Diastereoselective aziridination of alkenes using 3-acetoxyamino-2-(1-hydroxyalkyl)quinazolin-4(3*H*)-ones in the presence of titanium(IV) *tert*-butoxide

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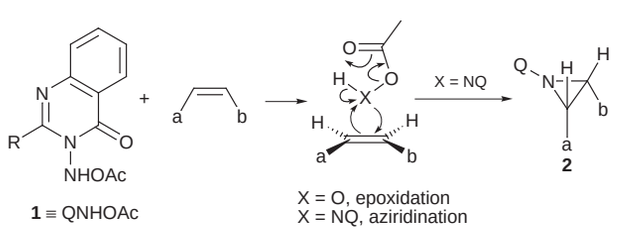
3-Amino-2-[(*S*)-1-hydroxy-2,2-dimethylpropyl]quinazolin-4(3*H*)-one 9 (Q^2NH) was prepared in four steps from (*S*)-*tert*-leucine in 43% yield without the need for chromatography. The corresponding 3-acetoxyaminoquinazolinone 10 (Q^2NHOAc), prepared in dichloromethane solution by reaction of 9 with lead tetraacetate, reacts with alkenes in the presence of titanium(IV) *tert*-butoxide to give the corresponding aziridines diastereoselectively. With styrene and butadiene the corresponding aziridines 12a (65%) and 15a (85%) are obtained completely diastereoselectively. Indene gave the expected *endo*-*N*-invertomer of aziridine 16a as the kinetically-formed product (86%) also completely diastereoselectively: equilibration to give a 8 : 1 ratio of *exo* : *endo* *N*-invertomers occurs above 0 °C. From an X-ray structure determination of aziridine 12a, the sense of diastereoselectivity in its formation is in agreement with the transition state model 14. Aziridinations of methyl acrylate and of *tert*-butyl acrylate give respectively 23a (65%) and 24a (53%), highly diastereoselectively (dr ≥ 20:1) and with the same sense of diastereoselectivity as identified by an X-ray crystal structure determination on 24a and chemical correlation of esters 23a and 24a *via* the acid 25.

Aziridinations of α-methylstyrene and methyl methacrylate are less completely diastereoselective; isoprene reacts completely diastereoselectively at its unsubstituted double bond but with little diastereoselectivity at its methyl-substituted double bond and the regioselectivity of aziridination on the two double bonds is 1.4:1 respectively by comparison to 1 : 4.7 in the absence of titanium(IV) *tert*-butoxide.

The use made of aziridines as synthetic relay intermediates still lags considerably behind that made of epoxides. One major reason is the comparative dearth of methods for direct conversion of alkenes into aziridines and, in particular, methods which accomplish this stereoselectively.[1] Thus, whereas *tert*-butyl hydroperoxide, in the presence of a metal catalyst (Mo, V or Ti) converts alkenols into epoxides,[2] substituted hydroxylamines under these, or any other conditions, do not effect the analogous conversion to aziridines. Likewise, nitrogen equivalents of peroxy acids are not known to be aziridinating agents (see however below).

Evans[3] and, independently, Jacobsen[4] and Katsuki[5] have prepared *N*-tosylaziridines highly enantioselectively from alkenes and *N*-tosylimino(phenyl)-λ³-iodane PhI=NTs by using copper catalysts complexed with enantiopure ligands. However, this method is not invariably stereospecific and is normally applied to *trans*- or cyclic *cis*-alkenes.

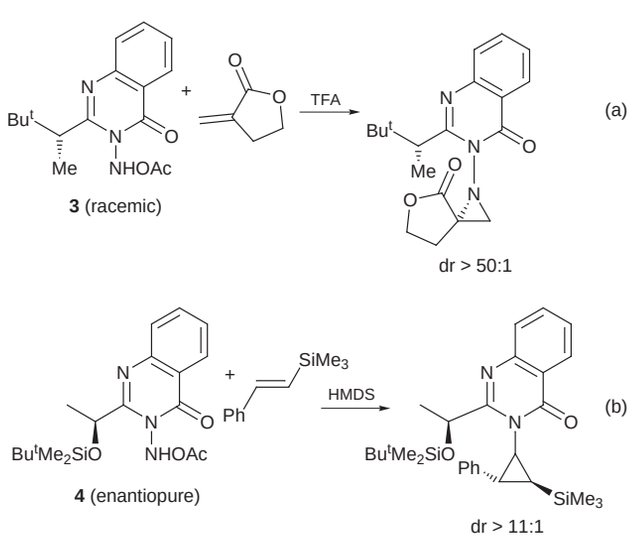
3-Acetoxyaminoquinazolinones **1** are, exceptionally, nitrogen equivalents of peroxyacetic acid and like the latter they react stereospecifically with alkenes with retention of alkene configuration in the three-membered ring product **2** (Scheme 1).[6]



Scheme 1

Unlike peroxyacids however, QNHOAc **1** reacts, often in good yields, with electron-deficient alkenes, *e.g.* methyl acrylate, under neutral conditions.

