.38 |
| Temperature         | 190(2) K |
| Wavelength          | 0.71073 Å |
| Crystal system      | Monoclinic |
| Space group         | P2₁ |
| Unit cell dimensions |  
| a = 8.789(2) Å  | alpha = 90° |
| b = 11.035(3) Å | beta = 111.20(4)° |
| c = 9.229(4) Å  | gamma = 90° |
| Volume, Z           | 834.5(5) Å³, 2 |
| Density (calculated)| 1.239 Mg/m³ |
| Absorption coefficient | 0.082 mm⁻¹ |
| F(000)              | 332 |
| Crystal size        | 0.56 x 0.44 x 0.16 mm |
| 0 range for data collection | 3.00 to 25.01° |
| Limiting indices    | 0 ≤ h ≤ 10, -1 ≤ k ≤ 13, -10 ≤ l ≤ 10 |
| Reflections collected | 1764 |
| Independent reflections | 1662 (R_{int} = 0.0341) |
| Absorption correction | Not applied |
| Refinement method   | Full-matrix least-squares on F² |
| Data / restraints / parameters | 1662 / 1 / 208 |
| Goodness-of-fit on F² | 1.122 |
| Final R indices [I>2σ(I)] | R₁ = 0.0415, wR₂ = 0.0972 |
| R indices (all data) | R₁ = 0.0509, wR₂ = 0.1106 |
| Absolute structure parameter | 0(2) |
| Largest diff. peak and hole | 0.171 and -0.179 eÅ⁻³ |
2.2 Crystal structure data for aziridine 137
Table 1. Crystal data and structure refinement for 137

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<td>Wavelength</td>
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<td>Crystal system</td>
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<tr>
<td>Space group</td>
<td>C2/c</td>
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<th>Unit cell dimensions</th>
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<td></td>
<td>c = 15.758(2) Å, gamma = 90°</td>
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<td>Crystal size</td>
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<td>2 range for data collection</td>
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<td>Independent reflections</td>
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<td>Absorption correction</td>
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<td>Refinement method</td>
<td>Full-matrix least-squares on F²</td>
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<td>Data / restraints / parameters</td>
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<td>Goodness-of-fit on F²</td>
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2.3 Crystal structure data for dienylamine 141
Table 1. Crystal data and structure refinement for 141

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<td>Crystal system</td>
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<td>Space group</td>
<td>P2₁</td>
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<td>Independent reflections</td>
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<td>Refinement method</td>
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2.4 Crystal structure data for sulphide 172
Table 1. Crystal data and structure refinement for p-lab.172

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<td>Crystal system</td>
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<td>Space group</td>
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<td>Completeness to 25.00$^\circ$</td>
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2.5 Crystal structure data for trifluoroacetate 186
Table 1. Crystal data and structure refinement for 186

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<tr>
<td>Unit cell dimensions</td>
<td>a = 9.1753(11) Å, α = 108.846(11)°</td>
</tr>
<tr>
<td></td>
<td>b = 10.3076(12) Å, β = 97.423(12)°</td>
</tr>
<tr>
<td></td>
<td>c = 10.376(2) Å, γ = 94.182(11)°</td>
</tr>
<tr>
<td>Volume, Z</td>
<td>914.0(2) Å³, 2</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.437 Mg/m³</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.119 mm⁻¹</td>
</tr>
<tr>
<td>F(000)</td>
<td>412</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.72 x 0.55 x 0.44 mm</td>
</tr>
<tr>
<td>θ range for data collection</td>
<td>2.10 to 24.99°</td>
</tr>
<tr>
<td>Limiting indices</td>
<td>0 ≤ h ≤ 10, -11 ≤ k ≤ 11, -12 ≤ l ≤ 12</td>
</tr>
<tr>
<td>Reflections collected</td>
<td>3213</td>
</tr>
<tr>
<td>Independent reflections</td>
<td>3136 (R(int) = 0.0285)</td>
</tr>
<tr>
<td>Absorption correction</td>
<td>Not applied</td>
</tr>
<tr>
<td>Refinement method</td>
<td>Full-matrix least-squares on F²</td>
</tr>
<tr>
<td>Data / restraints / parameters</td>
<td>3135 / 0 / 253</td>
</tr>
<tr>
<td>Goodness-of-fit on F²</td>
<td>1.098</td>
</tr>
<tr>
<td>Final R indices [I&gt;2σ(I)]</td>
<td>R1 = 0.0462, wR2 = 0.1127</td>
</tr>
<tr>
<td>R indices (all data)</td>
<td>R1 = 0.0597, wR2 = 0.1234</td>
</tr>
<tr>
<td>Largest diff. peak and hole</td>
<td>0.254 and -0.323 eÅ⁻³</td>
</tr>
</tbody>
</table>
2.6 Crystal structure data for aziridine 239
Table 1. Crystal data and structure refinement for 239

<table>
<thead>
<tr>
<th>Identification code</th>
<th>9904</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empirical formula</td>
<td>$C_{14}H_{10}F_3I_3O_3$</td>
</tr>
<tr>
<td>Formula weight</td>
<td>325.25</td>
</tr>
<tr>
<td>Temperature</td>
<td>200(2) K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Monoclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>$P2_1/n$</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>$a = 9.5161(13)$ Å, $\alpha = 90^\circ$</td>
</tr>
<tr>
<td></td>
<td>$b = 9.9120(14)$ Å, $\beta = 97.25(2)^\circ$</td>
</tr>
<tr>
<td></td>
<td>$c = 14.341(3)$ Å, $\gamma = 90^\circ$</td>
</tr>
<tr>
<td>Volume, Z</td>
<td>1341.9(4) Å$^3$, 4</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.610 Mg/m$^3$</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.143 mm$^{-1}$</td>
</tr>
<tr>
<td>F(000)</td>
<td>664</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.76 x 0.36 x 0.23 mm</td>
</tr>
<tr>
<td>θ range for data collection</td>
<td>2.43 to 26.00°</td>
</tr>
<tr>
<td>Limiting indices</td>
<td>0 ≤ h ≤ 11, -1 ≤ k ≤ 12, -17 ≤ l ≤ 17</td>
</tr>
<tr>
<td>Reflections collected</td>
<td>3128</td>
</tr>
<tr>
<td>Independent reflections</td>
<td>2635 ($R_{int} = 0.0166$)</td>
</tr>
<tr>
<td>Absorption correction</td>
<td>Not applied</td>
</tr>
<tr>
<td>Refinement method</td>
<td>Full-matrix least-squares on $F^2$</td>
</tr>
<tr>
<td>Data / restraints / parameters</td>
<td>2635 / 0 / 208</td>
</tr>
<tr>
<td>Goodness-of-fit on $F^2$</td>
<td>1.073</td>
</tr>
<tr>
<td>Final R indices [I&gt;2σ(I)]</td>
<td>$R_1 = 0.0397$, $wR_2 = 0.0937$</td>
</tr>
<tr>
<td>R indices (all data)</td>
<td>$R_1 = 0.0550$, $wR_2 = 0.1032$</td>
</tr>
<tr>
<td>Largest diff. peak and hole</td>
<td>0.158 and -0.257 eÅ$^{-3}$</td>
</tr>
</tbody>
</table>
References


120. W. T. Gattrell and I. S. T. Lochrie, personal communication.


127. H. A. Albar, personal communication.


