Desilylative elimination of the quinazolinone ring from 1-(4-oxoquinazolin-3-yl)-2-silylaziridines; preparation of an N–H aziridine in high enantiomeric excess by *in situ* nucleophilic addition to the derived azirine

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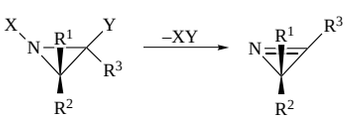
Aziridination of vinylsilanes PhCH=CHSiR$_3$ (R = Me, Et, Ph) with enantiopure 3-acetoxyaminoquinazolinone 11 gives the corresponding aziridines 12 [diastereoisomer ratio (dr) 10:1], 18 (dr 13:1) and 20 (dr 2:1). Desilylative elimination of the quinazolinone from these aziridines by caesium fluoride in the presence of cyanide gives aziridine 14 by cyanide addition to the 3-unsubstituted azirine 13, produced *in situ*. Acylation of aziridine 14 with (*S*)-acetoxypropionyl chloride gives *N*-acylaziridine 16; the good correlation between the diastereoisomer ratios of aziridines 12, 18 and 20 and those of the *N*-acylaziridine 16 produced in each case suggests that intermediate azirine 13 is configurationally stable.

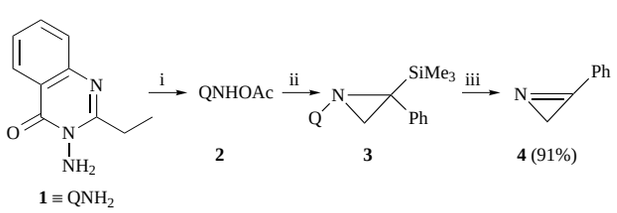
There are a small number of methods available for the synthesis of azirines by elimination of two adjacent substituents on an aziridine ring (Scheme 1).[1]



Scheme 1

The importance of these methods is that they provide access to enantiopure azirines from enantiopure aziridines: other routes to azirines do not lend themselves to the preparation of single enantiomers.

We have shown previously that one example of the conversion shown in Scheme 1 is that shown in Scheme 2.[2] Here, fluoride mediated elimination of $SiMe_3$ and the quinazolinone ring (Q) from aziridine **3** gives 3-phenylazirine **4** in good yield.

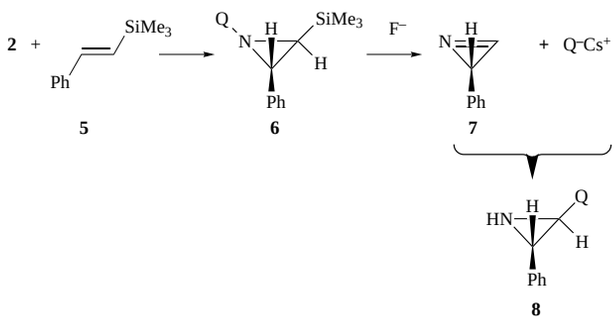


Scheme 2 *Reagents and conditions:* i, $Pb(OAc)_4$, CH_2Cl_2, −20 °C, ii, 1-phenyl-1-trimethylsilylethene, CsF, DMF

3-Acetoxyaminoquinazolinones, *e.g.* **2** (QNHOAc; prepared from 3-aminoquinazolinones **1**), are efficient aziridinating agents for a range of alkenes including vinylsilanes. Ring-opening of the derived aziridine ring, followed by N–N bond cleavage, provides a route to useful (Q-free) products.[3] However, the aziridine to azirine conversion **3** ⟶ **4** is the only way we have found so far to cleave the Q–N bond and retain the three-membered ring.

We have also shown previously that desilylative elimination of Q from the aziridine **6** gives aziridine **8** (Scheme 3).[4] This aziridine to azirine to aziridine transformation arises from re-addition of Q^- to the intermediate azirine **7** as a consequence of the greater reactivity of 3-unsubstituted azirines towards nucleophilic attack.

The present work[5] was undertaken with two aims: (i) to intercept the reactive 3-unsubstituted azirines *e.g.* **7**, produced *in situ* in Scheme 3, with nucleophiles other than Q^- and thus to prepare useful Q-free aziridines; (ii) to use this aziridine to azirine to aziridine conversion to prepare enantiopure Q-free aziridines.

