Aziridination of β-substituted styrene derivatives with 3-acetoxyaminoquinazolin-4(3*H*)-ones: probing transition state geometry from changes in diastereoselectivity

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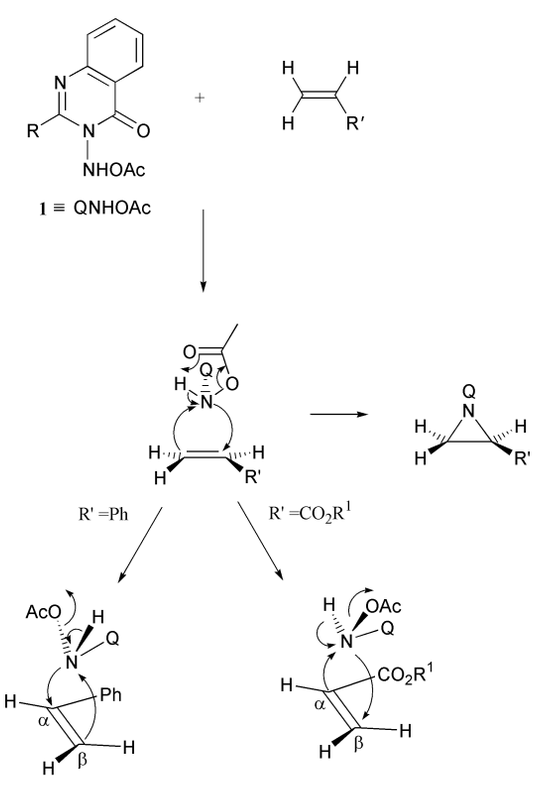
Reaction of (*S*)-3-acetoxyamino-2-[1-(*t*-butyldimethylsilyloxy)ethyl]quinazolin-4(3*H*)-one **5** (Q^1NHOAc) with styrene and R(*β*)-substituted *E*-styrenes (R = $SiMe_3$, Me, CH_2Cl, $CHCl_2$) gives the corresponding aziridines diastereoselectively. The diastereoselectivity increases in the same sense from 5 : 1 ⟶ 20 : 1 as the electron-withdrawing character of R increases [H(Me), CH_2Cl, $CHCl_2$] but is accompanied by a decrease in yield of aziridine. A similar increase in diastereoselectivity is found in the reaction of 3-acetoxyamino-2-(2,3,3-trimethylpropyl)quinazolin-4(3*H*)-one **38** (Q^4NHOAc) with the same *β*-substituted styrenes.

An explanation for these observations is offered based on a tighter, more symmetrical transition state for the aziridination of styrenes bearing the more electron-withdrawing β-substituents and is supported by SCF calculations.

Introduction

3-Acetoxyaminoquinazolinones **1** (QNHOAc) are ambiphilic aziridinating agents for alkenes: they react in comparable yields with alkenes of grossly different electron availability *e.g.* styrene and *α,β*-unsaturated esters (Scheme 1).[1] In the transition states



Scheme 1

(TS#s) for aziridination the planes containing alkene and the Q ring are approximately parallel with an attractive (*endo*) overlap of the (Q)C=O with the *π*-system of the alkene substituent (**2**, **3**).

However, the mechanism of reaction in TS# **2** is thought to differ from that in TS# **3**: in aziridination of styrene, TS# **2**, C_β–N bond formation is believed to run ahead of N–C_α bond formation[2] whereas in aziridination of acrylates **3**, N–C_β bond formation runs ahead of C_α–N bond formation *i.e.* the TS# takes on some Michael addition character.[3] In neither case is any intermediate involved *i.e.* the reactions are concerted but asynchronous. The configurations at the sp^3-hybridised[4] NHOAc chiral centres in **2** and **3** are opposite because attack on this nitrogen is assumed to be S_N2 in character. Thus the ambiphilicity of QNHOAc arises from its ability to respond to the different electron availability of the alkene by a change in mechanism.

Aziridination with QNHOAc **1** is analogous to epoxidation with peroxyacetic acid but QNHOAc **1** is the more versatile reagent because peroxyacids do not react well with electron-deficient alkenes, *i.e.* acrylates.

The location of R, the Q-2 substituent, in TS#s **2** and **3** means that with R = R*, a chiral group, diastereoselective aziridination of prochiral alkenes is feasible.[5a,b] The work described in this paper was initiated as a result of the observation that aziridination of (*E*)-*β*-trimethylsilylstyrene with Q^1NHOAc **5**, prepared *in situ* by *N*-acetoxylation of Q^1NH_2 **4** with lead tetraacetate (LTA) was more diastereoselective [dr (diastereoisomer ratio) 11 : 1][6] than styrene itself (dr 5 : 1) (Scheme 2).[7]

It seemed that the effect of the trimethylsilyl group on the diastereoselectivity must be electronic in origin because in the presumed TS# **8** for aziridination of this alkene, little, if any, steric interaction of the trimethylsilyl group with the (Q^1)-2-substituent would be expected. To understand this electronic effect and hence to extend its application to increase diastereoselectivity in aziridination more generally, we have studied the aziridinations of a variety of *β*-substituted styrenes with Q^1NHOAc and the results are summarised in Scheme 3. The only other homogeneous product isolated from these reactions

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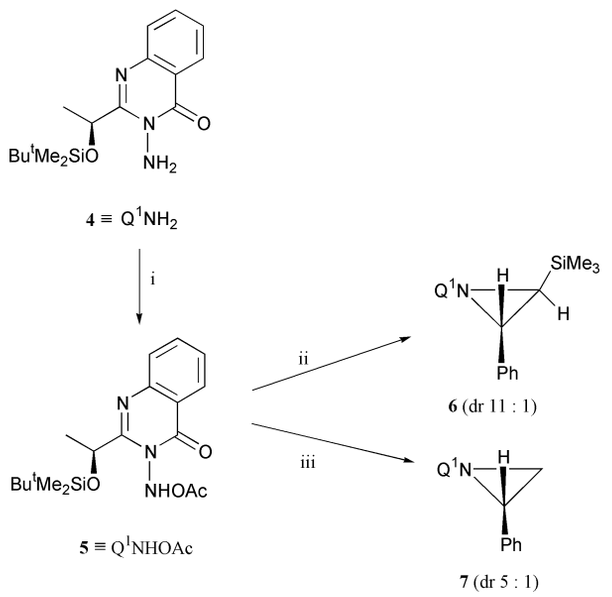
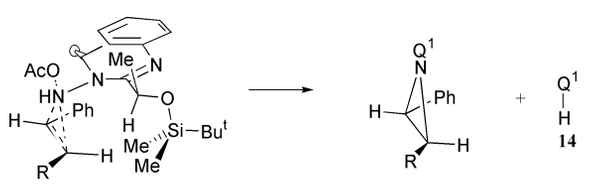


Scheme 2 *Reagents*: i, $Pb(OAc)_4$, CH_2Cl_2; ii, (*E*)-PhCH=CHSiMe$_3$; iii, styrene.



		Yield%	dr
6	R = $SiMe_3$	56	11:1
7	R = H	68	5:1
9	R = Me	60	5:1
10	R = CH_2Cl	51	10:1
11	R = $CHCl_2$	41	20:1
12	R = Ph	51	3:1
13	R = CO_2Me	49	3:1

Scheme 3

was the 3*H*-quinazolinone **14**, a known decomposition product of Q^{1}NHOAc.

In the reaction of Q^{1}NHOAc **5** with (*E*)-*β*-methylstyrene, both diastereoisomers of aziridine **9** are present as mixtures of *N*-invertomers by NMR spectroscopy in deuteriochloroform of the crude reaction product. Unravelling of the diastereoisomer ratio present was facilitated after separating the aziridine from unchanged *β*-methylstyrene by chromatography and then by partial separation of the diastereoisomers (13 : 1 ratio after Kieselgel chromatography). The major diastereoisomer was present as a 1.3 : 1 (Q/Ph *cis* : *trans*) ratio of *N*-invertomers and the minor diastereoisomer as a 2.2 : 1 ratio favouring Q/Ph *trans*. This conclusion was arrived at from observation of the chemical shifts of the C*H*Ph aziridine ring protons (Fig. 1): protons *cis* to the quinazolinone ring have been previously shown to be deshielded relative to those which are *trans*.[8]

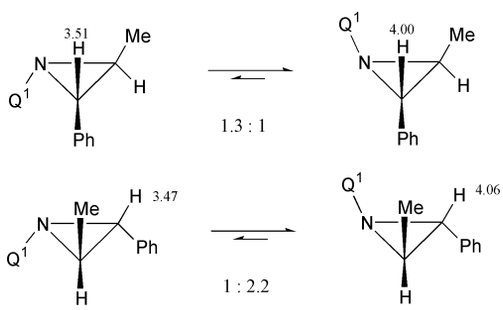


Fig. 1 Invertomer ratios for diastereoisomeric aziridines **9**.

Examination of the crude reaction mixture shows that the diastereoisomer ratio for aziridine **9** is 5 : 1. The enhancement in dr from 5 : 1 ⟶ 13 : 1 above is important because it allows a distinction between signals in the NMR spectrum from both *N*-invertomers of the same diastereoisomer (a ratio which is not affected by chromatography because interconversion is fast on the real timescale in solution) and signals from different diastereoisomers.

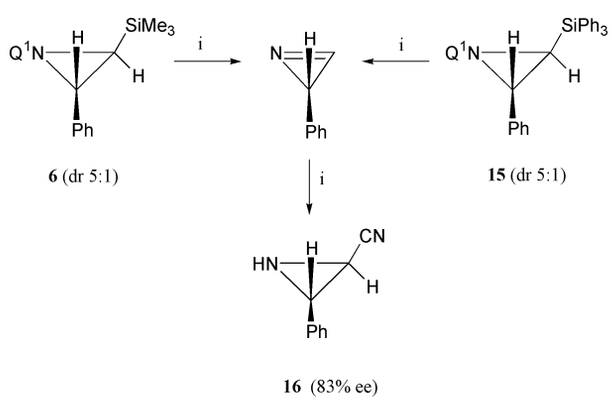
Aziridination of (*E*)-*β*-chloromethylstyrene using Q^{1}NHOAc **5** and purification of the crude product **10** using a Chromatotron gave the major diastereoisomer as a crystalline solid (*N*-invertomer ratio 3.5 : 1 favouring Q and Ph *cis*) and the minor diastereoisomer as an oil (*N*-invertomer ratio 2 : 1 favouring Q and Ph *cis*). Re-examination of the crude reaction product showed that the initial diastereoisomer ratio was 10 : 1.

