Aziridination of 2- and 3-phenyl-substituted allylic alcohols with 3-acetoxyaminoquinazolinones: probing the nature of the transition state from the diastereoselectivity of aziridination

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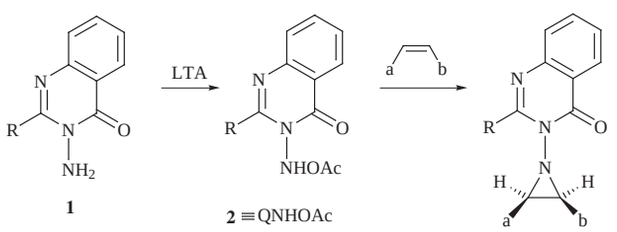
Aziridination of phenyl-substituted allylic alcohol **10** with 3-acetoxyaminoquinazolinone **3** (Q^1NHOAc) and with **22** (Q^2NHOAc) has been studied. The diastereoselectivity of these reactions is markedly changed by carrying them out in the presence of aqueous sodium hydrogen carbonate solution and under these conditions aziridinations of **10** and of its ester analogue **5** with Q^2NHOAc give the same magnitude and sense of diastereoselectivity (with Ph≡CO_2Me). An explanation for these changes in diastereoselectivity is offered based upon differences in the nature of the hydrogen bonding in the transition states for aziridination of **10** with and without the presence of acetic acid.

A versatile method for aziridination of alkenes uses 3-acetoxyaminoquinazolinones **2** (QNHOAc) prepared in solution by *N*-acetoxylation of 3-aminoquinazolinones **1** with lead tetraacetate (LTA) (Scheme 1).[1]



1

2 ≡QNHOAc
3 R = Et≡ Q^1NHOAc

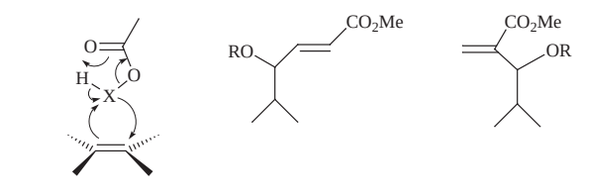
Scheme 1

The main advantages of this method are (i) a range of alkenes of different electron availability can be used including styrene and α,β-unsaturated esters, (ii) the reaction is stereospecific with retention of configuration in the alkene and (iii) high or complete diastereoselectivity is possible when R is a chiral group (R*).[2–4]

The mechanism of aziridine ring formation in Scheme 1 would appear to resemble that by which peroxyacetic acid reacts with alkenes (see **4**) but there are differences which arise from involvement of the quinazolinone ring in the aziridination mechanism. Thus our previous study[5] of aziridine ring formation from ester-substituted allylic alcohol **5** and Q^1NHOAc **3** lead to the proposed transition state (TS#) **9** in which *endo*-overlap of the ester carbonyl oxygen and the quinazolinone 4-position as shown[6] is essential for the reaction to occur. The other important features of this TS# **9** are (i) N–C_β bond formation (Michael addition) runs ahead of C_α–N bond formation, (ii) displacement of the acetoxy group from the exocyclic nitrogen takes place *via* an S_N2-type substitution with formation of the C_α–N bond and (iii) the presence of hydrogen bonding between the allylic hydroxy group of alcohol **5** and the acetoxy group of Q^1NHOAc **3**: inversion at the sp^3-hybridised exocyclic nitrogen is known to be fast on the time-scale of the aziridination although slow on the NMR time-scale.[7]

Our derivation of TS# **9** involved a comparison of both the magnitude and sense of diastereoselectivity in aziridinations of isomeric ester-substituted allylic alcohols **5** and **7** and their *O*-acetates **6** and **8**.[5]

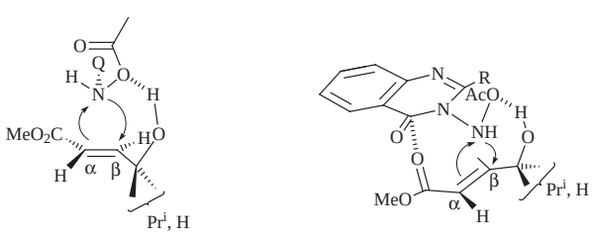
In this paper are described our results from aziridination of



4 X = O; epoxidation
X = NQ; aziridination

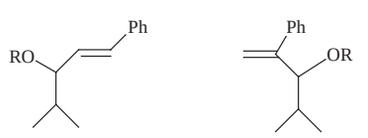
5 R = H
6 R = Ac

7 R = H
8 R = Ac



9 front view

9 side view



10 R = H
12 R = Ac

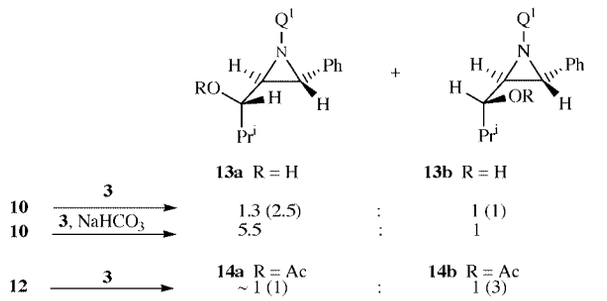
11 R = H

the analogous phenyl-substituted allylic alcohols **10** and **11** and *O*-acetate **12**.[8] This study was undertaken in an attempt to determine the effect on the aziridination TS# **9** of the change to a much more electron-available (phenyl-substituted) double bond. Our eventual goal in this work is the rational design of a range of chiral 2-substituents in QNHOAc **2** (R = R*), based on a detailed knowledge of the TS#, in order to bring about the complete reagent-controlled diastereoselective aziridination of a range of alkenes.

As in our previous work using alcohols **5** and **7**, the purpose of the hydroxy group in alcohols **10** and **11** was to offer an opportunity for the *N*-acetoxy group of the QNHOAc **2** to hydrogen bond in the transition state for aziridination. The substitution at the chiral centre in alcohols **10** and **11** was kept identical to that in **5** and **7** to allow direct comparison between reaction of two types of alkene to be made.

Results

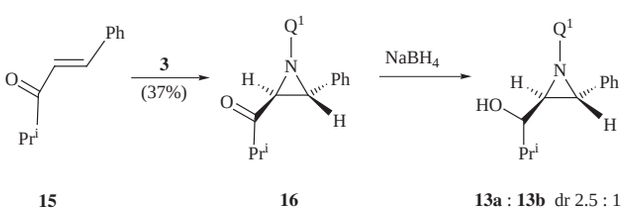
Aziridination of allylic alcohol **10** with Q[1]NHOAc **3** was carried out as described previously[5] and gave a mixture of the diastereoisomers **13a** and **13b** (Scheme 2) in a 1.3 : 1 ratio from analysis of the NMR spectrum of the crude reaction product and by comparison with spectra of the pure separated diastereoisomers (see below).