The presence of the Q ring in QNHOAc **1** has a retarding effect on the rate of *N*-inversion in the aziridine products **2** in Scheme 1 which has allowed us to probe into the mechanism and transition state geometry for the reaction (see below).[6] A further advantage in the presence of the Q ring is that a chiral centre can be incorporated at the 2-position (**1**, R = R*) and used to bring about reagent-controlled diastereoselectivity in aziridinations of prochiral alkenes.[7] We have shown that high or complete diastereoselectivity can be obtained using the chiral groups in the 3-acetoxyaminoquinazolinones **3**[8]† and **4**[9] as in Scheme 2.

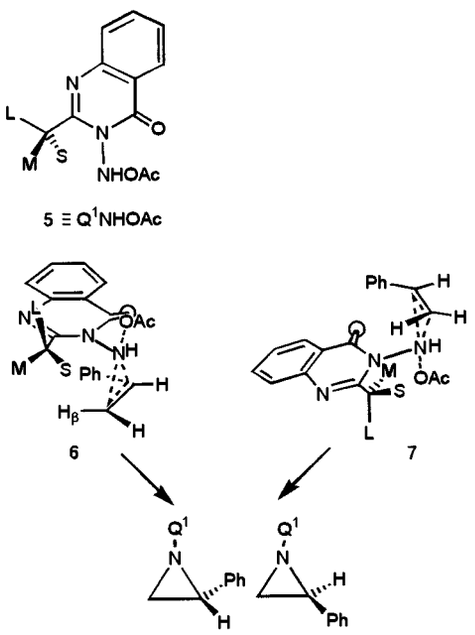


Scheme 2

† At the time the aziridinating species was thought to be the nitrene (refs. 7 and 8).

In reagent-controlled diastereoselective additions to alkenes as in Scheme 2 where asymmetric induction arises from a chiral centre present in the reagent, there must be defined sites for three different substituents on this chiral centre in attack on one face of the prochiral alkene. In terms of our previously derived transition state model[10,11] for aziridination of *e.g.* styrene with Q^1NHOAc **5** (one enantiomer), diastereoselectivity is only obtained if transition state **6** is favoured over **7** or *vice versa* *i.e.* where there are defined sites for M and S if it is assumed that approach of the alkene is opposite to the largest group L.

Although the preferred sites for M and S will clearly be affected by their proximity to the substituents in the alkene (and in particular H_β), the relative energies of **6** and **7** (Scheme 3)



Scheme 3

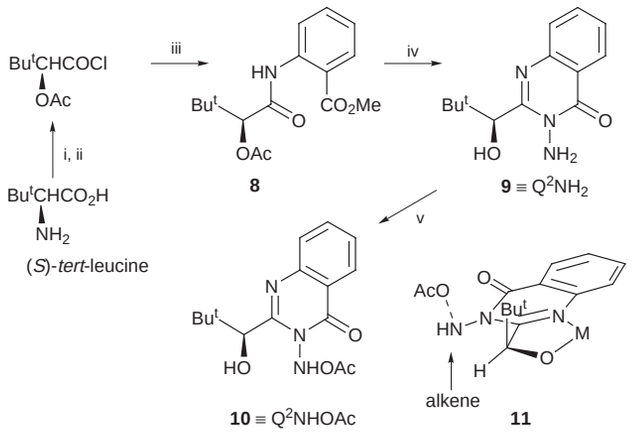
will also depend on conformational preferences arising from rotation around the (LMS)C-quinazolinone bond. Thus the high diastereoselectivity of reaction **6** is believed to arise from a conformational preference in **4** (independent of the presence of the alkene), in which the Bu^tMe_2SiO–C bond is close to the plane of the quinazolinone ring and the O–Si bond is orthogonal to it.[12]

A well-known device for limiting the freedom to rotate around a bond linking a chiral centre to a C=N or C=O double bond is to use a metal atom to chelate one of the substituents on the chiral centre to the nitrogen or oxygen of this double bond. We therefore synthesised 3-acetoxyaminoquinazolinone **10** (Q^2NHOAc) to examine the diastereoselectivity of its reactions with alkenes in the presence of chelating metals.[13]

Our expectation was that chelation as in **11** would direct attack of the alkene from the face of the quinazolinone *anti* to the *tert*-butyl group. Synthesis of Q^2NH_2 **9**, the precursor of Q^2NHOAc **10**, was accomplished in 43% overall yield from commercially available (*S*)-*tert*-leucine by the route shown in Scheme 4 without the need for chromatography at any stage.