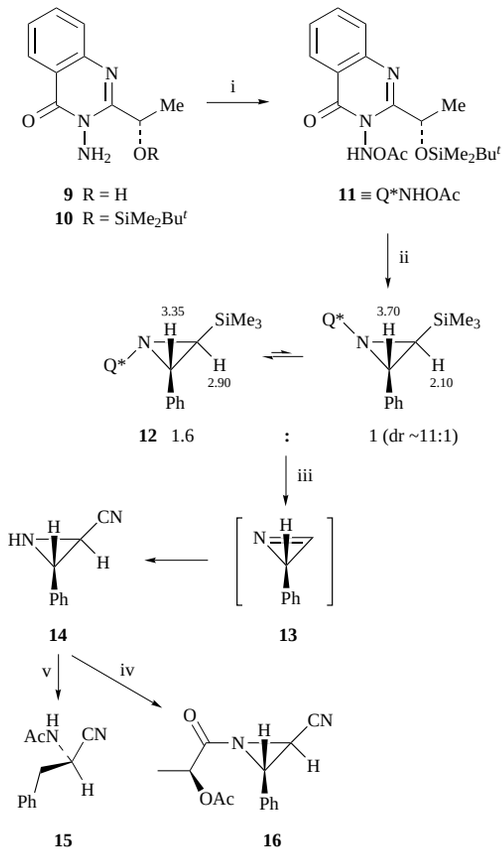


Scheme 3

Aziridination of β-trimethylsilylstyrene **5** was carried out with the previously prepared 3-acetoxyaminoquinazolinone **11** (Q*NHOAc)[6] (Scheme 4) in which the quinazolinone 2-substituent is derived from (*S*)-lactic acid. Q*NHOAc **11** is prepared *in situ* by *N*-acetoxylation of 3-aminoquinazolinone **10**: the yield for the preparation of silyl ether **10** from the corresponding alcohol **9** has been improved. The yield of aziridine **12** was significantly improved in the presence of hexamethyldisilazane (HMDS).

The ^{1}H NMR spectrum of aziridine **12** was complicated by the presence of invertomers at the aziridine nitrogen (ratio 1.6:1). Assignments of the relative configuration at this ring nitrogen in both invertomers of **12** (Scheme 4) were made from the effect on their equilibrium[7] ratio of the change from trimethylsilyl to triethylsilyl (see below): these assigments are also consistent with the expected deshielding effect of the quinazolinone (carbonyl) on the *cis*-substituted aziridine ring proton[7] (see appended chemical shifts of these protons in both invertomers of aziridine **12**).

Aziridination using 3-acetoxyaminoquinazolinones is invariably stereospecific with retention of the alkene configuration in the aziridine product.[8] In the ^{1}H NMR spectrum of aziridine **12** there were only two sets of signals and their assignment to diastereoisomers differing in configuration at the aziridine ring nitrogen (*N*-invertomers) rather than at both aziridine ring chiral centres was eventually confirmed by the transformations outlined below. In the ^{13}C NMR spectrum of aziridine **12**, however, three of the four aziridine ring carbons (2 invertomers) were accompanied by a small peak which suggested the pres-



Scheme 4 *Reagents and conditions:* i, $Pb(OAc)_4$, CH_2Cl_2, −20 °C, ii, **5**, HMDS, iii, CsF, DMF, KCN, iv, (*S*)-$CH_3CH(OAc)COCl$, NEt_3, v, H_2, Pd/C, Ac_2O

ence of the minor diastereoisomer (ratio major : minor ~ 11 : 1). This minor diasteroisomer, apparently also present as a mixture of *N*-invertomers, will, as indicated above, have the same relative configuration but opposite absolute configurations at the aziridine ring carbon centres compared with those of the major diastereoisomer.

Aziridine **14**[9] (Scheme 4) mp 58–60 °C $[\alpha]_D$ −153.1 (*c* 1.0, EtOH), was isolated in 76% yield by desilylative elimination of Q* from aziridine **12** with caesium fluoride in DMF in the presence of potassium cyanide (3 equiv.). The relative configuration at its ring carbons follows from the magnitude of the coupling constant between the protons at these positions (2.5 Hz) which is characteristic for *trans* aziridine ring protons and hence a *trans* Ph/CN relationship.[10] Addition of cyanide to the 3-unsubstituted azirine **13**, therefore, is highly stereoselectively *anti* to the 2-phenyl group.