Scheme 2

The major diastereoisomer **13a** was separated as a colourless solid (32%) and after flash chromatography, the minor diastereoisomer **13b** was obtained also as a colourless solid (27%). Assignment of stereostructures to these diastereoisomers was straightforward and based on the chemical shift of the hydroxy and allylic methine (Pr^{i}C*H*O*H*) protons in their NMR spectra which we have previously correlated with relative configuration in these aziridine alcohols.[5] Thus the major diastereoisomer **13a** has δ 5.19 (O*H*) and δ 3.4 (Pr^{i}C*H*OH) whereas in the minor diastereoisomer **13b** these two protons resonate at δ 2.51 and δ 4.4 respectively. These stereostructural assignments were confirmed by an X-ray crystal structure determination on the major diastereoisomer **13a**.[8]

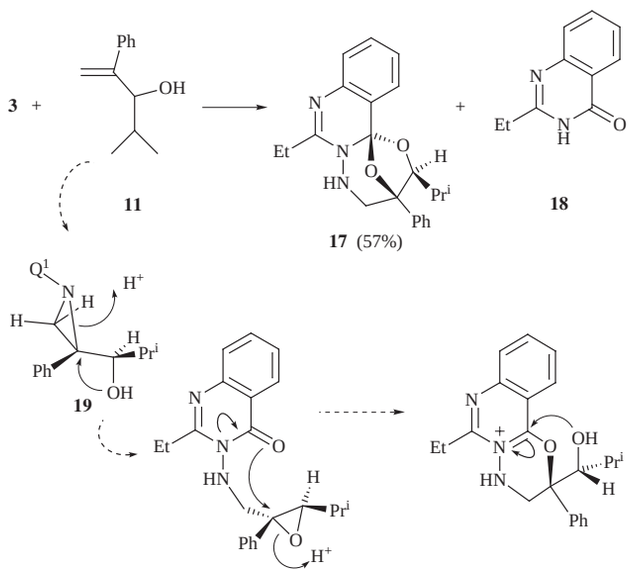
That the two aziridine alcohols **13a** and **13b** were epimeric at the isobutanol chiral centre was confirmed when they were obtained in a 2.5 : 1 ratio (major : minor as above) by sodium borohydride reduction of the aziridinyl ketone **16**. This ketone **16** was obtained by aziridination of the α,β-unsaturated ketone **15** with Q[1]NHOAc **3** (Scheme 3).



Scheme 3

Aziridination of **12**, the *O*-acetate of alcohol **10** with Q[1]NHOAc **3** (Scheme 2) gave a mixture of the two aziridines **14a** and **14b** and together with a by-product whose structure has not been identified (ratio† **14a** : **14b** : by-product 1 : 2 : 1). After flash chromatography a small sample of aziridine **14b** was eluted as a crystalline solid but the mixture of aziridine **14a** and the by-product was not separated. Assignments of relative configuration to aziridines **14a** and **14b** (Scheme 2) followed from the chemical shift of the Pr^{i}C*H*OAc protons at δ 4.85 and δ 5.36 respectively in their NMR spectra and were confirmed by *O*-acetylation of the corresponding alcohols **13a** and **13b** with pyridine and acetic anhydride. Significantly, in the acetylation of alcohol **13a**, a mixture of acetate **14a** and the by-product in a 2.3 : 1 ratio was obtained whereas alcohol **13b** gave only the corresponding acetate **14b**. Since the by-product in the aziridination of allylic acetate **12**, therefore, is apparently derived exclusively from further reaction of diastereoisomer **14a**, the initial diastereoisomer ratio of **14a** : **14b** formed in this aziridination is ~1 : 1 (see Scheme 2).

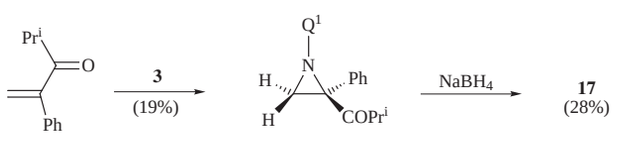
Aziridination of the isomeric allylic alcohol **11** using Q[1]NHOAc **3** was also carried out under the same conditions. The major product (57% isolated yield) was a crystalline solid shown to be cyclic acetal **17** by an X-ray crystal structure determination:[8] the only other product identified was the 3*H*-quinazolinone **18** (Scheme 4).



Scheme 4

The proposed mechanism for formation of acetal **17** in Scheme 4 includes ring-opening of the first-formed aziridine **19** by a Payne-type rearrangement with inversion of configuration followed by ring-opening of the resulting epoxide by the quinazolinone oxygen, again with the inversion of configuration.[9]

In an attempt to prepare the diastereoisomer of aziridine **19** which was not identified in the products from aziridination of allylic alcohol **11**, we prepared the aziridine ketone **21** (in low yield) from reaction of α,β-unsaturated ketone **20** with Q[1]NHOAc **3** (Scheme 5). In reduction of the keto-group



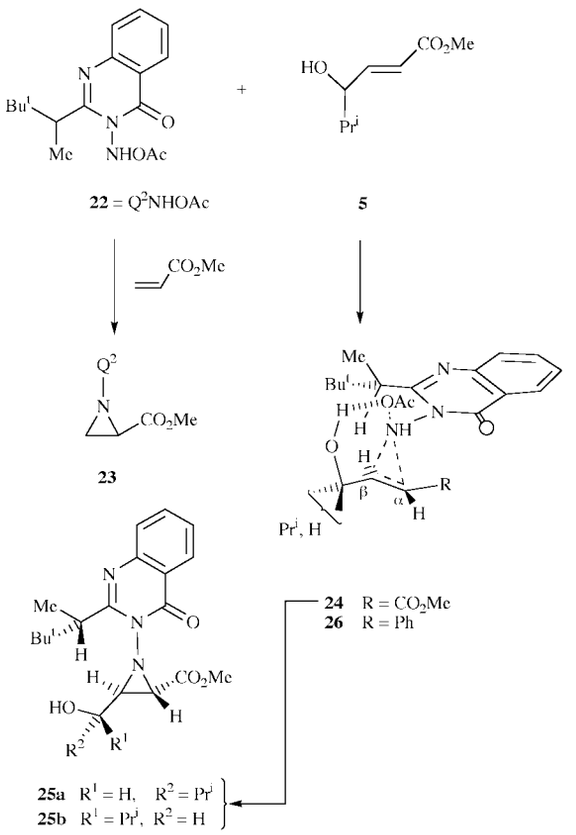
Scheme 5

with sodium borohydride formation of both diastereoisomeric aziridine alcohols was anticipated but, in the event, the only homogeneous product isolated after chromatography was the acetal **17** (28%).

Aziridination using chiral Q[2]NHOAc 22

We have also previously studied aziridination of racemic ester-substituted allylic alcohol **5** with the racemic Q[2]NHOAc **22** (Scheme 6).[8] Although four aziridine diastereoisomers could have been formed in this reaction, in practice only two, **25a** and **25b** are obtained (ratio 6 : 1) and these differ in configuration only at the isobutanol chiral centre. By contrast, reaction of methyl acrylate with Q[2]NHOAc **22** gave a 2.5 : 1 ratio of aziridine diastereoisomers **23**.[2] Our rationalisation of the complete reagent-controlled diastereoselectivity in formation of aziridines **25a** and **25b** used TS[#] **24** where, with attack on the

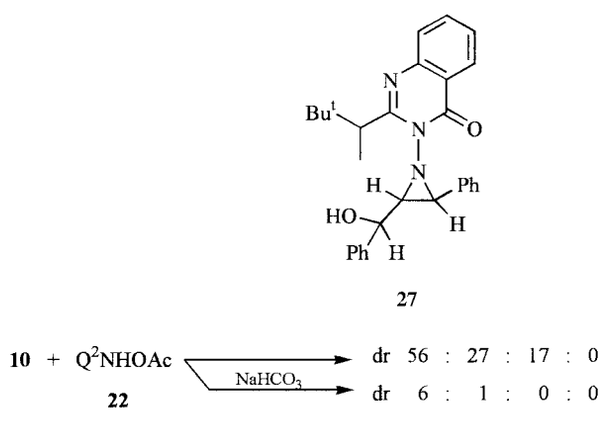
† This ratio is based on the assumption that the NMR signal for the by-product (δ 4.71, dd, *J* 9.5 and 5.8) corresponds to one proton.