For the (*E*)-*β*-dichloromethylstyrene-derived aziridine **11**, measurement of the diastereoisomer ratio (20 : 1) and the aziridine *N*-invertomer ratio (7 : 1) in the major diastereoisomer was again facilitated when the latter was obtained as a crystalline solid after silica chromatography. An NMR spectrum of the mother liquor from this crystallisation after evaporation showed it was enriched in the minor diastereoisomer of aziridine **11**.

Aziridination of (*E*)-stilbene gave a 3 : 1 ratio of diastereoisomers of **12**. A small sample of the minor diastereoisomer was separated by column chromatography: the major diastereoisomer was obtained as a crystalline solid. Likewise, methyl cinnamate gave a 3 : 1 ratio of diastereoisomers of aziridine **13** with the major one separable by chromatography. In neither of these cases **12** or **13** was the absolute configuration at the two chiral centres determined.

Stereostructures of aziridines 6, 7 and 9–11

The stereostructure of the major diastereoisomer of aziridine **6** was previously shown to be that having the 2*S*,3*S* configuration by chemical correlation (Scheme 4) together with an X-ray crys-

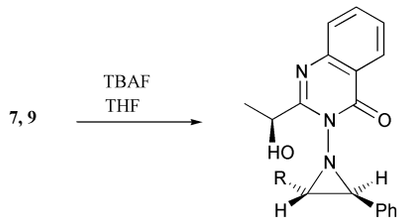


Scheme 4 *Reagents*: i, KCN, CsF, CH_3CN.

tal stucture determination[6] of the minor diastereoisomer of the related aziridine **15**: both of the major diastereoisomers of aziridines **6** and **15** gave the same product **16** by the aziridine–azirine–aziridine sequence in Scheme 4.[9]

X-Ray crystal structures[7] of the major diastereoisomers of aziridines **10** and **11** revealed that these also had the same absolute configuration at the 2-position as **6**. Both crystal structures showed the Q-group *cis* to the phenyl ring and this is presumably the major *N*-invertomer in solution since the chemical shifts of the PhC*H* aziridine ring protons in each case are at higher field than those of the corresponding protons in the minor *N*-invertomers (see above).

For determination of the absolute configuration of the major diastereoisomers of styrene- and (*E*)-*β*-methylstyrene-derived aziridines **7** and **9**, both were converted to the corresponding (Q)-2-(1-hydroxyethyl) compounds **17** and **18** by desilylation using tetrabutylammonium fluoride (TBAF) (Scheme 5).



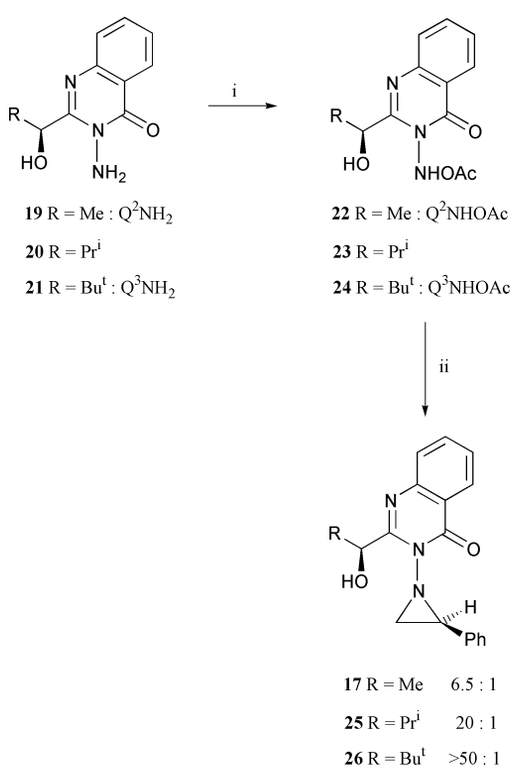
7 (dr 5:1) → **17** R = H (dr 5:1)

9 (dr 5:1) → **18** R = Me (dr 5:1)

Scheme 5

Aziridine **17** was obtained from aziridine **7** (dr 5 : 1) as a 5 : 1 ratio of diastereoisomers which were separated by Chromatotron chromatography. Similarly, aziridine **9** (dr 5 : 1) was converted into aziridine **18** (dr 5 : 1) without any apparent interconversion of diastereoisomers: the major diastereoisomer was separated as a crystalline solid.

Previously we had shown that 3-acetoxyamino-2-(1-hydroxyalkyl)quinazolinones **22**–**24**, prepared *in situ* by acetoxylation of the corresponding 3-aminoquinazolinones **19**–**21**, react with styrene diastereoselectively in the presence of titanium(IV) *tert*-butoxide (TTB) to give aziridines **17**, **25** and **26** respectively (Scheme 6).[5a] The major diastereoisomer of aziridine **17** produced was identical to the major one obtained by desilylation of aziridine **7** in Scheme 5.



19 R = Me : Q^2NH_2

20 R = Pr^i

21 R = Bu^t : Q^3NH_2

22 R = Me : Q^2NHOAc

23 R = Pr^i

24 R = Bu^t : Q^3NHOAc

17 R = Me 6.5 : 1

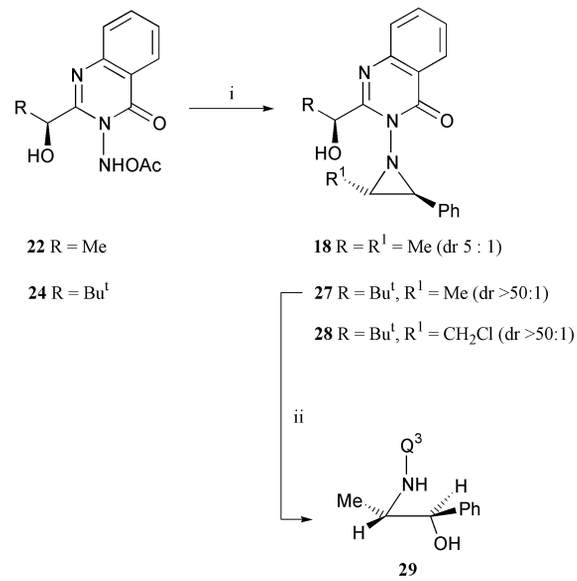
25 R = Pr^i 20 : 1

26 R = Bu^t >50 : 1

Scheme 6 *Reagents*: i, LTA, CH_2Cl_2, −20 °C; ii, $Ti(OBu^t)_4$, styrene.

Evidence for the same preferred sense of diastereoselectivity in formation of aziridines **17**, **25** and **26** came from the excellent correlation in their NMR spectra for the chemical shifts of aziridine ring and RC*H*OH protons in major and minor diastereoisomers. The absolute configuration for aziridine **26** at the 3-membered ring carbon was shown to be (*S*) from X-ray crystallography by relating it to the [(*S*)-*tert*-leucine-derived] inducing centre in the Q2-substituent. From the correlations above, it follows that the configuration at the phenyl-substituted 3-membered ring carbon in the major diastereoisomer of aziridine **17** and hence aziridine **7** is also (*S*).[5a]

In this work aziridination of (*E*)-*β*-methylstyrene with Q^2NHOAc **22** was also carried out in the presence of TTB and aziridine **18** was isolated as a 5 : 1 ratio of diastereoisomers (Scheme 7) with the major one identical to the crystalline major diastereoisomer isolated by desilylation of aziridine **9** (Scheme 5). The diastereoisomer of **18** shown is that which would be formed using our previous TS# model for aziridination of styrene (see below). Aziridination of (*E*)-*β*-methylstyrene with Q^3NHOAc **24** in the presence of TTB gave aziridine **27** as a single diastereoisomer from NMR examination of the crude reaction mixture: some aziridine ring-opening to alcohol **29** took place on silica chromatography.



22 R = Me

24 R = Bu^t

18 R = R^1 = Me (dr 5 : 1)

27 R = Bu^t, R^1 = Me (dr >50:1)

28 R = Bu^t, R^1 = CH_2Cl (dr >50:1)

29

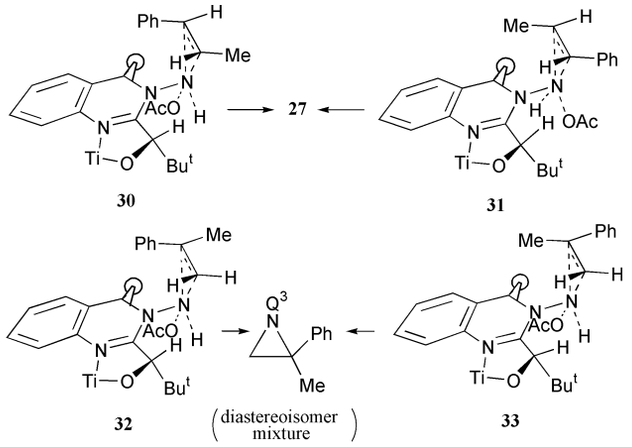
Scheme 7 *Reagents*: i, (*E*)-RCH=$CHPh_2$, $Ti(OBu^t)_4$; ii, silica chromatography.

When aziridination of (*E*)-*β*-methylstyrene with Q^3NHOAc **24** was carried out in the absence of TTB, the diastereoselectivity was, as expected, much reduced (dr 2 : 1). After separation of the minor diastereoisomer by chromatography, it was shown to be absent from the crude reaction product **27** by NMR spectroscopy.

Although the identity in configuration at C-2 in aziridines **18** and **27** could not be confirmed by the ^1H NMR correlation used for aziridines **17** and **26** above, it seems very likely from the correspondence in behaviour of *β*-methylstyrene and styrene in the aziridinations in Schemes 5–7 that the *β*-methyl substituent has virtually no effect upon the stereochemistry of these aziridinations and that the configuration at the aziridine ring chiral centres in **9** is acccordingly 2*S*,3*S*.

The complete diastereoselectivity in aziridination of (*E*)-*β*-methylstyrene with Q^3NHOAc **24** in the presence of TTB to give aziridine **27** deserves some comment when taken in conjunction with our previous observation that aziridination of *α*-methylstyrene under the same conditions gave a 5 : 1 ratio of diastereoisomers.[5a] Our TS# model for aziridination of (*E*)-*β*-methylstyrene that leads to diastereoisomer **27** has the phenyl *endo* and *cis* to the Q-ring as in **30**. However, the sense of diastereoselectivity would remain unchanged even if some competitive aziridination took place *via* TS# **31** since the same face of the alkene is being attacked. Attack *via* TS# **31** seems less likely than *via* **30** in any case because of steric interaction between the *N*-acetoxy and *tert*-butyl groups. Attack *via* analogous TS#s **32** and **33** on α-methylstyrene, however, would lead to diastereoisomeric aziridines because opposite faces of the alkene would be involved: the *N*-acetoxy and *tert*-butyl groups would be *anti* in either case (Scheme 8).