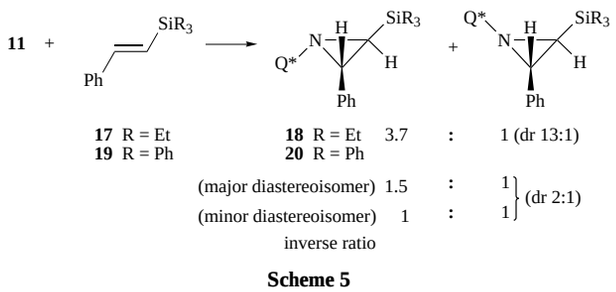
The absolute configuration at these aziridine ring positions was assigned as 2*R*,3*S* after hydrogenation and *in situ* acetylation to give 2-acetylamino-3-phenylpropionitrile **15**, $[\alpha]_D$ +45.1 (*c* 0.78, EtOH), a rotation of opposite sign to that reported ($[\alpha]_D$ −56.8[11]) for a sample prepared from (*S*)-phenylalanine. The enantiopurity of aziridine **14** (83% ee) was determined by reaction with enantiopure (*S*)-α-acetoxypropionyl chloride to give the two diastereoisomers of aziridine **16** (ratio 10 : 1 by comparison with a 1 : 1 mixture prepared by its reaction with racemic 2-acetoxypropionyl chloride).

Aziridination of β-triethylsilylstyrene **17** with Q*NHOAc **11** (Scheme 5) yielded results analogous to those above. In aziridine **18**, the *N*-invertomer ratio was now 3.7 : 1 and there is an excellent correlation between the chemical shifts of aziridine ring proton signals in both major and minor invertomers of aziridines **12** and **18** (Table 1).

With the reasonable assumption that an increase in the size of the trialkylsilyl group favours that invertomer having this group and the Q* group *trans*, the configuration at the aziridine

Table 1 Chemical shift (δ) correlation between major and minor *N*-invertomers of aziridines **12** and **18**

	δ_H (ppm)	
Signal	**12**	**18**
C*H*Ph major inv.	3.35	3.4
C*H*Si major inv.	2.90	2.90
C*H*Ph minor inv.	3.70	3.88
C*H*Si minor inv.	2.10	2.15



Scheme 5

ring nitrogen in major and minor invertomers of **12** and **18** can be assigned as illustrated in Schemes 4 and 5.

The presence of both diastereoisomers of aziridine **18** was indicated by the presence of additional small doublets for the aziridine ring protons in its ^{1}H NMR spectrum in C_6D_6 at δ 4.2, 3.58, 3.32 and 2.18 (2 *N*-invertomers) besides the larger doublets at δ 4.30, 3.45, 3.10 and 2.25 (ratio major : minor diastereoisomers ~ 13 : 1).

Desilylative elimination of Q* from aziridine **18** in the presence of potassium cyanide, following the procedure in Scheme 4, and reaction of the aziridine **14** obtained with (*S*)-2-acetoxypropionyl chloride gave *N*-acylaziridine **16** as a 13 : 1 ratio of diastereoisomers (ee 86%).

Aziridination of β-triphenylsilylstyrene **19** with Q*NHOAc **11** in the presence of HMDS gave aziridine **20** (41%) as a 2 : 1 ratio of diastereoisomers. A crystalline sample of the minor diastereoisomer was obtained by trituration with light petroleum and, from its ^{1}H NMR spectrum, is present in solution as a 1 : 1 ratio of *N*-invertomers. Examination of the ^{1}H NMR spectrum of the crude reaction mixture revealed that the major diastereoisomer consisted of two invertomers (ratio 1.5 : 1).† Unlike aziridine **12** the aziridine ring proton signals in the NMR spectra of both diastereoisomers of **20** are clearly anisochronous.