Scheme 6

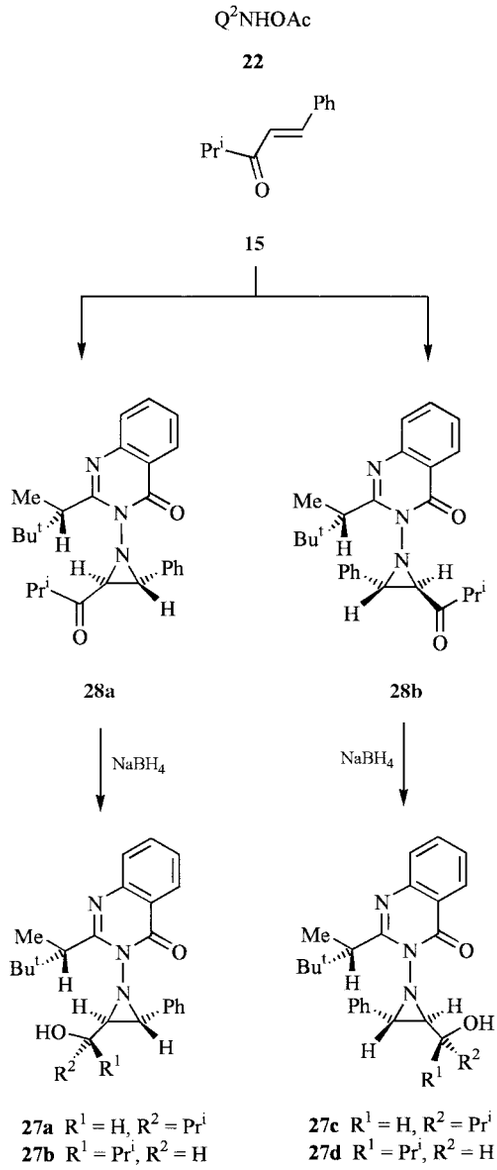
diastereoface shown, the site preferences of the substituents on the Q²-2 chiral centre are influenced by the proximity of the *N*-acetoxy group.

The aziridination of allylic alcohol **10** with Q²NHOAc **22** has now been examined to assess the effect of replacement of the ester in **5** by a phenyl group. From examination by NMR spectroscopy of the crude reaction product, three of the four possible diastereoisomers of aziridine **27** appeared to be present in a ratio 56:27:17 (Scheme 7). Separation by flash chromatography gave a mixture (6:1) of the two more abundant diastereoisomers as a colourless solid but the least abundant diastereoisomer was not isolated.



Scheme 7

To confirm that the relationship between these three products in the crude reaction mixture was a diastereoisomeric one, we synthesised all four diastereoisomers **27a**–**d** by aziridination of α,β-unsaturated ketone **15** with Q²NHOAc **22** and reduction of each of the separated diastereoisomeric aziridinyl ketones **28a** and **28b** with sodium borohydride (Scheme 8).



Scheme 8

The NMR spectrum of the mixture of aziridinyl alcohols from reduction of ketone diastereoisomer **28a** showed that it contained the two major diastereoisomers (*56*:*27*:17) from the aziridination in Scheme 7. This ketone **28a** was also identified as the Swern oxidation product of alcohol **27a** when a pure sample of this alcohol became available. From inspection of the NMR spectrum of the mixture from sodium borohydride reduction of the other aziridinyl ketone **28b**, one of the aziridinyl alcohol products was identical to that present as the minor diastereoisomer (56:27:*17*) arising from the aziridination in Scheme 7.

Assignments of relative configuration to ketones **28a** and **28b** were possible after an X-ray structure determination of **28b** became available (Fig 1):‡ assignments of relative configuration

‡ *X-Ray crystallography*. *Crystal data for* **27b**: Chemical formula $C_{26}H_{31}N_3O_2$, formula weight M = 417.54, crystal system monoclinic, a = 14.405(5), b = 29.119(6), c = 12.006(3) Å, β = 108.8(1)°, space group $C2/c$, μ 0.074 mm^{-1}, R Values $R1$ = 0.0719, $wR2$ = 0.233 for all data, unit cell dimensions 0.52 × 0.41 × 0.24 mm, unit cell volume V = 4768(2) Å^3, temperature of data collection 173 K, Z 8, measured independent reflections and R(int) 4166 R_{int} = 0.018 [2798 having $F > 4\sigma(F)$].

CCDC reference number 207/342. See http://www.rsc.org/suppdata/p1/1999/2121 for crystallographic files in .cif format.

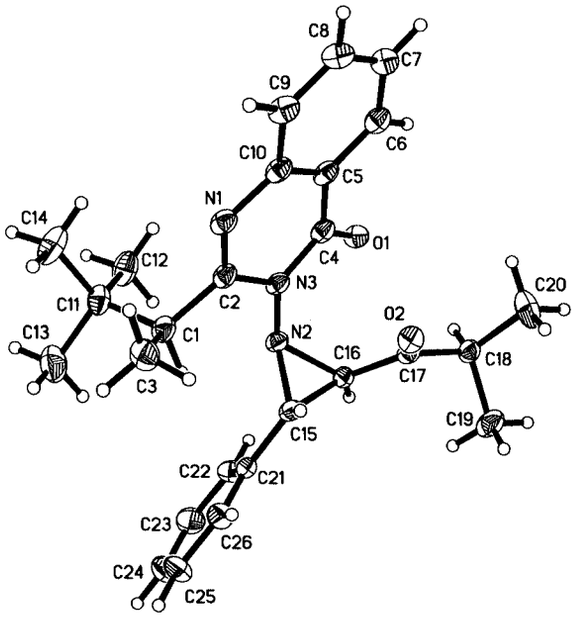


Fig. 1 Structure of **28b** showing the atom labelling scheme. Displacement parameters are shown at the 30% probability level.

for each of the alcohols **27a**–**d** then followed from δ for Pr^i-C*H*OH in the NMR spectra of the alcohol mixtures **27a**,**b** and **27c,d** (Scheme 8).

Aziridination of allylic alcohols 10 and 5 in the presence of saturated sodium hydrogen carbonate solution

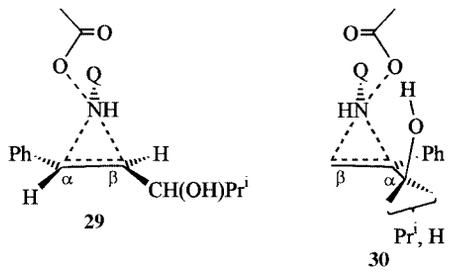
We have previously reported[10] that the rate of aziridination of styrene relative to methyl acrylate with solutions of QNHOAc **2** (R = Pr^i) is retarded in the presence of aqueous sodium hydrogen carbonate and have attributed this effect to the removal of acetic acid normally present in the reaction mixture. Aziridinations by Q^2NHOAc **22** of both allylic alcohols **5** and **10** were carried out in the presence of aqueous sodium hydrogen carbonate to determine what effect the removal of acetic acid had on the diastereoselectivity of the these reactions (*cf.* Schemes 6 and 7).

For aziridination of allylic alcohol **5** with Q^2NHOAc **22** in the presence of aqueous sodium hydrogen carbonate, there was no measurable change in the ratio of diastereoisomers **25a**:**25b** produced. However, for aziridination of allylic alcohol **10** with Q^2NHOAc **22** under the same conditions, NMR spectroscopic examination of the crude reaction mixture revealed that only **27a** and **27b** were present in a 6:1 ratio respectively. Thus, in the presence of aqueous sodium hydrogen carbonate, the outcome of aziridinations of allylic alcohols **5** and **10** is the same (with $CO_2Me \equiv Ph$) both in the sense of the resulting diastereoselectivity—the relative configurations of **25a**, **25b** and **27a**, **27b** are identical—and in the numerical ratio of the two diastereoisomers produced in each case.

The presence of aqueous sodium hydrogen carbonate solution also affected the diastereoselectivity in aziridination of allylic alcohol **10** with Q^1NHOAc **3** and the ratio of aziridines **13a**:**13b** produced was changed from 1.3:1 to 5.5:1 (Scheme 2).

Discussion

To simplify this discussion we start with the proposal that aziridinations of phenyl-substituted allylic alcohols **10** and **11** under the standard conditions proceed *via* TS#s **29** and **30** respectively. Hydrogen bonding between the allylic hydroxy and the *N*-acetoxy group therefore is absent in TS# **29** but is feasible in TS# **30**, a situation complementary to that for aziridination



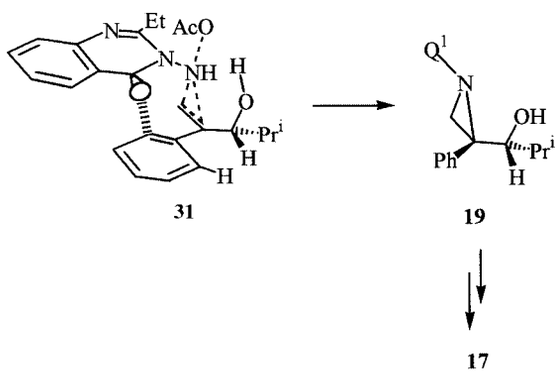
of ester-substituted allylic alcohol analogues **5** (see **9**) and **7** respectively.