Aziridination of *β*-chloromethylstyrene with Q^3NHOAc **24** was also completely diastereoselective giving **28** (Scheme 7).



Scheme 8

Prior to obtaining confirmation of the absolute configuration of aziridine **10** by X-ray crystallography, we had attempted to do this by chemical correlation. Desilylation of the major diastereoisomer by TBAF gave two products in a 1.6 : 1 ratio identified as the aziridine **34a** and the imine **35** (Scheme 9a).

Previously we had prepared a diastereoisomer **34b** of aziridine **34a** by intramolecular aziridination of the 3-acetoxyaminoquinazolinone **36** (Scheme 9b).[4]

The NMR spectra of these two aziridines **34a** and **34b** were consistent with their assigned diastereoisomeric relationship particularly in the similarity of chemical shifts and coupling constants for the OCH_2CH unit but in the dissimilarities for the CH_3CH protons arising from their different environments. Since both aziridines **34a** and **34b** have the same absolute configuration for the chiral centre adjacent to the 2-position of the Q-ring they must be epimeric at both aziridine ring chiral centres (aziridination of double bonds by QNHOAc is always stereospecific).

Aziridination using Q[4]NHOAc 38

We also briefly examined aziridination of some of the β-substituted styrene derivatives used above with (racemic) Q[4]NHOAc **38** and the results are summarised in Scheme 10. The X-ray crystal structure of the major diastereoisomer of aziridine **40** (Fig. 2) was obtained. The major diastereoisomer of aziridine **41** was obtained as a crystalline solid.

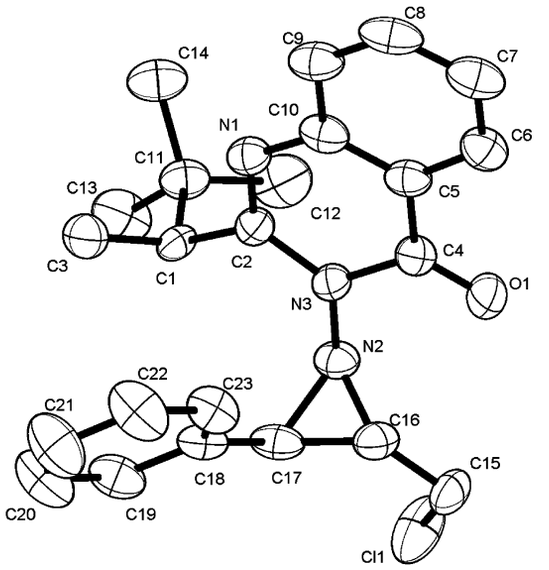
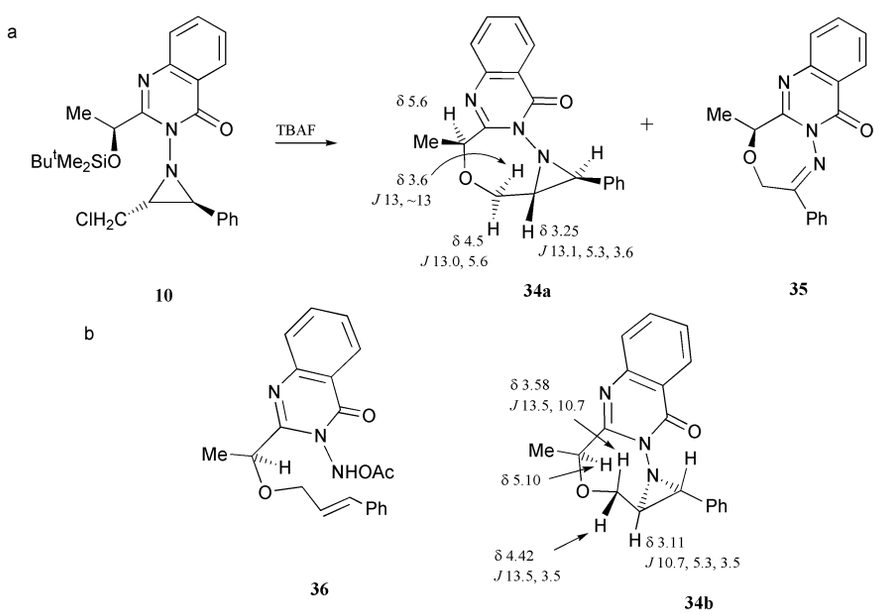


Fig. 2 The molecular structure of **40** showing the atom label scheme and 30% displacement probability ellipsoids. H atoms are omitted for clarity.

Discussion

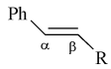
Aziridination with Q[1]NHOAc **5** of styrene and *β*-substituted styrenes to give **6**, **7**, **9**–**11** all proceed in the same diastereosense to give the same absolute configuration at the phenyl-bearing aziridine C-2 position. As the *β*-substituent changes from H(Me) ⟶ CH_2Cl ⟶ $CHCl_2$, *i.e.* becomes more electron-withdrawing, there is an increase in diastereoselectivity but a decrease in yield. Aziridination with Q[4]NHOAc **38** shows the same trend of increased diastereoselectivity but reduced yield with the same *β*-substituent changes if it is assumed that aziridination takes place in the same diastereosense in each case.

Although the changes in activation energy bringing about the changes in diastereoselectivity in these aziridinations are small, it is the trend of increasing dr with substituent electronegativity which is significant. Our explanation for this trend is based on the assumption that the effect of increasing the electron-withdrawing character of the *β*-substituent reduces the extent by which C_β–N bond formation runs ahead of N–C_α in the TS[#] for aziridination of these electron-available alkenes (**2** in Scheme 1).

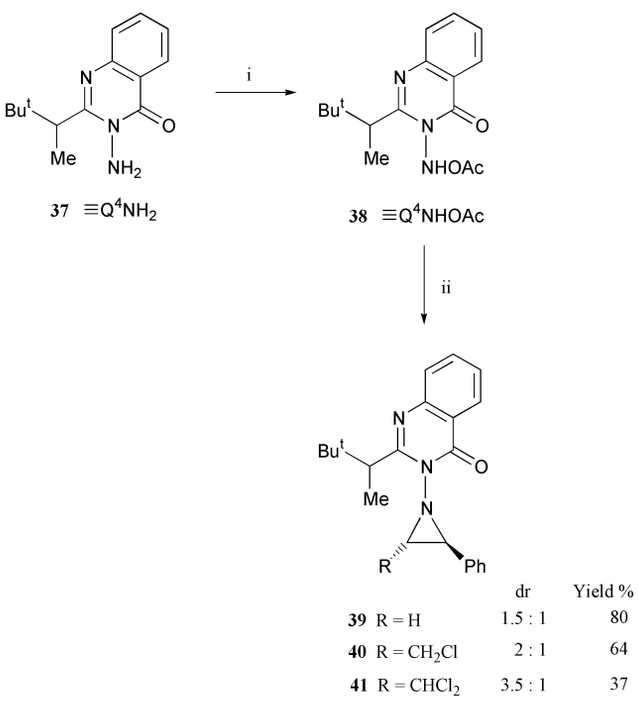


Scheme 9

Table 1 Energy levels (hartrees) and calculated orbital coefficients of C_α and C_β for some of the β-substituted styrenes used in Scheme 3



	HOMO			LUMO		
R	E	C_α	C_β	E	C_α	C_β
H	−0.3016	0.1794 0.1581	0.2579 0.2344	0.1119	0.1786 0.2993	−0.2415 −0.4325
Me	−0.2923	0.2058 0.1823	0.2636 0.2421	0.1152	0.1693 0.2910	−0.2569 −0.4225
CH_2Cl	−0.3100	0.1625 0.1403	0.2177 0.1937	0.1004	0.1823 0.3038	−0.2118 −0.3318
$CHCl_2$	−0.3170	0.1518 0.1255	0.2158 0.1986	0.0940	0.1943 0.3237	−0.2098 −0.3260
SiH_3	−0.3064	0.1727 0.1490	0.2587 0.2388	0.0913	0.2238 0.3590	−0.2214 −0.3616



37 ≡Q^4NH_2 **38** ≡Q^4NHOAc

	dr	Yield %
39 R = H	1.5 : 1	80
40 R = CH_2Cl	2 : 1	64
41 R = $CHCl_2$	3.5 : 1	37

Scheme 10 *Reagents*: i, LTA, CH_2Cl; ii, (*E*)-RCH=CHPh.

Using *ab initio* SCF calculations and a double zeta basis set (6-319*), the orbital coefficients at C_α and C_β and HOMO and LUMO energy levels for some of the *β*-substituted styrenes used in Scheme 3 were calculated (Table 1).

According to our mechanism for electron-available alkenes[2] the aziridination involves overlap of $HOMO_{alkene}$ and $LUMO_{Q^1NHOAc}$ (the N–OAc σ* orbital) and $LUMO_{alkene}$ with $HOMO_{Q^1NHOAc}$ (the *N*HOAc lone pair) with the ordering of HOMO and LUMO levels resembling that in Fig. 3 for styrene.

Since the aziridination is primarily electrophilic attack by Q^1NHOAc, we have chosen LUMO (Q^1NHOAc) and HOMO (alkene) for the reaction scheme, a choice illustrated by the fact that $LUMO_{Q^1NHOAc}$–$HOMO_{alkene}$ overlap is larger than $LUMO_{alkene}$–$HOMO_{Q^1NHOAc}$ overlap, in Fig. 3.

It is clear from the Table that the effect of increasing the electron-withdrawing character of the β-substituent from H ⟶ CH_2Cl ⟶ $CHCl_2$ is to lower both the HOMO and LUMO levels of the alkene which increasingly favours $LUMO_{alkene}$–$HOMO_{Q^1NHOAc}$ overlap.