A sample of aziridine **20** containing a 5 : 1 ratio of major : minor diastereoisomers, recovered after removal of the bulk of the crystalline minor diastereoisomer, was also subjected to desilylative elimination of Q* in the presence of potassium cyanide as in Scheme 4 above. Derivatisation of the resulting aziridine **14** in this case gave a 5 : 1 ratio of diastereoisomers of *N*-acylaziridine **16**.

The correlation in each case between the diastereoisomer ratios in aziridines **12**, **18** and **20** and those in the derived aziridine **16** suggests that azirine **13** is configurationally stable under the reaction conditions.

Confirmation of the absolute configuration of the major diastereiosomers of aziridines **12**, **18** and **20** was provided by an X-ray crystal structure of the minor diastereoisomer of the β-triphenylsilylstryrene-derived aziridine **20**.[13]

The preferred sense of diastereoselectivity in formation of aziridines **12**, **18** and **20** is the same in each case since they all give the *same* major diastereoisomer of *N*-acylaziridine **16** when each is subjected to the desilylative-elimination/acylation procedure in Scheme 4. With the known relative configuration

† Assignment of invertomer identities in this major diastereoisomer (Scheme 5) is made on the basis of relative chemical shift positions of the aziridine ring protons (*cf.* for **12**).

of the chiral centres in the minor diastereoisomer of aziridine **20** (X-ray) and the known absolute configuration of the chiral centre in the quinazolinone 2-position [derived from (*S*)-lactic acid], the stereostructures of the major diastereoisomers of **12**, **18** and **20** can be deduced and are as illustrated in Schemes 4 and 5.

Further work to establish the generality of the N–(Q*) aziridine to azirine to aziridine interconversion is in progress together with an examination of the origin of the unexpectedly high diastereoselectivity in the aziridination of vinylsilanes **5** and **17** with Q*NHOAc **11**.[13]

Experimental

Unless otherwise indicated, ^{1}H NMR spectra were run at 25 °C and 250 MHz in $CDCl_3$ solution with $SiMe_4$ as internal standard and ^{13}C spectra at 75 MHz in the same solvent. IR Spectra were run as solutions in dichloromethane. Optical rotations were measured using a Perkin-Elmer 341 Polarimeter and are recorded in units of 10^{-1} deg cm^2 g^{-1}. For other instrumentation and general experimental details see ref. 14.

Improved procedure for preparation of 3-amino-2-[(1*S*)-1-*tert*-butyldimethylsilyloxyethyl]-3,4-dihydroquinazolin-4-one 10

3-Aminoquinazolinone **9**[3] (5.67 g, 27.7 mmol), *tert*-butyldimethylsilyl chloride (5.00 g, 33.2 mmol) and imidazole (4.70 g, 69.1 mmol) were dissolved in DMF (11 cm^3) and stirred at room temperature for 2 days. Water (30 cm^3) was then added and the aqueous layer was extracted with light petroleum (4 × 50 cm^3). The combined organic extracts were washed with brine (2 × 50 cm^3), dried and reduced to ~20 cm^3 by evaporation under reduced pressure. Seeding with amino alcohol **9** and scratching the side of the flask removed a small amount of this unchanged starting material, and evaporation of the separated light petroleum gave 3-aminoquinazolinone **10** as a colourless oil (7.07 g, 80%) identical with that obtained previously.[6]

Aziridination of β-trimethylsilylstyrene 5 with Q*NHOAc 11

Dichloromethane (5 cm^3) was cooled to −15 °C, lead tetraacetate (LTA) (0.76 g, 1.2 mmol) was added and the solution stirred until the LTA dissolved. A solution of 3-aminoquinazolinone **10** (0.50 g, 1.6 mmol) in dichloromethane (2 cm^3) was then added with stirring over 5 min and the mixture stirred at −15 °C for a further 5 min. After cooling to −30 °C, the mixture was filtered rapidly through a small column containing Celite using a low positive pressure of nitrogen into a stirred solution of β-trimethylsilylstyrene **5**[15] (0.33 g, 1.9 mmol) and HMDS (1.0 cm^3, 4.7 mmol) in dichloromethane (1 cm^3) held at −30 °C. The reaction mixture was allowed to warm to room temperature over 1 h with stirring before addition of dichloromethane (10 cm^3). After washing the mixture with saturated aqueous sodium hydrogen carbonate, the organic layer was separated, dried and the solvent removed under reduced pressure to give an oil (0.77 g).