In these TS#s **29** and **30** it is assumed that C_β–N bond formation is running ahead of N–C_α bond formation: the partial carbocation generated in the reaction at C_α is stabilised by the phenyl ring. It is, therefore, the change in the nature of the alkene from an electrophile (in **5** and **7**) to a nucleophile (in **10** and **11**) which is responsible for the change in configuration at the exocyclic nitrogen in QNHOAc and hence the possibility of hydrogen bonding only in TS# **30**.

In Scheme 2, the ratio of aziridine alcohol diastereoisomers **13a** and **13b** and their corresponding *O*-acetates **14a** and **14b**, from aziridination of phenyl-substituted allylic alcohol/acetates **10/12** with Q^1NHOAc **3**, are given along with the ratios (in parentheses) from aziridination of ester-substituted allylic alcohol/acetate analogues **5/6**. It is clear from comparison of these ratios that there is little correspondence between them: if hydrogen bonding is present in the TS# for aziridination of ester-substituted allylic alcohol **5**, as is believed to be the case (see TS# **9**), then an analogous hydrogen bonding is unlikely to be present in the TS# for aziridination of phenyl-substituted allylic alcohol **10**.

A similar conclusion follows from the gross differences in diastereoselectivity from aziridinations of ester- and phenyl-substituted allylic alcohols **5** and **10** respectively with Q^2NHOAc **22** (Schemes 6 and 7). Again if, as is believed, there is hydrogen bonding present in the aziridination of **5** as in TS# **24**, such a hydrogen bond is very likely absent in the TS# for the reaction of **10**.

On the other hand, formation of acetal **17** from attempted aziridination of allylic alcohol **11** is not inconsistent with a TS# **31** (*cf.* **30**) in which hydrogen bonding is present leading to aziridine **19** and thence to acetal **17** (Scheme 9). In this TS# **31**



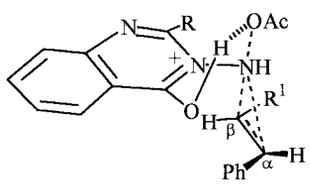
Scheme 9

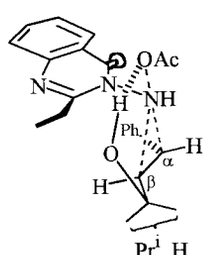
the attractive interaction between the phenyl ring and the Q^1 carbonyl group (dashed line)[11] resembles that between the ester and the Q^1 carbonyl in TS# **9** and has for a long time been thought to be an important[1] although not indispensable[12] factor in aziridination of styrene derivatives. The configuration at the isobutanol chiral centre as in TS# **31** is thought to be preferred because steric interaction between the isopropyl and the *o*-proton of the phenyl ring is thereby avoided.[13] Whether the hydrogen bonding present in TS# **31** is between the allylic

hydroxy group and the *N*-acetoxy group, however, is presently not clear (see below).

The effect of the presence of aqueous sodium hydrogen carbonate solution on the diastereoselectivity of aziridination of allylic alcohol **10** with Q^2NHOAc **22** (Scheme 7) is striking: the identity both in the sense of diastereoselectivity and in the numerical ratio of diastereoisomers of the aziridinations in Schemes 6 and 7 under these conditions strongly suggests that both reactions proceed *via* analogous TS#s **24** and **26** (see Scheme 6).

To rationalise these results we propose that, in the presence of acetic acid, aziridination of phenyl-substituted allylic alcohol **10** takes place *via* a TS# resembling **32**. Here *O*-protonation of the Q^2 carbonyl group makes the exocyclic nitrogen more electrophilic with the presence of positive charge on (Q^2)N-3. Moreover, breaking of the N–OAc bond is assisted by *intramolecular* hydrogen bonding with the *O*-bonded proton. Diastereoselectivity arising from TS# **32** is expected to be low as is found to be the case (dr 56:27:17). Note that for aziridine ring formation from electron-available alkenes *e.g.* **10**, the TS# **32** has C_β–N bond formation running ahead of N–C_α bond formation and so protonation of the departing acetoxy will very likely accelerate the reaction.





32 R = CHBu^t(Me), R^1 = CH(OH)Pr^i **34**

33 R = Et, R^1 = CH(OH)Pr^i

35 R = Et, R^1 = H

By contrast, in the TS# **9** for aziridination of ester-substituted allylic alcohol **5**, *intermolecular* hydrogen bonding between the alcohol and the *N*-acetoxy group is preferred. *O*-Protonation of the Q^2 carbonyl oxygen (as in TS# **32**) is less favoured because the nucleophilicity of the exocyclic nitrogen Q^2NHOAc **3** is thereby reduced (N–C_β bonding formation runs ahead of C_α–N bond formation) and in any case the acetoxy group is *anti* to this Q^2-carbonyl oxygen.

The effect of adding base to the aziridination of allylic alcohol **10** (Scheme 7) is to remove acetic acid and hence to bring about a change in TS# from **32**→**26** as a result of the now more favourable intermolecular hydrogen bonding. It is the similarity between TS# **24** and **26** which leads to the identical diastereoselectivity for the two aziridinations in Schemes 6 and 7.

The change in diastereoselectivity in aziridination of allylic alcohol **10** with Q^1NHOAc **3** brought about by the presence of sodium hydrogen carbonate solution (from 1.3:1→5.5:1) is in agreement with an analogous switch from TS# **33** to TS# **34**. It is noteworthy that in the presence of the base this substrate-controlled diastereoselectivity (5.5:1) is almost identical to that substrate-controlled diastereoselectivity element in aziridination of allylic alcohol **10** with Q^2NHOAc **22** above (6:1). This near-identity is not unexpected in view of the similarity between TS#s **34** and **26** and the likely absence of any influence in **26** of the (chiral) substituent at (Q)C-2 on the site preferences at hydrogen and isopropyl at the isobutanol chiral centre.§

§ In the TS# **31** for aziridination of allylic alcohol **11** with Q^1NHOAc in the presence of acetic acid, hydrogen bonding is possible either with the protonated (Q)C=O and/or with the allylic hydroxy group.

What is the likely mechanism of aziridination with *e.g.* Q^1NHOAc **3** of styrene itself, based on the foregoing results and our interpretation of them? In TS#s **26** and **34** there is presumably some partial carbocation character generated on C_β but in neither case is this thought to be as developed as the carbanion build-up in TS#s **9** and **24** which we believe to be more 'unsymmetrical'. For styrene itself, the absence of any carbocation stabilising feature at C_β is likely to make TS# **35** the preferred one in the presence of acetic acid, and TS# **35**, without the proton on the Q^1 carbonyl oxygen, preferred in the absence of acetic acid.

Conclusions

The diastereoselectivities of aziridination of phenyl-substituted allylic alcohols **10** and **11** with Q^1NHOAc **3** or Q^2NHOAc **22** are very different from those of their ester-substituted analogues **5** or **7**. These differences are ascribed to one of mechanism for aziridination of the two different types of double bond in the presence of acetic acid. In the presence of aqueous sodium hydrogen carbonate solution, however, aziridinations of phenyl- and ester-substituted allylic alcohols **10** or **5** with Q^2NHOAc **22** result in the same diastereoselectivity and in aziridination of **10** with either Q^1NHOAc **3** or Q^2NHOAc **22** the substrate-controlled diastereoselectivity elements are also identical. These changes in diastereoselectivity brought about by removal of acetic acid from the reaction mixture are ascribed to a change in the nature of the hydrogen bonding in the TS# for aziridination of allylic alcohol **10** and include a change in configuration at the pyramidal exocyclic nitrogen Q*N*HOAc.