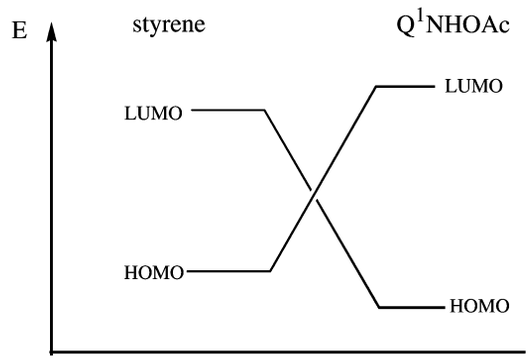
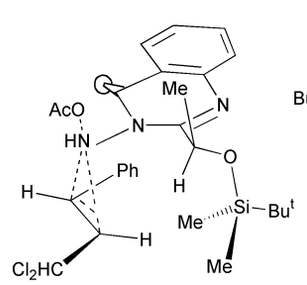


Fig. 3

In addition, as the electron-withdrawing character of the β-substituent increases, there is in the $LUMO_{alkene}$ a progressive increase in the magnitude of the C_α coefficient and a corresponding decrease in the C_β-coefficient that will increasingly favour bond making at the C_α-position. The same effects, moreover, are brought about by *β*-substitution of SiH_3 in styrene (as a model for $SiMe_3$) (Table).

Overall, the effect of favouring increased N–C_α bond formation in the TS[#] will be to make it more symmetrical and tighter with formation of the two 3-membered ring bonds more but not completely synchronous. An increase in diastereoselectivity is expected, *i.e.* in formation of aziridine **11**, because of the increased site selectivity of the three substituents on the inducing Q2-chiral centre. Thus using our previous TS[#] model for this aziridination,[2] **42** will become favoured over **43** because of the augmented interaction between H_β and CH*Me*OSi in the latter.



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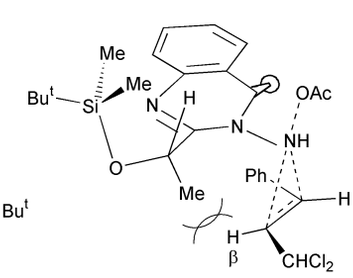

43

There is in TS[#] **42**, a stereoelectronic effect which favours the conformation around the Q2–C bond shown with the C–O bond at the chiral centre almost in the plane of the Q ring and

the O–Si bond orthogonal to this plane:[10] the two methyl groups on silicon then direct the methyl and hydrogen on the chiral centre to the sites shown. It is this stereoelectronic effect which is responsible for the superior levels of diastereoselectivity using Q^1NHOAc **5** over Q^4NHOAc **38** in spite of the better size differentiation in the substituents on the inducing chiral centre in Q^4NHOAc **38**.

The progressive decrease in yield with increasing electron-withdrawal by the *β*-substituent in Schemes 3 and 10 is a reflection of the inherent electrophilic character of the QNHOAc species: only in TS[#] **3** with back donation by the oxygen of the *α*,*β*-unsaturated ester carbonyl is the nucleophilic reactivity of the Q*N*HOAc brought to the fore in Michael addition to the double bond.

Experimental

For general experimental details, see ref. [11]. Unless otherwise indicated, NMR spectra were run at 250 MHz in deuteriochloroform solutions with tetramethylsilane as internal standard. (*E*)-β-Dichloromethylstyrene was prepared by the literature method[12] and routinely crystallised from light petroleum before use. All calculations were carried out using the standard facilities provided by Gaussian 941.[13]

General procedure 1 for aziridination

The 3-aminoquinazolinone QNH_2 (1 eq.) and acetic acid-free lead tetraacetate (LTA) (1.1 eq.) were added alternately and continuously in very small portions over 15 min. to a vigorously stirred solution of dry dichloromethane (1 cm^3 per 100 mg of QNH_2) cooled with a dry ice–acetone bath held at −20 to −25 °C. After stirring for a further 5 min to give a solution of the 3-acetoxyaminoquinazolinone, a solution of the alkene (1.5–3.5 eq.) in dichloromethane (500 mg QNH_2 per 1 cm^3) was added and then the temperature of the solution was allowed to rise to ambient stirring throughout. Lead diacetate was separated and (on a 500 mg QNH_2 scale) washed with dichloromethane (15 cm^3) the organic solution washed successively with saturated aqueous sodium hydrogen carbonate (15 cm^3) and water (15 cm^3), dried with magnesium sulfate and the solvent removed by evaporation under reduced pressure.

General procedure 2 for aziridination in the presence of HMDS

A solution of 3-acetoxyaminoquinazolinone at −20 °C was prepared as described above, separated from lead di-acetate at this temperature (on a small scale a Pasteur pipette can be used) and the cold solution added dropwise over 2 min. to a stirred solution of the alkene (1.5–3.5 eq.) in dichloromethane (1 cm^3/500 mg) containing HMDS (2–3 eq.) maintained at −20 °C (bath temperature). The temperature of the stirred solution was then allowed to rise to ambient and the reaction worked-up as described above.

General procedure 3 for aziridination in the presence of titanium(IV) *tert*-butoxide (TTB)

A cold (−20 °C) solution of 3-acetoxyaminoquinazolinone freed from lead diacetate prepared as described above was added dropwise over 2 min to a stirred solution of the alkene (1.5–3.5 eq.) in dichloromethane (1 cm^3 per 500 mg QNH_2) containing TTB (2 eq.) maintained at −20 °C (bath temperature). After 5 min the cooling bath was removed and the temperature of the stirred solution was allowed to rise to ambient. The reaction mixture was then poured into saturated hydrogen carbonate solution, the gelatinous precipitate produced filtered off (Celite), the organic layer separated, washed with brine, dried and solvent evaporated under reduced pressure.

Aziridination of styrene with Q^1NHOAc 5

General procedure 2 was followed using Q^1NH_2 **4**[9] (0.2 g, 0.63 mmol), LTA (0.31 g, 0.69 mmol), HMDS (0.20 g, 1.25 mmol) and styrene (0.13 g, 1.25 mmol) in dry dichloromethane (2 cm^3). After work-up, examination of the residue by NMR spectroscopy indicated two diastereoisomers of aziridine **7** were present in a 5 : 1 ratio from integral comparison of signals at *δ* 2.71 and 2.65 ppm respectively and comparison with previously reported spectra.[4]

Aziridination of β-methylstyrene with Q^1NHOAc 5

General procedure 2 was followed using Q^1NH_2 **4**[9] (1 g, 3.13 mmol), LTA (1.53 g, 3.45 mmol), HMDS (1 g, 6.28 mmol) and β-methylstyrene (0.74 g, 6.28 mmol) in dry dichloromethane (15 cm^3). The crude product was chromatographed over silica with light petroleum–ethyl acetate (10 : 1) as eluent to give a mixture of *aziridine* **9** diastereoisomers (R_f 0.30) as a colourless oil (0.82 g, 60%). (Found: M^+ 435.234. $C_{25}H_{33}N_3O_2Si$ requires *M* 435.234) ν_{max}/cm^{-1} 1675s and 1600s; *m*/*z* (%) 435 (M^+, 6), 247 (72), 132 (100) and 73 (30); δ_H (400 MHz) (d_5-pyridine) (mixture of *N*-invertomers) major *N*-invertomer (Ph and Q^1 *cis*) 0.00 (3H, s, CH_3SiCH_3), 0.06 (3H, s, CH_3-SiCH_3), 0.68 (9H, s, Bu^t), 0.98 (3H, d, *J* 5.0, azir. CH_3), 1.52 (3H, d, *J* 6.2, CH_3CHO), 2.87 (1H, dq, *J* 6.0 and 5.0, azir. H-3), 3.51 (1H, d, *J* 6.0, azir. H-2), 5.18 (1H, q, *J* 6.2, CH_3C*H*O), 6.99–7.67 [8H, m, 6-H, 7-H, 8-H(Q) and C*H*Ph] and 8.20 [1H, dd, *J* 8.0 and 1, 5-H(Q)]; minor *N*-invertomer (observable signals) *δ* 1.01 (3H, d, *J* 5.0, azir. CH_3), 1.64 (3H, d, *J* 6.2, CH_3CHO), 3.80 (1H, dq, *J* 5.6 and 5.0, azir. H-3), 4.00 (1H, d, *J* 5.6, azir. H-2), 5.47 (1H, q, *J* 6.2, CH_3C*H*O) and 8.28 [1H, d, *J* 8.0, 5-H(Q)]. From integral comparison of signals at *δ* 5.18 and 5.47, the *N*-invertomer ratio was 1.3 : 1; minor diastereoisomer (mixture of *N*-invertomers) major *N*-invertomer (phenyl and Q^1 *trans*); (observable signals) *δ* 2.92 (1H, dq, *J* 5.0 and 6.0, azir. H-3), 4.06 (1H, br d, *J* 5, azir. H-2) and 5.41 (1H, q, *J* 6.2, CH_3C*H*O); minor *N*-invertomer (observable signal) *δ* 3.47 (1H, d, *J* 5.6, azir. H-2). From integral comparison of signals at *δ* 4.06 and 3.47, the *N*-invertomer ratio was ~2 : 1. The ratio of diastereoisomers present was 5 : 1 from integral comparison of signals at *δ* 5.18 + 5.47 : 4.06 + 3.47 in the crude reaction product.

Kieselgel chromatography of the 5 : 1 ratio of diastereoisomers with light petroleum–ethyl acetate as eluent gave a fraction containing the two diastereoisomers in a 13 : 1 ratio from integral comparison of signals *inter alia* at *δ* 5.18 + 5.47 : 4.06 + 3.47.