Chromatography over silica, previously washed with light petroleum–ethyl acetate (4:1) containing 2% triethylamine, and elution with light petroleum–ethyl acetate (4:1) gave (2S,3S)-1-{2-[(1S)-1-tert-*butyldimethylsilyloxyethyl*]-4-*oxo*-3,4-*dihydroquinazolin*-3-*yl*}-2-*phenyl*-3-*trimethylsilylaziridine* **12** (R_F 0.30) (0.27 g, 35%) (Found: M$^+$, 493.2580. $C_{27}H_{39}N_3O_2Si_2$ requires *M*, 493.2580); ν_{max}/cm^{-1} 1920m, 1680s and 1600m; δ_H(1.6:1 ratio of *N*-invertomers); major invertomer (observable signals) 8.15 [d, *J* 7.5, 5-H(Q)], 5.03 (q, *J* 6.0, C*H*OSi), 3.35 (d, *J* 7.5, C*H*Ph) and 2.9 (d, *J* 7.5, C*H*SiMe$_3$); minor invertomer (observable signals) 8.05 [d, *J* 7.9, 5-H(Q)], 5.25 (q, *J* 6.0, C*H*OSi), 3.70 (d, *J* 7.2, C*H*Ph) and 2.10 (d, *J* 7.2, C*H*Si); signals for both invertomers at 6.9–7.6 (m, 8 H), 1.4 (m), 0.7–1.85 (m) and −0.1 to −0.2 (m), (total 27 H); δ_C major diastereoisomer (2 *N*-invertomers) 163.4 (s), 163.3 (s), 160.3 (s), 159.3 (s), 148.8 (s), 148.6 (s), 140.7 (s), 136.3 (d), 136.0 (d), 134.8 (d), 132.0 (d), 131.6 (d), 131.4 (d), 131.1 (d), 130.7 (d), 130.3 (d), 130.0 (d), 129.5 (d), 129.1 (d), 128.9 (d), 128.8 (d), 124.3 (s), 69.8 (d), 68.6 (d), 55.9 (d), 52.3 (d), 51.3 (d), 46.2 (d), 33.1 (d), 28.6 (q), 24.3 (q), 21.4 (s), 20.8 (s), 1.5 (q), 0.4 (q) and 0.0 (q); minor diastereoisomer (observable signals) 56.1 (d), 52.3 (d) and 50.8 (d).