Experimental

For general experimental details see refs. 5 and 10. Unless otherwise indicated NMR spectra were recorded at 300 MHz in $CDCl_3$ with tetramethylsilane as an internal standard.

(*E*)-3-Hydroxy-4-methyl-1-phenylpent-1-ene **10** was prepared by addition of cinnamaldehyde to a well-stirred solution of isopropylmagnesium chloride in ether (supplied by Aldrich) and obtained as a colourless oil, bp 158–159 °C/0.5 mmHg (lit.[14] 170 °C/0.7 mmHg). (*E*)-4-Methyl-1-phenylpent-1-en-3-one **15** was prepared by the Swern procedure (described below for alcohol **27a**) from alcohol **10** (2 g, 1.4 mmol) and triethylamine (7.92 cm^3, 0.057 mol) in dry dichloromethane (4 cm^3). The crude product was distilled, bp 125–126 °C/0.1 mmHg (lit.[15] 164 °C/26 mmHg) to give the ketone **15** (1.45 g, 73%). (*E*)-3-Acetoxy-4-methyl-1-phenylpent-1-ene **12** was prepared from the corresponding alcohol **10** (2 g, 11 mmol) by acetylation with acetic anhydride (5 cm^3) and pyridine (5 cm^3) as described previously.[5] After work-up the acetate **12** (1.6 g, 67%) obtained was used in aziridination experiments below without further purification, δ_H (90 MHz, $CDCl_3$) 7.3 [1H, 5 × C*H*(Ph)], 6.69 (1H, d, *J* 15, PhC*H*=CH), 6.21 (1H, dd, *J* 15 and ~7, PhCH=C*H*), 5.24 (1H, t, *J* ~7, C*H*OAc), 2.03 (4H, s, OCOCH_3, m, C*H*Me$_2$) and 1.00 [6H, t, *J* 6, CH(CH_3)$_2$]. 3-Hydroxy-4-methyl-2-phenylpent-1-ene **11** was prepared by addition of a solution of α-bromostyrene (3 g, 16 mmol) in dry ether (5 cm^3) dropwise to a well-stirred slurry of magnesium turnings (0.23 g, 8 mmol) in dry ether (5 cm^3) and stirring continued until the magnesium dissolved. After 20 min isobutyraldehyde (0.85 cm^3, 9.37 mmol) was added dropwise over 10 min and the reaction mixture stirred for 6 h before hydrochloric acid (2 M, 4 cm^3) was added. The reaction mixture was transferred to a separating funnel, the ether layer separated and washed with water (16 cm^3), dried, and the ether removed under reduced pressure. Distillation of the residue gave the required allylic alcohol **11** as a clear oil (21.6 g, 77%), ν_{max}/cm^{-1} 3607s, 1634w, 1604w; δ_H 7.4 [m, 5 × C*H*(Ph)], 5.46 (1H, d, *J* 1.3, =C*H*H), 5.40 (1H, dd, *J* 1.3 =CH*H*), 4.50 (1H, d, *J* 5.3, C*H*OH), 2.8 [1H, s, br, CHO*H*, (exch. D_2O)], 1.87 (1H, m, C*H*Me$_2$), 1.05 (3H, d, *J* 6.7,

CH_3CHCH_3) and 1.03 (3H, d, *J* 6.7, CH_3CHCH_3); δ_C 151.3 (*C*=CH_2), 140.6 [C(Ph)], 128.1 (2 × C), 127.5, 127.4, 127.2 [5 × C*H*(Ph)], 113.6 (*C*H_2=C), 78.6 (*C*HOH), 31.4 (*C*HMe_2) and 19.2 and 16.4 (CH_3CHCH_3). 4-Methyl-2-phenylpent-1-en-3-one **20** was prepared by Swern oxidation of the foregoing alcohol using the method described for alcohol **27a** below and obtained as an oil, bp 125–126 °C/0.5 mmHg (77%) (Found: M^+ 174.1045, $C_{12}H_{14}O$ requires M^+ 174.1044); ν_{max}/cm^{-1} 1670s, 1610m, 1600m and 1500w; δ_H ($CDCl_3$, 90 MHz) 7.13 [m, 5 × CH(Ph)], 5.91 (1H, s, =C*H*H), 5.82 (1H, s, =CH*H*), 3.25 (1H, septet, *J* 7.5, C*H*Me_2) and 1.19 [6H, d, *J* 7.4, $(CH_3)_2CH$)]; *m*/*z* (%) 174 (M^+, 78), 131 (29) and 103 (100) (lit.[14]: no analysis given).

Aziridination of allyl alcohol 10 with Q[1]NHOAc 3

A solution of Q[1]NHOAc **3** was prepared from 3-aminoquinazolinone (**1**, R = Et, 1 g, 5.29 mmol) and LTA (2.46 g, 5.55 mmol) in dry dichloromethane (12 cm^3) at −12 to −20 °C as described previously[5] and allylic alcohol **10** (1.3 g, 7.41 mmol) added. After work up, the crude product, containing a 1.3 : 1 ratio of aziridine diastereoisomers from comparison of the integral of signals at δ 4.4 and 3.4 in its NMR spectrum (see below), was chromatographed over silica using ethyl acetate–light petroleum (1 : 4) as eluent to give the major *aziridine* diastereoisomer **13a** (R_f 0.34) as colourless crystals (0.61 g, 32%), mp 115–116 °C (from ethanol) (Found: C, 72.7; H, 7.0; N, 11.5. $C_{22}H_{25}N_3O_2$ requires C, 72.7; H, 6.95; N, 11.55); ν_{max}/cm^{-1} 3450s,br, 1655s and 1600m; δ_H 8.30 [1H, dd, *J* 8 and 1.1, 5-H(Q)], 7.69 [1H, ddd, *J* ~8, ~7 and 1, 7-H(Q)], 7.53 [1H, d, *J* 8, 8-H(Q)], 7.43 [1H, dd, *J* ~8 and ~7, 6-H(Q)], 7.1 [m, 5 × C*H*(Ph)], 5.19 (1H, d, *J* 2.3, CHO*H* (exch. D_2O)], 3.7 (2H, m, azir. H-2, H-3), 3.4 (1H, m, C*H*OH), 2.90 (1H, dq, *A*BX_3, J_{AB} 16.3, J_{AX} 7.3, C*H*HCH_3), 2.34 (1H, dq, A*B*X_3, J_{AB} 16.3, J_{BX} 7.3, CH*H*CH_3), 1.96 (1H, m, C*H*Me_2), 1.10 (3H, t, *J* 7.3, CH_2CH_3), 1.05 (3H, d, *J* 7.1, CH_3CHCH_3) and 0.95 (3H, d, *J* 7.1, CH_3CHCH_3); *m*/*z* (%) 363 (M^+, 1), 291 (30), 290 (100), 200 (56), 175 (31), 174 (24) and 173 (28). An X-ray structure determination on **13a** was carried out on a crystal grown in ethanol.[8] Further elution with the same solvent mixture gave the minor *aziridine* diastereoisomer **13b** (R_f 0.27) as an off-white solid (0.51 g, 27%), mp 95–97 °C (from ethanol) (Found: C, 72.5; H, 6.95; N, 11.5. $C_{22}H_{25}N_3O_2$ requires C, 72.7; H, 6.95; N, 11.55%); ν_{max}/cm^{-1} 3470s,br, 1660s and 1595s; δ_H 8.25 [1H, dd, *J* 8 and 1, 5-H(Q)], 7.65 [1H, ddd, *J* 8, 7 and 1, 7-H(Q)], 7.50 [1H, d, *J* 8, 8-H(Q)], 7.44 [1H, d, *J* 8 and 7, 6-H(Q)], 7.1 [m, 5 × CH(Ph)], 4.40 (1H, d, *J* 5.3, C*H*OH), 4.07 (1H, d, br, *J* ~6, azir. H-3), 3.94 (1H, d, *J* 6, azir. H-2), 2.96 (1H, dq, ABX_3, J_{AB} 14.7, J_{AX} 7.3, C*H*HCH_3), 2.51 [1H, s, br, CHO*H*, (D_2O exch.)], 2.40 (1H, dq, *A*BX_3, J_{AB} 14.7, J_{BX} 7.3, CH*H*CH_3), 1.95 [1H, m, C*H*$(CH_3)_2$], 1.15 (3H, t, *J* 7.3, CH_2CH_3) and 1.04 (6H, 2 × d, *J* 6, CH_3CHCH_3); *m*/*z* (%) 363 (M^+, 0.1), 290 (40), 257 (22), 200 (54), 175 (100), 174 (49), 173 (40) and 84 (25).