Aziridination of (*E*)-cinnamyl chloride with Q^1NHOAc 5

General procedure 2 was followed using Q^1NH_2 **4**[9] (1 g, 3.13 mmol), LTA (1.53 g, 3.45 mmol), HMDS (1.52 g, 9.40 mmol) and cinnamyl chloride (1.43 g, 9.40 mmol) in dry dichloromethane (15 cm^3). Chromatography of the product over silica with light petroleum–ethyl acetate (15 : 1) as eluent gave the major *aziridine* diastereoisomer **10** (R_f 0.29) as an oil which solidified after trituration with light petroleum and crystallised as a colourless solid (0.75 g, 51%) mp 119–121 °C (from ethanol). $[\alpha]_D = -378$ (*c* = 0.5, $CHCl_3$) (Found: C, 63.5; H, 6.9; N, 8.9. $C_{25}H_{32}ClN_3O_2Si$ requires C, 63.85; H, 6.85; N, 8.95%); δ_H (400 MHz) (mixture of *N*-invertomers) major *N*-invertomer (phenyl and Q^1 *cis*): 0.09 (3H, s, CH_3SiCH_3), 0.11 (3H, s, CH_3SiCH_3), 0.70 (9H, s, Bu^t), 0.88 (3H, d, *J* 6.1, CH_3CHO), 3.76 (1H, dd, *J* 11.5 and 7.1, C*H*HCl), 3.78 (1H, d, *J* 3.9, azir. H-2), 4.13 (1H, m, azir. H-3), 4.48 (1H, dd, *J* 11.5 and 3.9, CH*H*Cl), 5.05 (1H, q, *J* 6.1, CH_3C*H*O), 6.80–7.62 [8H, m, 6-H, 7-H, 8-H(Q) and C*H*(Ph)] and 8.24 [1H, dd, *J* 8.5 and 0.6, 5-H(Q)]; minor *N*-invertomer (observable signals) *δ* 1.43 (3H, d, *J* 6.4, CH_3CHO), 3.24 (1H, m, azir. H-3), 3.61 (1H, dd, *J* 11.9 and 7.5 C*H*HCl), 4.54 (1H, d, *J* 4.6, azir. H-2), 5.43 (1H, q,

J 6.4, CH_3CHO) and 8.18 [1H, d, *J* 7.9, 5-H(Q)]. From integral comparison of the signals at δ 4.48 and 4.54, the ratio of major : minor *N*-invertomers was 3.5 : 1; ν_{max}/cm^{-1} 2950m, 2860m, 1675s and 1600m; *m*/*z* (%) 469 (M^+, 1), 247 (68), 166 (44), 130 (51), 117 (32), 103 (48), 91 (30), 77 (55), 75 (55), 73 (100) and 57 (23). A crystal of aziridine **10** suitable for X-ray crystallography was obtained by crystallisation from ethanol.

Repetition of reaction above and chromatography of the crude product using a Chromatotron with light petroleum–ethyl acetate (15 : 1) as eluent, gave a pure sample of minor *aziridine* **10** diastereoisomer (R_f 0.29) as a colourless oil. $[\alpha]_D$ = 54 (*c* = 1, $CHCl_3$) (Found: M^+ 469.195. $C_{25}H_{32}ClN_3O_2Si$ requires *M* 469.195); δ_H (mixture of *N*-invertomers) major *N*-invertomer (phenyl and Q *cis*) −0.03 (3H, s, CH_3SiCH_3), −0.01 (3H, s, CH_3SiCH_3), 0.83 (9H, s, Bu^t), 1.60 (3H, d, *J* 6.1, CH_3CHO), 3.69 (1H, d, *J* 3.9, azir. H-2), 3.77 (1H, dd, *J* 11.5 and 7.5, C*H*HCl), 4.33 (1H, dd, *J* 11.5 and 3.9, CH*H*Cl), 4.40 (1H, m, azir. H-3), 4.95 (1H, q, *J* 6.1, CH_3CHO), 6.99–7.66 [8H, m, 6-H, 7-H, 8-H(Q) and C*H*(Ph)] and 8.22 [1H, d, *J* 8.5, 5-H(Q)]; minor *N*-invertomer (observable signals) δ 0.00 (3H, s, CH_3SiCH_3), 0.04 (3H, s, CH_3SiCH_3), 0.85 (9H, s, Bu^t), 1.63 (3H, d, *J* 6.1, CH_3CHO), 3.25 (1H, m, azir. H-3), 3.61 (1H, dd, *J* 11.5 and 7.5, C*H*HCl), 4.65 (1H, d, *J* 3.9, azir. H-2), 5.38 (1H, q, *J* 6.1, CH_3CHO) and 8.19 [1H, d, *J* 8.5, 5-H(Q)]. From integral comparison of the signals at δ 4.33 and 4.65, the ratio of major : minor *N*-invertomers was 2 : 1; an NMR spectrum (400 MHz) of the crude product above showed the ratio of major : minor aziridine diastereoisomers of **10** was 10 : 1 from integral comparison of signals at δ 4.48 + 4.54 : 4.33 + 4.65 ppm; *m*/*z* (%) 469 (M^+, 0.7), 412 (34), 247 (100), 166 (25), 130 (20), 129 (24), 117 (22) and 73 (27).

Aziridination of (*E*)-β-dichloromethylstyrene with Q^1NHOAc 5

General procedure 2 was followed using Q^1NH_2 **4**[9] (0.4 g, 1.25 mmol), LTA (0.61 g, 1.38 mmol), HMDS (0.61 g, 3.76 mmol) and *β*-dichloromethylstyrene (0.68 g, 3.76 mmol) in dry dichloromethane (5 cm^3). Flash chromatography of the product over silica with light petroleum–ethyl acetate (15 : 1) as eluent gave the major *aziridine* **11** diastereoisomer (R_f 0.29) as a colourless solid (0.26 g, 41%) mp 130–132 °C (from ethanol), $[\alpha]_D$ = −366 (*c* = 1, $CHCl_3$) (Found: C, 59.5; H, 6.25; N, 8.4. $C_{25}H_{31}Cl_2N_3O_2Si$ requires C, 59.5; H, 6.2; N, 8.35%); δ_H (mixture of *N*-invertomers) major *N*-invertomer (phenyl and Q *cis*) 0.00 (3H, s, CH_3SiCH_3), 0.02 (3H, s, CH_3SiCH_3), 0.70 (9H, s, Bu^t), 0.83 (3H, d, *J* 6.3, CH_3CHO), 3.96 (1H, d, *J* 5.4, azir. H-2), 4.48 (1H, dd, *J* 5.4 and 3.8, azir. H-3), 4.98 (1H, q, *J* 6.3, CH_3CHO), 6.39 (1H, d, *J* 3.8, $CHCl_2$), 6.90–7.70 [8H, m, 6-H, 7-H, 8-H(Q) and C*H*(Ph)] and 8.13 [1H, dd, *J* 7.8 and 1, 5-H(Q)]; ν_{max}/cm^{-1} 2950m, 3060m, 2860m, 1670s and 1600s; *m*/*z* (%) 503 (M^+, 0.2), 446 (26), 247 (100), 164 (26), 130 (24), 75 (34) and 73 (65); minor *N*-invertomer (observable signals) δ 1.58 (3H, d, *J* 6.3, CH_3CHO), 3.25 (1H, dd, *J* 5.4 and 3.8, azir. H-3), 5.63 (1H, q, *J* 6.3, CH_3CHO), 5.81 (1H, d, *J* 3.8, azir. H-2) and 6.53 (1H, d, *J* 5.4, $CHCl_2$). From integral comparison of the signals at δ 4.98 and 5.63, the ratio of major : minor *N*-invertomers was 7 : 1; minor diastereoisomer (observable signal) δ 3.86 (1H, d, *J* 5.4, azir. H-2). Examination of the NMR spectrum of the crude product showed the ratio of major : minor diastereoisomers of aziridine **11** was 20 : 1 from comparison of the signals at δ 3.96 and 3.86 ppm. A crystal of aziridine **11** suitable for X-ray crystallography was grown by crystallisation from ethanol.

Identification of the major diastereoisomer of aziridine 7: desilylation of aziridine 7

To a solution of the crude aziridine **7** prepared as described above (0.20 g, 0.48 mmol) in THF (3 cm^3) at 0 °C was added a solution of tetrabutylammonium fluoride (TBAF) in THF (1 M, 0.25 g, 0.96 mmol) and the mixture stirred for 30 min at 0 °C and then at room temp. for 15 min. The reaction mixture was poured into ether (10 cm^3), the solution washed with water (10 cm^3), brine (10 cm^3), dried and then evaporated under reduced pressure to give a yellow oil whose NMR spectrum showed the presence of two aziridine **17** diastereoisomers in a ratio 5 : 1 from integral comparison of signals at δ 2.75 and 2.65 ppm respectively. This mixture was separated using a Chromatotron and eluting with light petroleum–ethyl acetate (5 : 1) to give the major *aziridine* **17** diastereoisomer (R_f 0.18) as a colourless oil (0.1 g, 69%). $[\alpha]_D$ = 320 (*c* = 0.8, $CHCl_3$) (Found: M^+ 307.132. $C_{18}H_{17}N_3O_2$ requires *M* 307.132); δ_H 1.51 (3H, d, *J* 6.3, CH_3CHOH), 2.75 (1H, dd, *J* 5.0 and 1.9, azir. H-3 *trans* to Q^1), 3.70 (1H, dd, *J* 7.9 and 1.9, azir. H-3 *cis* to Q^1), 4.03 (1H, dd, *J* 7.9 and 5.0, azir. H-2), 4.49 (1H, d, *J* 7.6, CH_3CHOH), 5.15 (1H, dq, *J* 7.6 and 6.3, CH_3CHOH), 7.30–7.78 [8H, m, 6-H, 7-H, 8-H(Q) and C*H*(Ph)] and 8.22 [1H, dd, *J* 7.9 and 1, 5-H(Q)]; ν_{max}/cm^{-1} 1670s and 1600s; *m*/*z* (%) 307 (M^+, 31), 264 (40), 262 (64), 216 (63), 201 (27), 189 (60), 175 (20), 173 (100), 172 (81), 147 (26), 130 (27), 119 (33), 118 (74), 117 (66), 103 (61), 91 (77), 90 (42), 84 (20) and 76 (34).

Further elution with light petroleum–ethyl acetate (5 : 1) gave the minor *aziridine* **17** diastereoisomer also as a colourless oil (0.03 g, 20%). $[\alpha]_D$ = −94 (*c* = 0.5, $CHCl_3$) (Found: M^+ 307.132. $C_{18}H_{17}N_3O_2$ requires *M* 307.132); δ_H 1.50 (3H, d, *J* 6.3, CH_3CHOH), 2.65 (1H, dd, *J* 5.0 and 1.9, azir. H-3 *trans* to Q), 3.49 (1H, dd, *J* 7.9 and 1.9, azir. H-3 *cis* to Q), 4.46 (1H, dd, *J* 7.9 and 5.0, azir. H-2 and d, *J* 7.6, CH_3CHOH), 5.35 (1H, dq, *J* 7.6 and 6.3, CH_3CHOH), 7.38–7.78 [8H, m, 6-H, 7-H, 8-H(Q) and C*H*(Ph)] and 8.21 [1H, dd, *J* 7.9 and 1, 5-H(Q)]; *m*/*z* (%) 307 (M^+, 22), 264 (25), 262 (38), 216 (77), 201 (29), 189 (39), 174 (21), 173 (73), 172 (58), 134 (72), 130 (21), 119 (56), 118 (49), 115 (36), 105 (55), 104 (26), 103 (56) 92 (71), 91 (100), 90 (31), 78 (37), 77 (42) and 76 (25).