Aziridination of β-triethylsilylstyrene 17 with Q*NHOAc 11

A solution of Q*NHOAc **11** in dichloromethane (10 cm^3) was prepared from 3-aminoquinazolinone **10** (1.00 g, 3.1 mmol) and LTA (1.53 g, 3.1 mmol) as described above and reacted with a solution of β-triethylsilylstyrene **17**[16] (0.82 g, 3.8 mmol) containing HMDS (0.76 g, 4.7 mmol) in dichloromethane (2 cm^3). After the work-up described above, chromatography over silica and elution with light petroleum–ethyl acetate–triethylamine (89:9:2) gave (2S,3S)-1-{2-[(1S)-1-tert-*butyldimethylsilyloxyethyl*]-4-*oxo*-3,4-*dihydroquinazolin*-3-*yl*}-2-*phenyl*-3-*triethylsilylaziridine* **18** (R_F 0.49) as an oil (0.88 g, 40%) (Found: C, 67.65; H, 8.6; N, 7.75. $C_{30}H_{45}N_3O_2Si_2$ requires C, 67.25; H, 8.45; N, 7.85%); ν_{max}/cm^{-1} 1680s and 1595m; δ_H(2:1 ratio of *N*-invertomers) major invertomer (observable signals) 8.20 [d, *J* 7.5, 5-H(Q)], 6.80–7.60 (m, 8 H), 5.07 (q, *J* 7, C*H*CH$_3$), 3.40 (d, *J* 7.9, C*H*Ph), 2.90 (d, *J* 7.9, C*H*Si) and 1.40 (d, *J* 7, CHC*H*$_3$); minor invertomer (observable signals) 5.30 (q, *J* 6, C*H*CH$_3$), 3.88 (d, *J* 7.5, C*H*Ph) and 2.15 (d, *J* 7.5, C*H*Si); signals from both invertomers at 1.00 (m), 0.85 (m) and 0.00 (m) (total 30 H); δ_C(161.3 and 161.0) (s), (158.3 and 157.3) (s), 146.3 (s), 138.5 (s), 132.7 (d), 134.0 (d), 129.2 (d), 128.9 (d), 128.4 (d), 128.0 (d), 127.1 (d), 126.7 (d), 126.4 (d), 122.0 (s), (67.5 and 66.2) (d), (53.0 and 49.7) (d), 46.4 (d), 42.7 (d), 26.2 (q), 21.9 (d), 20.9 (d), (18.9 and 18.5) (s), 7.9 (q) and 2.7 (t); δ_H(C_6D_6) major diastereoisomer (3.7:1 ratio of *N*-invertomers) major invertomer (assignable signals) 8.3 [d, *J* 7.5, 5-H(Q)], 6.70–7.60 (m, 8 H), 5.25 (q, *J* 6, C*H*CH$_3$), 3.45 (d, *J* 7.9, C*H*Ph), 3.10 (d, *J* 7.9, C*H*Si) and 1.40 (d, *J* 6, CHC*H*$_3$); minor invertomer (assignable signals) 5.60 (q, *J* 6.1, C*H*CH$_3$), 4.30 (d, *J* 7, C*H*Ph) and 2.25 (d, *J* 7, C*H*Si); minor diastereoisomer (~1:1 ratio of invertomers) (assignable signals) 4.28 (d, *J* 7.5, C*H*Ph), 3.58 (d, *J* 7.5, C*H*Ph), 3.32 (d, *J* 7.5, C*H*Si) and 2.18 (d, *J* 7.5, C*H*Si); the ^{1}H NMR of the crude reaction mixture in C_6D_6 showed the ratio of major:minor diastereoisomers as ~13:1 from comparison of signal intensity for the aziridine ring protons above; *m*/*z* 535 (M$^+$, 3.9%), 417 (42.6), 376 (100) and 247 (43.1).

Aziridination of β-triphenylsilylstyrene 19 with Q*NHOAc 11

A solution of Q*NHOAc **11** in dichloromethane (25 cm^3) was prepared from 3-aminoquinazolinone **10** (2.00 g, 6.3 mmol) and LTA (3.05 g, 6.9 mmol) as described earlier (but without filtration through Celite) and β-triphenylsilylstyrene **19**[16,17] (2.50 g, 6.9 mmol) and HMDS (2.0 cm^3, 9.4 mmol) were added at −30 °C. After reaction and work-up as described previously, the crude product was chromatographed over silica eluting with light petroleum–ethyl acetate (4:1) to give aziridine **20** (1.74 g, 41%) as a 2:1 ratio of diastereoisomers from comparison of the aziridine ring proton signals in the ^{1}H NMR spectrum (see below). Trituration with light petroleum gave the minor diastereoisomer (2R,3R)-1-{2-[(1S)-1-tert-*butyldimethylsilyloxyethyl*]-4-*oxo*-3,4-*dihydroquinazolin*-3-*yl*}-2-*phenyl*-3-*triphenylsilylaziridine* **20** as a colourless solid, mp 151–152 °C (from ethanol) (Found: M$^+$ 679.3050. $C_{42}H_{45}N_3O_2Si_2$ requires *M*, 679.3050); ν_{max}/cm^{-1} 1680s and 1600s; δ_H major diastereoisomer (1.5:1 ratio of *N*-invertomers) major invertomer 8.15 [d, *J* 7.5, 5-H(Q)], 7.80 (m, 4 H), 7.40 (m, 15 H), 7.00 (m, 3 H), 5.3 (q, *J* 6.2, C*H*CH$_3$), 4.20 (d, *J* ~7.5, C*H*Ph), 2.90 (d, *J* 7.5, C*H*SiPh$_3$), 1.05 (d, *J* 6.2, CHC*H*$_3$), 0.70 [s, SiC(C*H*$_3$)$_3$] and −0.05 [s, Si(C*H*$_3$)$_2$]; minor *N*-invertomer (observable peaks) 5.05 (d, *J* 6.0, C*H*CH$_3$), 4.00 (d, *J* 7.3, C*H*Ph) and 3.40 (d, *J* 7.3, C*H*SiPh$_3$); minor diastereoisomer (1:1 ratio of *N*-invertomers), signals for both invertomers at 8.45 [d, *J* 7.5, 5-H(Q)], 7.95 (m, 4