Aziridination of α,β-unsaturated ketone 15 with Q[1]NHOAc 3

A solution of Q[1]NHOAc **3** in dichloromethane (12 cm^3) at −20 °C was prepared from 3-aminoquinazolinone **1** (R = Et) (1 g, 5.29 mmol) and LTA (2.46 g, 5.55 mmol) as described previously and α,β-unsaturated ketone **15** (1.3 g, 7.41 mmol) added. After work-up, the solid product crystallised to give the *aziridinyl ketone* **16** (0.71 g, 37%) as colourless crystals, mp 124–125 °C (from ethanol) (Found: M^+ 361.1790. $C_{22}H_{23}N_3O_2$ requires M^+ 361.1790); ν_{max}/cm^{-1} 1675s and 1600s; δ_H 8.14 [1H, d, *J* 7.9, 5-H(Q)], 7.6 [2H, m, 7-H and 8-H(Q)], 7.4 [6H, m, 6-H(Q), 5 × CH(Ph)], 4.1 (2H, s, azir. H-2, H-3), 3.34 [1H, septet, *J* 6.8, C*H*$(CH_3)_2$], 2.8 (2H, m, CH_2CH_3), 1.30 (6H, 2 × d, *J* 6.8, CH_3CHCH_3) and 1.29 (3H, t, *J* 7.3, CH_2CH_3); δ_C 202.0 (Pr^iC=O), 159.3 [*C*=O(Q)], 155.5 [N=C(Q)], 145.1 [*C*–N=C(Q)], 144.6 [*C*(Ph)], 133.4, 128.7, 128.6, 126.6, 126.3, 126.1, 125.7 [4 × CH(Q), 5 × CH(Ph)], 120.8 [*C*–C=O(Q)], 54.3, 53.8 (azir. *C*-2, *C*-3), 41.0 (*C*HMe_2), 27.6 (CH_2CH_3), 17.2, 16.1 (CH_3CHCH_3) and 14.5 (CH_2CH_3); *m*/*z* (%) 361 (M^+, 2.4), 291 (66), 290 (100), 262 (21), 200 (29), 173 (20), 130 (21), 117 (20) and 116 (28).

Reduction of aziridinyl ketone 16 with sodium borohydride

To a stirred solution of ketone **16** (0.5 g, 14 mmol) in dry methanol (10 cm^3) was added sodium borohydride (0.15 g, 3 mmol) in small portions over 20 min and the reaction mixture stirred until the starting ketone disappeared as monitored by TLC. The reaction mixture was poured into water (60 cm^3) and the bulk of the methanol removed by evaporation under reduced pressure. The residual solution was extracted with dichloromethane (30 cm^3) and the organic extract dried and evaporated under reduced pressure. An NMR spectrum of the crude product showed the presence of aziridinyl alcohol diastereoisomers **13a/13b** in a 2.5 : 1 ratio from comparison of signals at δ 3.40 and 4.40.

Aziridination of *O*-acetate 12

Aziridination of **12** (0.75 g, 3.7 mmol) was carried out using Q[1]NHOAc **3** prepared from 3-aminoquinazolinone **1** (R = Et) (0.5 g, 2.65 mmol) and LTA (1.23 g, 2.77 mmol) in dry dichloromethane (6 cm^3). The crude product contained aziridine diastereoisomers **14a** and **14b** from signals in its NMR spectrum at δ 5.36 and 4.85 together with an unidentified by-product (δ 4.71) in a ratio **14a** : **14b** : by-product = 1 : 2 : 1. Chromatography over silica and elution with ethyl acetate–light petroleum (1 : 4) gave a pure sample of the major diastereoisomer of *aziridine acetate* **14b** (R_f 0.29) as colourless crystals (0.05 g, 5%), mp 118–120 °C (from ethanol) (Found: C, 70.85; H, 6.8; N, 10.25. $C_{24}H_{27}N_3O_2$ requires C, 71.1; H, 6.7; N, 10.35%); ν_{max}/cm^{-1} 1740s, 1670s and 1600s; δ_H 8.25 [d, *J* 8.2, 5-H(Q)], 7.65 [ddd, *J* 8, 7 and 1.5, 6-H(Q)], 7.49 [d, *J* 8, 8-H(Q)], 7.44 [1H, dd, *J* 8.2 and 7, 6-H(Q)], 7.1 [m, 5 × CH(Ph)], 5.36 (1H, dd, *J* 4.7 and 4.7, C*H*OAc), 4.4 (1H, m, br, azir. H-3), 3.76 (1H, d, *J* 5.7, azir. H-2), 3.00 (1H, dq, ABX_3, J_{AB} 16.3, J_{AX} 7.3, C*H*HCH_3), 2.4 (2H, m, C*H*Me_2, CH*H*CH_3), 2.14 (3H, s, $OCOCH_3$), 1.16 (3H, t, *J* 7.3, CH_2CH_3) and 1.06–1.04 (6H, 2 × d, *J* 6.3, CH_3CHCH_3); *m*/*z* (%) 405 (M^+, 1), 291 (22) and 290 (100).

Further elution gave a mixture of aziridine diastereoisomers **14a/14b** and the by-product (see above) (0.388 g). For the minor diastereoisomer of aziridine acetate **14a**, δ_H (observable signals) 4.85 (1H, dd, *J* 7.6 and 4.2, C*H*OAc), 4.46 (1H, dd, *J* 6.2 and 6, azir. H-3), 3.59 (1H, d, *J* 6, azir. H-2), 2.29 (3H, s, $OCOCH_3$), 1.16 (3H, t, *J* 7.3, CH_2CH_3), 1.05–1.03 (6H, 2 × d, *J* 6.2, CH_3CHCH_3). For the by-product, δ_H 5.51 (1H, d, br, *J* ~4), 4.71 (1H, dd, *J* 9.5 and 5.8), 2.89 (1H, dd, *J* 9.5 and 4.7), 2.07 (1H, m, C*H*Me_2), 1.96 (3H, s, $OCOCH_3$), 1.46 (3H, t, *J* 7.4, CH_2CH_3) and 0.96 (6H, 2 × d, *J* 6, CH_3CHCH_3).

Acetylation of aziridine alcohols 13a/13b

Acetylation of **13a**, mp 115–116 °C (0.5 g, 1.4 mmol) was carried out with acetic anhydride (2 cm^3) and pyridine (3 cm^3). After 3 h the reaction was worked-up as described previously and an NMR spectrum of the product showed the presence of the *minor* aziridine diastereoisomer **14a** produced in the aziridination of **12** above together with the same unknown by-product in a 2.1 : 1 ratio from comparison of signals at δ 4.85 and 4.71.

Acetylation of **13b**, mp 95–97 °C (0.5 g, 1.4 mmol) under the same conditions gave rise to a single aziridine *O*-acetate isolated as colourless crystals, mp 119–121 °C identical to the major diastereoisomer **14b** isolated in the aziridination above.