Aziridination of styrene with Q^2NHOAc–TTB

General procedure 3 was followed using Q^2NH_2 **19**[5b] (0.2 g, 0.98 mmol), LTA (0.48 g, 1.07 mmol) and added to a stirred solution of TTB (0.66 g, 1.95 mmol) and styrene (0.20 g, 1.95 mmol) in dry dichloromethane (2 cm^3) maintained at −20 °C (bath temperature). After work-up, examination of the residue by NMR spectroscopy showed the two aziridine **17** diastereoisomers (0.09 g, 31%) were present in a 6.5 : 1 ratio from integral comparison of signals at δ 2.75 and 2.65 ppm respectively in its NMR spectrum. These major and minor aziridine diastereoisomers were shown to be identical to the major and minor diastereoisomers isolated in the previous experiment by comparison of their NMR spectra.

Identification of the major diastereoisomer of aziridine 9: desilylation of aziridine 9

To a stirred solution of the aziridine **7** (dr 5 : 1) (0.25 g, 0.57 mmol) in THF (2 cm^3) at 0 °C was added a solution of TBAF in THF (1 M, 0.18 g, 0.68 mmol) and the mixture stirred for 30 min at 0 °C and then at room temp. for 15 min. The reaction mixture was poured into ether (10 cm^3), the solution washed with water (10 cm^3), then brine (10 cm^3), dried and concentrated under reduced pressure to give a colourless oil. Flash chromatography of the oil over silica with light petroleum–ethyl acetate (10 : 1) as eluent gave a mixture of *aziridine* **18** (R_f 0.34) as an oil (0.11 g, 59%) together with unchanged aziridine **9** (0.09 g, 38%). Trituration of the oil with light petroleum gave the major *aziridine* diastereoisomer **18** as a colourless solid mp 127–128 °C (from ethanol). $[\alpha]_D$ = −59 (*c* = 0.5, $CHCl_3$) (Found: C, 71.0; H, 5.95; N, 13.1. $C_{19}H_{19}N_3O_2$ requires C, 71.0; H, 6.0; N, 13.15%); δ_H (mixture of *N*-invertomers) major *N*-invertomer (phenyl and Q *trans*) 1.42 (3H, d, *J* 6.0, CH_3CHOH), 1.45 (3H, d, *J* 6.6, azir. CH_3), 3.08 (1H, dq, *J* 6.6 and 5.0, azir. H-3), 3.97 (1H, d, *J* 5.0, azir. H-2), 4.63 (1H, d, *J* 6.3, CH_3CHOH), 5.15 (1H, dq, *J* 6.3 and 6.0,

CH_3CHOH), 6.95–7.78 [8H, m, 6-H, 7-H, 8-H(Q) and C*H*(Ph)] and 8.23 [1H, dd, *J* 7.9 and 1, 5-H(Q)]; minor *N*-invertomer (observable signals) δ 1.31 (3H, d, *J* 6.6, azir. CH_3), 1.70 (3H, d, *J* 6.0, CH_3CHOH), 3.60 (1H, d, *J* 6.0, CH_3CHOH), 4.28 (1H, m, azir. H-3), 4.92 (1H, m, CH_3CHOH) and 8.12 [1H, d, *J* 7.9, 5-H(Q)]. From integral comparison of signals at δ 4.63 and 3.60, the *N*-invertomer ratio of the major aziridine diastereoisomer was 2.7 : 1; ν_{max}/cm^{-1} 1690s and 1600s; *m*/*z* (%) 321 (M^+, 5), 132 (100) and 118 (20). Observable signals from the minor diastereoisomer in the crude reaction product were present for major *N*-invertomer (phenyl and Q *trans*) at δ 4.15 (1H, d, *J* 5.0, azir. H-2) and for the minor *N*-invertomer at 3.50 (1H, d, *J* 5.0, azir. H-2) respectively with the ratio of *N*-invertomers 1.9 : 1 from comparison of these two signals. The NMR spectrum of the crude product showed the ratio of major : minor diastereoisomers was 5 : 1 from integral comparison of signals at δ 4.63 + 3.60 : 4.15 + 3.50 ppm.

Aziridination of β-methylstyrene with Q^{2}NHOAc 22–TTB

General procedure 3 was followed using Q^2NH_2 **19** [14] (0.4 g, 1.95 mmol), LTA (0.95 g, 2.15 mmol), TTB (1.33 g, 3.9 mmol) and *β*-methylstyrene (0.46 g, 3.9 mmol) in dry dichloromethane (6 cm^3). An NMR spectrum of the crude product showed two aziridine diastereoisomers present in a 5 : 1 ratio which were identical to the major and minor aziridines **18** respectively in the crude reaction product from the previous experiment.

Aziridination of β-methylstyrene with Q^{3}NHOAc 24–TTB

General procedure 3 was followed using Q^3NH_2 **21** [5a] (0.2 g, 0.81 mmol), LTA (0.4 g, 0.90 mmol), TTB (0.55 g, 1.62 mmol) and *β*-methylstyrene (0.19 g, 1.62 mmol) in dry dichloromethane (3 cm^3). An NMR spectrum of the crude product indicated only one aziridine diastereoisomer was present and, after trituration with ethanol, some of this aziridine crystallised out; a further quantity was obtained by Chromatotron chromatography with light petroleum–ethyl acetate as eluent (5 : 1) to give *aziridine* **27** (R_f 0.27) as a colourless solid (total 0.14 g, 49%) mp 157–158 °C (from ethanol). $[\alpha]_D$ = 60 (*c* = 0.5, $CHCl_3$) (Found: C, 72.35; H, 6.95; N, 11.4. $C_{22}H_{25}N_3O_2$ requires C, 72.7; H, 6.95; N, 11.55%); δ_H (mixture of *N*-invertomers) major *N*-invertomer (phenyl and Q *trans*): 0.68 (9H, s, Bu^t), 1.32 (3H, d, *J* 5.4, azir. CH_3), 3.21 (2H, m, azir. H-3 and H-2), 3.64 (1H, d, *J* 10.4, Bu^{t}CHO*H*), 4.70 (1H, d, *J* 10.4, Bu^{t}C*H*OH), 7.26–7.70 [8H, m, 6-H, 7-H, 8-H(Q) and C*H*(Ph)] and 8.20 [1H, dd, *J* 8.5 and 1.3, 5-H(Q)]; ν_{max}/cm^{-1} 1765w, 1680s and 1590s; *m*/*z* (%) 364 (MH^+, 63), 307 (20), 154 (100), 137 (52), 136 (71) and 132 (40); signals from the minor invertomer were observable at δ 0.93 (9H, s, Bu^t), 1.65 (3H, d, *J* 5.4, azir. CH_3). The ratio of *N*-invertomers was 3.6 : 1 from comparison of signals at δ 0.68 and 0.93.

Further elution with light petroleum–ethyl acetate (5 : 1) (Chromatotron) gave an oily ring-opened alcohol **29** (0.035 g, 11%). (Found: M^+ 382.213. $C_{22}H_{28}N_3O_3$ requires *M* 382.213); δ_H 0.86 (3H, d, *J* 6.6, $NHCHCH_3$), 1.03 (9H, s, Bu^t), 2.96 (1H, d, *J* 6.6, CHO*H*Ph), 3.62 (1H, d, *J* 10.1, Bu^{t}CHO*H*), 3.71 (1H, m, $CHCH_3$), 4.60 (1H, dd, *J* 6.6 and 6.0, C*H*OHPh), 5.28 (1H, d, *J* 10.1, Bu^{t}C*H*OH), 6.16 (1H, d, *J* 2.5, N*H*), 7.33–7.82 [8H, m, 6-H, 7-H, 8-H (Q) and C*H*(Ph)] and 8.28 [1H, dd, *J* 7.9 and 1.6, 5-H(Q)]; ν_{max}/cm^{-1} 3500m, 1680s, 1610w, 1595s and 1565s; *m*/*z* (%) 382 (M^+, 0.4), 274 (100), 256 (56), 215 (68), 176 (29), 175 (31) and 147 (22).

The above experiment was repeated, but in the absence of TTB. General procedure 1 was followed using Q^3NH_2 **21** [5a] (0.2 g, 0.81 mmol), LTA (0.4 g, 0.90 mmol) and *β*-methylstyrene (0.19 g, 1.62 mmol) in dry dichloromethane (3 cm^3). Examination of the NMR spectrum of the crude product showed two aziridine diastereoisomers were present in a 1.6 : 1 ratio from integration of signals at δ 4.70 : 4.95 + 4.63 with the major one identical to that isolated above. Chromatotron chromatography of the crude product with light petroleum–ethyl acetate as eluent (5 : 1) gave the minor diastereoisomer of *aziridine* **27** (R_f 0.42) as a colourless oil (0.07 g, 23%). (Found: M^+ 363.194. $C_{22}H_{25}N_3O_2$ requires *M* 363.194); δ_H major invertomer (phenyl and Q *trans*): 1.05 (9H, s, Bu^t), 1.33 (3H, d, *J* 5.4, azir. CH_3), 2.94 (1H, dq, *J* 5.4 and 5.4, azir. H-3), 3.80 (1H, d, *J* 10.4, Bu^{t}CHO*H*), 3.88 (1H, d, *J* 5.4, azir. H-2), 4.95 (1H, d, *J* 10.4, Bu^{t}C*H*OH), 6.91–7.76 [8H, m, 6-H, 7-H, 8-H(Q) and C*H*(Ph)] and 8.23 [1H, d, *J* 8.5, 5-H(Q)]; *m*/*z* (%) 363 (M^+, 0.7), 132 (100), 105 (29) and 83 (40); signals from the minor invertomer were observable at δ 0.93 (9H, s, Bu^t), 1.68 (3H, d, *J* 5.4, azir. CH_3), 2.78 (1H, d, *J* 8.8, Bu^{t}CHO*H*), 3.55 (1H, d, *J* 6.0, azir. H-2) and 4.63 (1H, d, *J* 8.8, Bu^{t}C*H*OH). The ratio of *N*-invertomers was 2.7 : 1 from comparison of signals at δ 4.95 and 4.63. Signals from this aziridine were absent from the spectrum of the crude product in the aziridination as above carried out in the presence of TTB.