H), 7.65 (m, 14 H) and 7.35 (m, 9 H), separate signals for invertomers at 5.50 (q, *J* 6.3, C*H*CH_3), 5.18 (q, *J* 6.3, C*H*CH_3), 4.95 (br d, *J* 7, C*H*Ph), 4.15 (d, *J* ~7, C*H*Ph), 3.55 (d, *J* 7, C*H*$SiPh_3$), 3.38 (d, *J* 7, C*H*$SiPh_3$), 1.78 (d, *J* 6.3, CHCH_3), 1.65 (d, *J* 6.3, CHCH_3), 1.08 [s, SiC(CH_3)$_3$], 0.88 [s, SiC(CH_3)$_3$] and 0.00, −0.09, −0.03 and −0.10 [s, Si(CH_3)$_2$].

Preparation of (2*R*,3*S*)-2-cyano-3-phenylaziridine 14 from aziridine 12

A flask containing dry caesium fluoride (2.37 g, 15.6 mmol) and potassium cyanide (0.30 g, 4.7 mmol) was flame-dried under vacuum then a solution of aziridine **12** (0.34 g, 1.56 mmol) in dry DMF (15 cm^3) was added and the mixture stirred overnight under nitrogen. Water (10 cm^3) was then added and the solution extracted with ethyl acetate (10 cm^3). The organic extract was washed with brine (3 × 10 cm^3), dried, the solvent evaporated under reduced pressure and the residue chromatographed over silica, eluting with light petroleum–dichloromethane–ethyl acetate (4:4:2) to give the *aziridine* **14** (0.10 g, 76%) (R_F 0.27, stained yellow with vanillin); $[\alpha]_D$ −153.1 (*c* 1.0, EtOH); mp 58–60 °C (EtOH); ν_{max}/cm^{-1} 3280s and 2220s; δ_H(−40 °C) (4:1 mixture of *N*-invertomers) major invertomer 7.43–7.29 [m, 5 × C-H(Ph)], 3.75 (dd, *J* 9.6 and 2.5, C*H*Ph), 2.43 (dd, *J* 7.7 and 2.6, C*H*CN) and 1.95 (dd, *J* 9.6 and 7.7, N*H*); minor invertomer (observable signals) 3.50 (dd, *J* 9.0 and 2.6, C*H*Ph), 2.88 (dd, *J* 9.6 and 2.6, C*H*CN) and 1.95 (dd, *J* 9.6 and 9, N*H*); *m*/*z* 144 (M^+, 19.3%), 143 (100), 116 (27.5), 90 (21), 89 (37) and 64 (23).

Reaction of aziridine 14 with (*S*)-2-acetoxypropionyl chloride

(*S*)-2-Acetoxypropionic acid[3] (0.60 g, 4.5 mmol) and thionyl chloride (3.26 g, 2.0 cm^3, 27.4 mmol) were stirred at room temperature for 2 h. Excess thionyl chloride was removed under reduced pressure and the residual acid chloride then added to a solution of aziridine **14** (0.10 g, 0.69 mmol) and triethylamine (0.46 g, 4.5 mmol) in diethyl ether (1 cm^3) maintained at 0 °C. The resulting solution was allowed to warm to room temperature, stirred overnight, then diluted with diethyl ether (10 cm^3), washed with saturated aqueous sodium carbonate (2 × 10 cm^3), dried and the solvent evaporated under reduced pressure. Chromatography of the crude product over silica and elution with light petroleum–ethyl acetate (4:1) gave (2R,3S)-1-[(2S)-2-*acetoxypropionyl*]-2-*cyano*-3-*phenylaziridine* **16** as an oil (0.06 g, 33%) (R_F 0.25) (Found: M^+, 258.100. $C_{14}H_{14}N_2O_3$ requires *M*, 258.100); δ_H major diastereoisomer 7.20–7.35 (m, 10 H), 5.00 (q, *J* 6.9, C*H*CH_3), 4.20 (d, *J* 2.5, C*H*CN), 2.95 (d, *J* 2.5, C*H*Ph), 1.80 (s, COCH_3) and 1.45 (d, *J* 6.9, CHCH_3); minor diastereoisomer (observable signals) 5.30 (q, *J* 6.9, C*H*CH_3), 3.90 (d, *J* 2.5, C*H*CN), 3.05 (d, *J* 2.5, C*H*Ph) and 1.70 (s, COCH_3). The ratio of major:minor diastereoisomers was 10:1 from comparison *inter alia* of signals at δ 4.20 and 3.90 above in the crude reaction product; δ_C 179.0 (s), 170.9 (s), 133.2 (s), 130.1 (d), 129.6 (d), 126.5 (d), 114.6 (s), 71.0 (d), 46.1 (d), 29.6 (d), 20.7 (q) and 18.0 (q); *m*/*z* 258 (M^+, 16.4%), 198 (10), 145 (13), 144 (90) and 117 (22).