Attempted aziridination of allylic alcohol 11 with Q[1]NHOAc 3

Reaction of **11** (0.74 g, 4.22 mmol) with a solution of Q[1]NHOAc **3** prepared from **1** (R = Et) (0.57 g, 3 mmol) and

LTA (1.4 g, 3.2 mmol) in dichloromethane (7 cm^3) as described previously[3] gave a solid product containing acetal **17** and 3*H*-quinazolinone **18** in the ratio 8 : 1 from comparison of signals in its NMR spectrum at δ 4.05 and 10.9 respectively. Crystallisation from ethanol gave the *acetal* **17** (0.62 g, 57%) as a colourless solid, mp 179–180 °C (Found: C, 72.6; H, 7.0; N, 11.5. $C_{22}H_{25}N_3O_2$ requires C, 72.7; H, 6.95; N, 11.55%); ν_{max}/cm^{-1} 3300w, 1595 and 1570s; δ_H 7.70 [1H, dd, *J* 7.8 and 1.3, 5-H(Q)], 7.4–7.2 [8H, m, 6-H, 7-H, 8-H(Q), 5 × CH(Ph)], 4.93 [1H, dd, *J* ~13.7 and 4, NH (D_2O exch.)], 4.05 (1H, dd, *J* 9.3 and 1.1, C*H*Pr^i), 3.80 (1H, dd, *J* 13.7 and 4, NC*H*H; after D_2O exch. becomes d, *J* 13.7), 3.67 (1H, ddd, *J* ~13.7, 13.7 and 1.1, NCH*H*; after D_2O exch. becomes dd, *J* 13.7 and 1.1), 2.7 (2H, m, C$H_2$$CH_3$), 2.2 (1H, m, $CHMe_2$), 1.30 (3H, t, *J* 7.5, CH_2CH_3) and 1.21 and 0.65 (6H, 2 × d, *J* 6.4, CH_3CHCH_3); δ_C 157.7, 143.2 [N=C(Q)], 137.1 [*C*–N=C(Q)], 130.6, 128.5, 128.3, 125.4, 124.7, 124.1 [4 × CH(Q), 5 × CH(Ph)], 119.4, 107.5 [*C*(Ph)], 94.0, 80.5, 49.0 (NCH_2), 28.2 ($CHMe_2$), 27.3 (CH_2CH_3), 21.5, 19 (CH_3CHCH_3) and 11.9 (CH_2CH_3); *m*/*z* (%) 363 (M^+, 100), 320 (70), 262 (62), 261 (27), 229 (25), 202 (30), 176 (22), 175 (35), 174 (76), 173 (72), 157 (37), 130 (32), 129 (27), 118 (31), 117 (28), 105 (38), 103 (37), 91 (22) and 77 (30). An X-ray crystal structure determination was carried out on a crystal of this acetal grown from ethanol.[8]

Aziridination of α,β-unsaturated ketone 20 with Q^1NHOAc 3

Aziridination of **20** (1.28 g, 7.4 mmol) with Q^1NHOAc **3** prepared from **1** (R = Et) (1 g, 5.29 mmol) and LTA (2.46 g, 5.5 mmol) as described previously and chromatography of the crude product over silica using ethyl acetate–light petroleum (1 : 4) as eluent gave *aziridine ketone* **21** (R_f 0.29) as colourless crystals (0.36 g, 19%), mp 163–165 °C (from ethanol) (Found: M^+ 361.1790. $C_{22}H_{23}N_3O_2$ requires M^+ 361.1789); ν_{max}/cm^{-1} 1745s, 1670s and 1595s; δ_H 8.31 [1H, d, *J* 7.2, H-5(Q)], 7.9–7.4 [8H, m, 6-H, 7-H, 8-H(Q), 5 × CH(Ph)], 3.44 (1H, s, azir. H-3 *cis* to COPh), 3.26 [1H, septet, *J* 6.7, C*H*Me_2), 3.07 (3H, m, azir. H-3 *cis* to Ph and C$H_2$$CH_3$), 1.45 (3H, t, *J* 6.9, CH_2CH_3), 1.04 and 0.83 (6H, 2 × d, *J* 7, CH_3CHCH_3); δ_C 203.8 (Pr^iC=O), 159.9 [*C*=O(Q)], 155.3 [N=C(Q)], 146.1 [*C*–N=C(Q)], 136.6 [*C*(Ph)], 133.6, 130.4, 128.8, 128.5, 127.1, 126.4, 125.6 [5 × CH(Ph), 4 × CH(Q)], 57.3 (azir. C-2), 48.6 (azir. C-3), 37.6 ($CHMe_2$), 27.0 (CH_2CH_3), 20.5 and 18.8 (CH_3CHCH_3) and 10.8 (CH_2CH_3); *m*/*z* (%) 361 (M^+, 18), 318 (38), 189 (47), 187 (26), 182 (54), 175 (41), 174 (100), 173 (67), 109 (50) and 103 (27).

Aziridination of allylic alcohol 10 with Q^2NHOAc 22

Aziridination of **10** (0.81 g, 4.6 mmol) was carried out with a solution of Q^2NHOAc **22** prepared from 3-aminoquinazolinone **1**[2] [R = Bu^t(Me)CH] (0.8 g, 3.3 mmol) and LTA (1.52 g, 3.4 mmol) in dichloromethane (10 cm^3) as described previously. A ^{1}H NMR spectrum of the crude product showed the presence of three diastereoisomers of the aziridine product **27** in a 56 : 27 : 17 ratio from integration comparison of signals at δ 3.66, 3.92 and 3.22 (see below). Chromatography over silica and elution with ethyl acetate–light petroleum (1 : 4) gave a fraction (0.994 g, 73%) containing the two major diastereoisomers above which crystallised from ethanol as a colourless solid containing **27a** and **27b** in a 6 : 1 ratio, mp 112–120 °C (Found: M^+ 419.2573. $C_{26}H_{33}N_3O_2$ requires M^+ 419.2573); ν_{max}/cm^{-1} 3410m, 1655s, 1610m and 1595m; δ_H ($CDCl_3$, 300 MHz) major diastereoisomer **27a**, 8.25 [1H, dd, *J* 7.9 and 1.6, 5-H(Q)], 7.7–6.85 [8H, m, H-6, H-7, H-8(Q) and 5 × CH(Ph)], 5.64 (1H, d, *J* 1.6, CHO*H*, exch. D_2O), 3.66 (1H, d, *J* 5.7, azir. H-2), 3.40 (2H, m, azir. H-3 and C*H*OH), 3.05 (1H, q, *J* 7.2, Bu^tCH), 1.92 (1H, septet, *J* 6.7, C*H*Me_2), 1.04 (3H, d, *J* 7.2, Bu^tCCH_3), 0.95 and 0.32 (6H, 2 × d, *J* 6.9, CH_3CHCH_3) and 0.88 (9H, s, Bu^t); minor diastereoisomer **27b** (observable peaks), 4.47 (1H, m, C*H*OH), 3.92 (1H, d, *J* 5.7, azir. H-2) and 3.76 (1H, dd, *J* 5.7 and 2.2, azir. H-3); *m*/*z* (%) 419 (M^+, 1), 347 (32), 346 (100), 174 (44), 173 (26), 130 (24), 118 (20), 117 (32), 116 (20), 91 (87) and 77 (20). The least abundant diastereoisomer **27c** was not eluted but was identified in the ^{1}H NMR spectrum of the crude reaction product by the presence of signals at δ_H 4.57 (1H, s, CHO*H*, D_2O exch.), 3.22 (2H, structured m, C*H*OH and MeC*H*).

Aziridination of allylic alcohol 10 with Q^2NHOAc 22 in the presence of saturated sodium hydrogen carbonate solution

A solution of Q^2NHOAc **22** was prepared from the corresponding 3-aminoquinazolinone (**1**, R = Bu^tMeCH, 0.7 g, 2.86 mmol)[2] and LTA (1.39 g, 3.14 mmol) as described previously and the cold solution added to a vigorously stirred (emulsion) mixture of **10** (0.42 g, 2.38 mmol), dichloromethane (10 cm^3) and saturated aqueous sodium hydrogen carbonate (15 cm^3) held at room temperature. Examination of the crude reaction mixture by NMR spectroscopy (250 MHz, $CDCl_3$) after work-up showed the presence of aziridine diastereoisomers **27a** and **27b** in 6 : 1 ratio from integral comparison of signals at δ 3.66 and 3.76 respectively. The crude product was triturated with light petroleum to free the *aziridine* diastereoisomer **27a** as a colourless solid (0.32 g, 32%) (from light petroleum–ethyl acetate) (Found: MH^+ 420.265. $C_{26}H_{34}N_3O_2$ requires MH^+ 420.265) identical with the major diastereoisomer isolated above. The minor diastereoisomer in the mixture above was identified as aziridine **27b** from the correlation below and was identical with the minor diastereoisomer isolated by chromatography in the aziridination above from signals in its NMR spectrum (250 MHz, $CDCl_3$) at 3.92 (1H, d, *J* 5.7, azir. H-2) and 3.76 (1H, dd, *J* 5.7 and 2.2, azir. H-3).