Further elution with light petroleum–ethyl acetate (5 : 1) gave the major *aziridine* diastereoisomer of **27** (R_f 0.31) as a colourless solid (0.09 g, 31%) identical with that isolated previously.

Aziridination of (*E*)-cinnamyl chloride with Q^{3}NHOAc 24–TTB

General procedure 3 was followed using Q^3NH_2 **21** [5a] (0.3 g, 1.21 mmol), LTA (0.59 g, 1.33 mmol), TTB (0.82 g, 2.42 mmol) and cinnamyl chloride (0.37 g, 2.42 mmol) in dry dichloromethane (5 cm^3). Crystallisation of the product by addition of ethanol gave *aziridine* **28** (R_f 0.29) as a colourless solid (0.22 g, 46%) mp 149–151 °C (from ethanol). $[\alpha]_D$ = +190 (*c* = 0.5, CH_2Cl_2) (Found: C, 66.15; H, 6.1; N, 10.35. $C_{25}H_{25}ClN_3O_2$ requires C, 66.4; H, 6.1; N, 10.55%); δ_H (mixture of *N*-invertomers) major *N*-invertomer (phenyl and Q *cis*): 0.75 (9H, s, Bu^t), 3.29 (1H, dd, *J* 11.3 and 9.4, C*H*HCl), 3.56 (1H, m, azir. H-3), 3.57 (1H, *J* 10.4, Bu^{t}CHO*H*), 3.66 (1H, d, *J* 5.0, azir. H-2), 4.30 (1H, dd, *J* 11.3 and 4.7, CH*H*Cl), 4.81 (1H, d, *J* 10.4, Bu^{t}CHO*H*), 7.0–7.80 [8H, m, 6-H, 7-H, 8-H(Q) and C*H*(Ph)] and 8.25 [1H, dd, *J* 7.9 and 1, 5-H(Q)]; ν_{max}/cm^{-1} 1660s and 1590s; *m*/*z* (%) 398 (M^+, 1.1), 348 (73), 312 (61), 214 (22), 189 (33), 176 (24), 175 (61), 168 (24), 166 (67), 147 (20), 132 (28), 130 (100), 117 (65), 116 (30), 115 (20), 104 (44), 103 (83), 77 (32), 76 (25) and 57 (33); minor *N*-invertomer (observable signals): δ 1.00 (9H, s, Bu^t), 3.98 (1H, d, *J* 5.0, azir. H-2), 4.50 (1H, s, br, Bu^{t}CHO*H*) and 8.02 [1H, dd, *J* 7.9 and 1, 5-H(Q)]; from integration comparison of the signals at δ 8.25 : 8.02 the ratio of *N*-invertomers was 4 : 1.

Desilylation of aziridine 10

To a stirred solution of aziridine **10** (0.09 g, 0.19 mmol) in THF (1 cm^3) at 0 °C was added a solution of TBAF in THF (1 M, 0.08 g, 0.29 mmol) and the mixture stirred for 30 min at 0 °C and then at room temp. for 15 min. The reaction mixture was poured into ether (5 cm^3), the solution washed with water (5 cm^3), then brine (5 cm^3), dried and concentrated under reduced pressure to give a colourless oil whose NMR spectrum showed the presence of aziridine ether **34a** and imine **35** in a 1.6 : 1 ratio from integration comparison of signals at δ 8.11 and 8.37 ppm respectively (see below). Flash chromatography of the product over silica with light petroleum–ethyl acetate (2 : 1) as eluent gave an oil (R_f 0.53) (0.03 g, 54%). Trituration of this oil with light petroleum gave the cyclic *aziridine ether* **34a** as a colourless solid, mp 171–173 °C (from ethanol). $[\alpha]_D$ = −104 (*c* = 0.8, $CHCl_3$) (Found: C, 71.2; H, 5.5; N, 13.1. $C_{19}H_{17}N_3O_2$ requires C, 71.45; H, 5.35; N, 13.15%); δ_H 1.84 (3H, d, *J* 7.2, CH_3CHO), 3.11 (1H, ddd, *J* 10.7, 5.3 and 3.5, azir. H-3), 3.27 (1H, d, *J* 5.3, azir. H-2), 3.58 (1H, dd, *J* 13.5 and 10.7, C*H*H), 4.42 (1H, dd, *J* 13.5 and 3.5, CH*H*), 5.10 (1H, q, *J* 7.2, CH_3CHO), 7.22–7.62 [8H, m, 6-H, 7-H, 8-H(Q) and C*H*(Ph)] and 8.11 [1H, ddd, *J* 8.2, 1.6 and 0.6, 5-H(Q)]; ν_{max}/cm^{-1} 1670s and 1590s; *m*/*z* (%) 319 (M^+, 23), 216 (89), 215 (100), 214 (27), 188 (21), 187 (27), 173 (93), 156 (20), 130 (21), 117 (60), 115

(34), 104 (20), 103 (21), 102 (25), 90 (20), 84 (25) and 77 (24). For comparison, signals of the other diastereoisomer **34b** are found at δ 1.75 (3H, d, *J* 7.0, CH_3CHO), 3.25 (1H, ddd, *J* 13.1, 5.3 and 3.6, azir. H-3), 3.4 (1H, d, *J* 5.3, azir. H-2), 3.6 (1H, dd, *J* 13.5 and *ca.* 13, C*H*H), 4.5 (1H, dd, *J* 13.1 and 3.6, CH*H*), 5.6 (1H, q, *J ca.* 7, CH_3CHO), 7.4–7.75 [8H, m, 6-H, 7-H, 8-H(Q) and C*H*(Ph)] and 8.25 [1H, ddd, *J* 7.7 and *ca.* 1, 5-H(Q)].[4]

Further elution of the column using the same solvent mixture gave imine **35** as a colourless oil (R_f 0.37) (0.015 g, 23%). (Found: M^+ 319.132. $C_{19}H_{17}N_3O_2$ requires *M* 319.132); δ_H: 1.67 (3H, d, *J* 6.6, CH_3CHO), 2.85 (2H, m, OCH_2), 3.05 (2H, m, CH_2CN), 5.06 (1H, q, *J* 6.6, CH_3CHO), 7.22–7.77 [8H, m, 6-H, 7-H, 8-H(Q) and C*H*(Ph)] and 8.37 [1H, dd, *J* 7.9 and 1.3, 5-H(Q)]; δ_C 17.12 (CH_3), 30.9 (CH_2CH_2), 33.4 (CH_2CH_2), 64.1 (CH_3CHO), 121.3 [*C*CO(Q)], 125.9–133.3 [4 × *C*H(Q) and 5 × *C*H(Ph)], 138.8 [*C*(Ph)], 144.8 [*C*=N(Q)], 145.2, 155.6, 157.4 [*C*–N(Q), N=*C*(Ph) and *C*O(Q)]; *m*/*z* (%) 319 (M^+, 68), 215 (26), 186 (20), 173 (27), 131 (41), 104 (43), 85 (91), 77 (44), 69 (41) and 57 (100).

Aziridination of stilbene with Q^1NHOAc 5

General procedure 2 was followed using Q^1NH_2 **4**[9] (0.2 g, 0.63 mmol), LTA (0.31 g, 0.69 mmol), HMDS (0.25 g, 1.54 mmol) and styrene (0.14 g, 0.75 mmol) in dry dichloromethane (3 cm^3). Flash chromatography of the crude product over silica with light petroleum–ethyl acetate (5 : 1) as eluent gave a pure sample of the minor *aziridine* **12** diastereoisomer (R_f 0.56) as a colourless oil (0.007 g, 2%). δ_H −0.20 (3H, s, CH_3SiCH_3), 0.00 (3H, s, CH_3SiCH_3), 0.95 (9H, s, Bu^t), 1.84 (3H, d, *J* 6.3, CH_3CHO), 3.95 (1H, d, *J* 6, azir. H-2 *trans* to Q), 4.88 (1H, d, *J* 6, azir. H-3 *cis* to Q), 4.95 (1H, q, *J* 6.3, CH_3CHO), 7.20–7.84 [13H, m, 6-H, 7-H, 8-H(Q) and C*H*(Ph)] and 8.16 [1H, d, *J* 7.8, 5-H(Q)].

Further elution with the same solvent mixture gave major *aziridine* **12** diastereoisomer (R_f 0.48) as an oil which, on trituration with light petroleum, gave a colourless crystalline product (0.053 g, 34%). $[a]_D$ = −599 (*c* = 0.6, $CHCl_3$) (Found: M^+ 497.250. $C_{30}H_{35}N_3O_2Si$ requires *M* 497.250); δ_H 0.00 (3H, s, CH_3SiCH_3), 0.02 (3H, s, CH_3SiCH_3), 0.69 (9H, s, Bu^t), 0.81 (3H, d, *J* 6.3, CH_3CHO), 3.69 (1H, d, *J* 6.0, azir. H-3 *trans* to Q), 4.61 (1H, d, *J* 6.0, azir. H-2 *cis* to Q), 5.07 (1H, q, *J* 6.3, CH_3CHO), 6.86–7.55 [13H, m, 6-H, 7-H, 8-H(Q) and C*H*(Ph)] and 8.14 [1H, d, *J* 7.8, 5-H(Q)]. From the NMR spectrum of the crude product the ratio of major : minor diastereoisomers was 3 : 1 from integration of signals at δ 5.07 and 4.95 ppm. ν_{max}/cm^{-1} 1660s and 1600s; *m*/*z* (%) 497 (M^+, 0.7), 247 (47), 195 (15) and 194 (100).