The same acylation procedure of aziridine **14** with (±)-(*S*)-2-acetoxypropionyl chloride gave *N*-acylaziridine **16** as a 1:1 ratio of diastereoisomers from comparison of the signals in the ^{1}H NMR spectrum of the product isolated as described above.

Hydrogenolysis–acetylation of aziridine 14

Aziridine **14** (0.12 g, 0.83 mmol) and acetic anhydride (0.11 g, 1.04 mmol) were dissolved in ethyl acetate (10 cm^3), palladium (10% on carbon) (0.20 g) was added and the solution hydrogenated at atmosphere pressure overnight. After separation of the palladium on carbon, the solution was evaporated under reduced pressure and the crude product chromatographed over silica eluting with light petroleum–ethyl acetate (7:3) to give (2R)-2-*acetamido*-3-*phenylpropionitrile* **15** (0.05 g, 32%) (R_F 0.48); $[\alpha]_D$ +45.1 (*c* 0.78, EtOH) {lit.,[11] $[\alpha]_D$ −56.8; −10.2 (*c* 2.5, EtOH)[12]}; δ_H 7.30 [m, 5 × CH(Ph)], 6.60 (d, *J* 8, N*H*CH), 5.10 (app., dt, *J* 8 and 7, CHCN), 3.05 (m, CH_2Ph) and 1.95 (s, COCH_3); δ_C 170.2 (s), 134.5 (s), 129.8 (d), 129.4 (d), 128.3 (d), 118.7 (s), 42.1 (t), 39.1 (d) and 23.1 (q); *m*/*z* 188 (M^+, 42.4%), 129 (95.8) and 91 (100). An authentic racemic sample was prepared[18] by acetylation of 2-amino-3-phenylpropionitrile[19] with acetic anhydride and pyridine and shown to be identical by ^{1}H NMR comparison.

Conversion of aziridine 18 into aziridine 14

The same procedure described above for conversion of aziridine **12** and **14** was applied to aziridine **18** (0.88 g, 1.6 mmol) using caesium fluoride (2.25 g, 14.8 mmol) and potassium cyanide (0.32 g, 4.9 mmol) in DMF (15 cm^3). After the same work-up, aziridine **14** was obtained (0.12 g, 50%). Reaction with (*S*)-2-acetoxypropionyl chloride–triethylamine as described above gave *N*-acylaziridine **16** as a 13:1 ratio of diastereoisomers from comparison of signals *inter alia* at δ 4.20 and 3.90 in the NMR spectrum of the crude reaction product.

Conversion of aziridine 20 into aziridine 14

A 5:1 mixture of diastereoisomers **20** (0.38 g, 0.56 mmol), obtained after removal of the bulk of the minor diastereoisomer by trituration with light petroleum (see above), was converted into aziridine **14** (44 mg, 55%) using caesium fluoride (1.77 g, 11.7 mmol) and potassium cyanide (0.25 g) in DMF (8 cm^3) as described above. Reaction with (*S*)-2-acetoxypropionyl chloride–triethylamine as above gave *N*-acylaziridine **16** as a 5:1 ratio of diastereoisomers from comparison of signals *inter alia* at δ 4.20 and 3.90 in the NMR spectrum of the crude reaction product.

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