Swern oxidation of aziridine alcohol 27a to ketone 28a

A flame-dried, two-necked flask was equipped with a septum cap, purged with nitrogen and cooled to −60 °C. A solution of oxalyl chloride in dichloromethane (2 M, 0.12 cm^3, 0.238 mmol) was added *via* a syringe followed by dimethyl sulfoxide (0.1 cm^3) dropwise as a solution in dry dichloromethane (0.5 cm^3). After 10 min **27a** (0.1 g, 0.238 mmol) was added as a solution in dichloromethane (1 cm^3) over 5 min followed by triethylamine (0.08 cm^3, 0.55 mmol) in one portion. The cooling bath was removed and the reaction temperature allowed to reach ambient before quenching with water (3 cm^3). The organic layer was separated and washed successively with hydrochloric acid (2 M, 5 cm^3), saturated sodium hydrogen carbonate (5 cm^3), saturated brine (5 cm^3) then dried and evaporated under reduced pressure to give *ketone* **28a** (0.1 g, 99%) as an oil (Found: M^+ 417.241. $C_{26}H_{31}N_3O_2$ requires M^+ 417.241); δ_H (250 MHz, $CDCl_3$) major *N*-invertomer (Q and phenyl *cis*), 8.11 [1H, d, *J* 8.2, 5-H(Q)], 6.9–7.6 [8H, m, H-6, H-7 and H-8(Q), 5 × CH(Ph)], 4.21 and 3.87 (2H, 2 × d, *J* 4.7, azir. H-2 and H-3), 3.1 (2H, m, C*H*Pr^i and Bu^tCHCH_3), 1.28 (3H, d, *J* 7.2, Bu^tCHCH_3), 1.15 (3H, d, *J* 6.9, CH_3CHCH_3), 1.13 (3H, d, *J* 6.9, CH_3CHCH_3) and 1.05 (9H, s, Bu^t); minor *N*-invertomer (observable signals) 8.26 [1H, d, *J* 1.6 and 7.9, 5-H(Q)], 4.45 and 3.96 (2H, 2 × d, *J* 5.3, azir. H-2 and H-3) and 0.9 (9H, s, Bu^t) (from integration comparison of the signals at δ 3.87 and 3.96 the ratio of *N*-invertomers was 2.8 : 1); ν_{max}/cm^{-1} 1710m, 1670s and 1590s; *m*/*z* (%) 417 (M^+, 1.3), 347 (79), 346 (100), 256 (26), 200 (26), 174 (82), 173 (42), 131 (31), 130 (29), 118 (21), 117 (30), 116 (42), 91 (23), 77 (22), 71 (30) and 57 (28).

Aziridination of ketone 15 using Q^2NHOAc 22

A solution of Q^2NHOAc **22** was prepared from the 3-aminoquinazolinone **1** [R = Bu^t(Me)CH] (0.3 g, 1.22 mmol) and LTA (0.6 g, 1.35 mmol) in dichloromethane (5 cm^3) as described previously and the α,β-unsaturated ketone **15** (0.43 g, 2.45 mmol) added. After work-up an NMR spectrum of the crude product showed the presence of aziridine ketones **28a** and **28b**

in a 1:2:4 ratio from comparison of signals at δ 4.21:4.05. Flash chromatography of the crude reaction product over silica with light petroleum–ethyl acetate (10:1) as eluent gave an oil (R_f 0.41) (0.22 g, 44%) which crystallised on trituration with ethanol to give *aziridine ketone* **28b** as a colourless solid, mp 166–168 °C (from ethanol) (Found: M^+ 417.241. $C_{26}H_{31}N_3O_2$ requires M^+ 417.241); δ_H (250 MHz, $CDCl_3$) (single *N*-invertomer) 8.08 [1H, d, *J* 8.2, 5-H(Q)], 7.7 [1H, m, H-8(Q)], 7.3–7.4 [7H, m, H-6 and H-7(Q), 5 × CH(Ph)], 4.05 and 3.80 (2H, 2 × d, *J* 4.7, azir. H-2 and H-3), 3.30 (1H, septet, *J* 6.9, C*H*Pr^i), 3.16 (1H, q, *J* 7.2, Bu^tCHCH_3), 1.33 (3H, d, *J* 7.2, Bu^tCHCH_3), 1.13 (3H, d, *J* 6.9, CH_3CHCH_3), 1.11 (3H, d, *J* 6.9, CH_3-$CHCH_3$) and 0.73 (9H, s, Bu^t); ν_{max}/cm^{-1} 1705m, 1665s and 1390s; *m*/*z* (%) 417 (M^+, 3.3), 347 (82), 346 (100), 256 (29), 200 (24), 174 (81), 173 (40), 172 (24), 131 (27), 130 (23), 117 (36), 116 (28), 84 (24) and 71 (30). An X-ray structure determination was obtained for this ketone **28b** on a crystal obtained from ethanol (see Fig. 1).

The minor diastereoisomer in the aziridination mixture above was not isolated but comparison of signals at δ 4.21 and 4.45 in the NMR spectrum of the crude reaction mixture with those from aziridine ketone **28a**, prepared by Swern oxidation of alcohol **27a** above, showed that they were identical.

Reduction of aziridine ketone 28b with sodium borohydride

Reduction of ketone **28b** (0.09 g, 0.22 mmol) was carried out as described above in methanol (3 cm^3) with sodium borohydride (0.013 g, 0.33 mmol). After disappearance of the starting ketone (~30 min, TLC) and work-up, examination of the crude reaction product by NMR spectroscopy indicated the presence of two aziridine alcohol diastereoisomers **27c** and **27d** in a 2.8:1 ratio from integration of signals at δ 4.49 and 2.72. Flash chromatography over silica and elution with light petroleum–ethyl acetate (8:1) gave the mixture of alcohols as a colourless oil (0.07 g, 78%) (Found: MH^+ 420.265. $C_{26}H_{34}N_3O_2$ requires MH^+ 420.265). For the major diastereoisomer **27c**, δ_H (250 MHz, $CDCl_3$) 8.28 [1H, d, *J* 7.9, 5-H(Q)], 6.9–7.7 [8H, m, H-6, H-7, H-8(Q), 5 × CH(Ph)], 4.49 [1H, s, $Pr^iCH(OH)$], 3.2 (2H, m, Pr^iCH and Bu^tCHCH_3), 2.9 (2H, m, azir. H-2 and H-3), 1.8 (1H, m, C*H*Pr^i), 1.3 (3H, d, *J* 7.2, Bu^tCHCH_3), 0.95 (6H, 2 × d, *J* 6.9, CH_3CHCH_3) and 0.68 (9H, s, Bu^t). [From comparison of the signal at δ 3.2, this aziridine alcohol diastereoisomer was identical to the minor diastereoisomer (dr 56:27:*17*) δ 3.22 in the crude reaction mixture from aziridination of **10** with Q^2NHOAc **22** (see above).] For the minor aziridine alcohol in the mixture above, δ_H (observable peaks) 3.6 (2H, m, Pr^i-C*HOH*), 2.72 (1H, s, br, azir. H-3) and 1.03 (3H, d, *J* 7.2, Bu^tCHCH_3); *m*/*z* (for mixture) 420 (MH^+, 100%).

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Paper 9/02577D