Aziridination of methyl cinnamate with Q^1NHOAc 5

General procedure 1 was followed using Q^1NH_2 **4**[9] (0.3 g, 0.94 mmol), LTA (0.46 g, 1.03 mmol) and methyl cinnamate (0.31 g, 1.88 mmol) in dry dichloromethane (4 cm^3). The NMR spectrum of the crude product revealed the presence of diastereoisomers of aziridine **13** (0.15 g, 33%) together with 3*H*-quinazolinone **14** in a 3 : 1 ratio, from integration of signals at δ 4.00 + 3.96 ppm and 9.28 respectively. Separation by flash chromatography over silica with light petroleum–ethyl acetate (7 : 1) as eluent gave major *aziridine* **13** diastereoisomer (R_f 0.32) as a colourless oil. (Found: M^+ 479.234. $C_{26}H_{33}N_3O_4Si$ requires *M* 479.224); δ_H −0.11 (3H, s, CH_3SiCH_3), 0.00 (3H, s, CH_3SiCH_3), 0.70 (9H, s, Bu^t), 1.24 (3H, d, *J* 6.3, CH_3CHO), 3.51 (3H, s, CO_2CH_3), 3.58 (1H, d, *J* 4.7, azir. H-3 or 2), 4.00 (1H, d, *J* 4.7, azir. H-2 or 3), 5.03 (1H, q, *J* 6.3, CH_3CHO), 7.25–7.55 [8H, m, 6-H, 7-H, 8-H(Q) and C*H*(Ph)] and 7.98 [1H, d, *J* 7.9, 5-H(Q)]; ν_{max}/cm^{-1} 1760s, 1710s and 1625s; *m*/*z* (%) 479 (M^+, 1), 422 (29), 248 (27), 247 (100) and 75 (22); observable signals from the minor diastereoisomer were present in the crude reaction product at δ −0.18 (3H, s, CH_3SiCH_3), −0.12 (3H, s, CH_3SiCH_3), 0.55 (9H, s, Bu^t), 1.62 (3H, d, *J* 6.3, CH_3CHO) and 3.96 (1H, d, *J* 4.7, azir. H-3 or 2). The NMR spectrum of the crude product showed the ratio of major : minor diastereoisomers was 3 : 1 from integration of signals at δ 4.00 and 3.96 ppm.

Aziridination of (*E*)-cinnamyl chloride with Q^4NHOAc 38

General procedure 2 was followed using Q^4NH_2 **37**[5b] (0.2 g, 0.82 mmol), LTA (0.4 g, 0.90 mmol), HMDS (0.26 g, 1.63 mmol) and cinnamyl chloride (0.25 g, 1.63 mmol) in dry dichloromethane (3 cm^3). Flash chromatography of the product over silica with light petroleum–ethyl acetate (12 : 1) as eluent gave a mixture of the aziridine **40** as a mixture of diastereoisomers (R_f 0.53) as a colourless oil (0.21 g, 64%) which crystallised after standing in the freezer (4–5 days); the major *aziridine* **40** diastereoisomer was obtained on addition of ethanol as a colourless solid, mp 94–96 °C (from ethanol). (Found: C, 69.6; H, 6.75; N, 10.45. $C_{25}H_{26}ClN_3O$ requires C, 69.75; H, 6.6; N, 10.6%); δ_H 0.36 (3H, d, CH_3CHBu^t), 0.88 (9H, s, Bu^t), 3.02 (1H, q, *J* 6.9, CH_3CHBu^t), 3.73 (1H, dd, *J* 11.3 and 3.7, CH*H*Cl), 3.78 (1H, d, *J* 5.6, azir. H-2), 3.96 (1H, ddd, *J* 7.5, 5.6 and 3.7, azir. H-3), 4.52 (1H, dd, *J* 11.3 and 7.5, C*H*HCl), 6.85–7.62 [8H, m, 6-H, 7-H, 8-H(Q) and C*H*(Ph)] and 8.25 [1H, dd, *J* 7.9 and 1.3, 5-H(Q)]; ν_{max}/cm^{-1} 1665s and 1590s; *m*/*z* (%) 395 (M^+, 9), 347 (25), 346 (100), 339 (21), 175 (42), 174 (46), 173 (23), 166 (41), 131 (34), 130 (66), 121 (26), 119 (40), 117 (62), 116 (28), 103 (29), 82 (26), 77 (26), 57 (33) and 51 (37). Observable signals from the minor diastereoisomer of aziridine **40** in the NMR spectrum of the crude reaction product were present at δ 0.73 (9H, s, Bu^t), 1.03 (3H, d, *J* 6.9 CH_3CHBu^t), 4.33 (1H, dd, *J* 11.3 and 3.7, CH*H*Cl) and 8.21 [1H, d, *J* 7.9, 5-H(Q)]. The NMR spectrum of the crude product showed the ratio of major : minor diastereoisomers present was 2 : 1 from integration of signals at δ 4.52 and 4.33 ppm. An X-ray structure determination was carried out for the major diastereoisomer of aziridine **40** on a crystal obtained from ethanol (see Fig. 2).

Aziridination of (*E*)-β-dichloromethylstyrene with Q^4NHOAc 38

General procedure 2 was followed using Q^4NH_2 **37**[5b] (0.2 g, 0.82 mmol), LTA (0.4 g, 0.90 mmol), HMDS (0.26 g, 1.63 mmol) and *β*-dichloromethylstyrene (0.18 g, 0.98 mmol) in dry dichloromethane (3 cm^3). Trituration of the oily product with light petroleum gave major *aziridine* **41** diastereoisomer as a colourless solid (0.1 g, 29%) mp 163–165 °C (from ethanol). (Found: C, 64.0; H, 5.9; N, 9.8. $C_{23}H_{25}Cl_2N_3O$ requires C, 64.2; H, 5.85; N, 9.75%); δ_H 0.28 (3H, d, *J* 6.6, CH_3CHBu^t), 0.72 (9H, s, Bu^t), 2.90 (1H, q, *J* 6.6, CH_3CHBu^t), 3.91 (1H, d, *J* 5.3, azir. H-2), 4.28 (1H, dd, *J* 5.3 and 3.5, azir. H-3), 6.39 (1H, d, *J* 3.5, $CHCl_2$), 6.83–7.50 [8H, m, 6-H, 7-H, 8-H(Q) and C*H*(Ph)] and 8.07 [1H, dd, *J* 8.2 and 1.6, 5-H(Q)]; ν_{max}/cm^{-1} 1665s and 1590s; *m*/*z* (%) 429 (M^+, 2), 347 (38), 346 (100), 174 (22), 117 (21) and 116 (23). Observable signals from the minor diastereoisomer of aziridine **41** were present in the NMR spectrum of the crude reaction mixture at δ 2.62 (1H, q, *J* 6.6, CH_3CHBu^t), 3.81 (1H, d, *J* 5.3, azir. H-2) and 4.68 (1H, m, azir. H-3). From the NMR spectrum of the crude product, the ratio of major : minor diastereoisomers of aziridine **41** is 3.5 : 1 from integration of signals at δ 3.91 and 3.81 ppm.

Crystal structure determination

Crystal data for 40.† $C_{23}H_{26}ClN_3O$, *M* = 395.92, monoclinic, space group $P2_1/c$, *a* = 9.750(9), *b* = 12.881(14), *c* = 16.715(9) Å, β = 95.70(6)°, *V* = 2089(3) $Å^3$, *T* = 200 K, *Z* = 4, μ(Mo-Kα) = 0.201 mm^{-1} colourless block, crystal dimensions 0.56 × 0.53 × 0.43 mm. Full matrix least squares based on F^2 gave R_1 = 0.056 for 2156 observed data ($F > 4\sigma(F)$) and wR_2 = 0.237 for all 2863 data, GOF = 1.072 for 257 parameters.

† CCDC reference number 169151. See http://www.rsc.org/suppdata/p2/b1/b107327n/ for crystallographic files in .cif or other electronic format.

Data were measured on a Siemens P4 diffractometer with graphite monochromated Mo-Kα radiation ($\lambda = 0.7107$ Å) using an ω scan technique. Three standard reflections monitored every 100 scans showed no significant variation in intensity, the reflections were corrected for Lorentz and polarisation effects.

The structure was solved by direct methods and refined by full-matrix least squares on F^2 using the program SHELXTL.[15] All hydrogen atoms were included in calculated positions (C–H = 0.96 Å) using a riding model. All atoms were refined using anisotropic displacement parameters.

References

1 R. S. Atkinson, *Tetrahedron*, 1999, **55**, 1519.
2 R. S. Atkinson, S. Ulukanli and P. J. Williams, *J. Chem. Soc., Perkin Trans. 1*, 1999, 2121.
3 R. S. Atkinson and P. J. Williams, *J. Chem. Soc., Perkin Trans. 1*, 1996, 1951.
4 R. S. Atkinson and P. J. Williams, *J. Chem. Soc., Perkin Trans. 1*, 1996, 205.
5 (*a*) R. S. Atkinson, A. P. Ayscough, W. T. Gattrell and T. M. Raynham, *J. Chem. Soc., Perkin Trans. 1*, 1998, 2783; (*b*) R. S. Atkinson and G. Tughan, *J. Chem. Soc., Perkin Trans. 1*, 1987, 2803.
6 R. S. Atkinson, M. P. Coogan and I. S. T. Lochrie, *Tetrahedron Lett.*, 1996, **37**, 5179.
7 Preliminary communication: R. S. Atkinson, T. A. Claxton, I. S. T. Lochrie and S. Ulukanli, *Tetrahedron Lett.*, 1998, **39**, 5113.
8 D. J. Anderson, D. C. Horwell and R. S. Atkinson, *J. Chem. Soc., Sect. C*, 1971, 624.
9 R. S. Atkinson, M. P. Coogan and I. S. T. Lochrie, *J. Chem. Soc., Perkin Trans. 1*, 1997, 897.
10 B. Gung, J. P. Melnick, M. A. Wolf and A. King, *J. Org. Chem.*, 1995, **60**, 1947; B. Gung and M. B. Francis, *Tetrahedron Lett.*, 1995, **36**, 2579.
11 R. S. Atkinson and S. Ulukanli, *J. Chem. Soc., Perkin Trans. 2*, 1999, 771.
12 M. S. Newman and P. K. Sujeeth, *J. Org. Chem.*, 1978, **43**, 4367.
13 Gaussian 94 (Revision B.2), M. Frisch, G. W. Trunks, H. B. Schlegel, P. M. W. Gill, B. G. Johnson, M. A. Robb, J. R. Cheeseman, T. A. Keith, G. A. Peterson, J. A. Montgomery, K. Paghavachari, M. A. Al-Laham, V. G. Zakrewski, J. V. Ortiz, J. R. Foresman, J. Cioslowski, B. B. Stefanov, A. Nanayakara, M. Challacombe, C. Y. Peng, P. Y. Ayala, W. Chen, M. W. Wong, J. L. Andres, E. S. Repogle, R. Gomperts, J. S. Binkley, C. Gonzales, R. L. Martin, D. J. Fox, D. J. Defrees, J. Baker, M. Head-Gordon, J. P. Stewart and J. A. Pople, Gaussin Inc., Pittsburgh, PA, 1993.
14 R. S. Atkinson, B. J. Kelly and J. Williams, *Tetrahedron*, 1992, **48**, 7713.
15 G. M. Sheldrick, SHELXTL ver. 6.10, Bruker AXS Inc., Madison, WI, USA, 2000.