In the NMR spectrum of 3-acetoxyaminoquinazolinone **3** at −20 °C, signals from two diastereoisomers are observable in a 4:1 ratio.[6] The additional chiral element is the pyramidal exocyclic nitrogen whose rate of inversion is slow on the NMR timescale.[14] In the NMR spectrum of Q^2NHOAc **10** at −20 °C, the corresponding two diastereoisomers were present in a 14:1 ratio from comparison of the two N*H*OAc singlets at δ 10.85 and 10.73 respectively.

Reaction of Q^2NHOAc **10** with styrene (1.2 equiv.) gave a 2:3 ratio of aziridine diastereoisomers **12a** and **12b** in excellent yield (Scheme 5) easily distinguishable by NMR spectroscopy. When this aziridination was repeated in the presence of titanium(IV) isopropoxide (2 mol equiv.) only aziridine diastereoisomer **12a** was formed (14%); the major product was 3-isopropoxyaminoquinazolinone **13** (59%). However, carrying out this aziridination in the presence of titanium(IV) *tert*-butoxide (2 mol equiv.) gave aziridine diastereoisomer **12a** in 65% isolated yield: signals from its diastereoisomer **12b** were absent from the NMR spectrum of the crude reaction product.



Scheme 4 *Reagents*: i, HNO_2, HOAc; ii, $SOCl_2$; iii, methyl anthranilate; iv, NH_2NH_2–EtOH; v, LTA–CH_2Cl_2

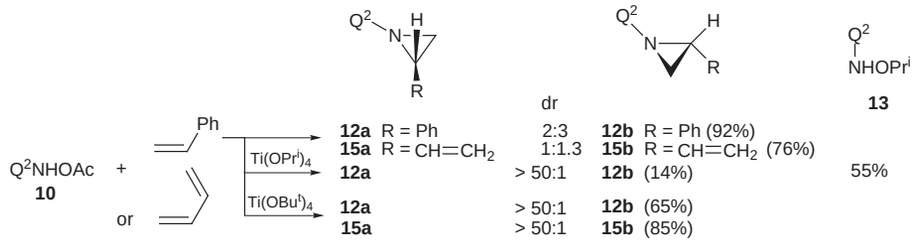
Identification of this single aziridine diastereoisomer as **12a** came from an X-ray crystal structure determination[13] and the sense of diastereoselectivity in formation of **12a** is in agreement with a titanium-chelated transition state **14** (R = Ph) (Scheme 6): *endo*-overlap[6] of the phenyl group of styrene with the quinazolinone ring as shown is believed to lead to the less stable invertomer of aziridine **12a′** which rapidly inverts at nitrogen to give **12a** (see below).

The same complete (>50:1) diastereoselectivity was obtained in aziridination of excess butadiene with Q^2NHOAc **10** but only in the presence of titanium(IV) *tert*-butoxide (Scheme 5). In this case the only material recovered was aziridine **15a** (85%) and all by-products are lost in the work up. Assignment of absolute configuration to aziridine **15a** is by analogy with that found for aziridine **12a** since a similar transition state **14** (R = CH=CH_2) is believed to be involved.‡§ Using indene (Scheme 6), there is some diastereoselectivity (3:1) in an aziridination carried out in the absence of titanium(IV) *tert*-butoxide but, in its presence, diastereoselectivity is again complete from inspection of the NMR spectrum of the crude reaction product. The additional strain in the bicyclic structure present in this aziridine **16** raises the barrier to aziridine *N*-inversion sufficiently to allow identification of the *endo*-*N*-invertomer **16a** as the sole kinetically-formed product. At room temperature, thermodynamic equilibration to give an 8:1 ratio of *exo*:*endo* **16a** occurs. Crystallisation of the product and dissolution in $CDCl_3$ at −20 °C gives an NMR spectrum in which only signals from the pure *exo*-invertomer **16a** are present (a second order asymmetric transformation). Conversion to the equilibrium 8:1 ratio of *exo*:*endo* **16a** took place over 40 min at room temperature. This increase in the aziridine *N*-inversion barrier is important because it has allowed us to carry out ring-opening reactions on individual *endo*- and *exo*-*N*-invertomers of **16**.[15]

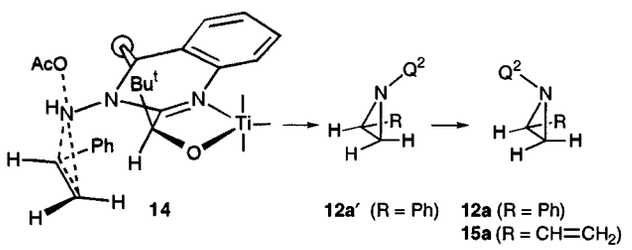
Whilst the diastereoselectivity of aziridination of styrene, butadiene and indene in the presence of titanium(IV) *tert*-

‡ In our preliminary communication (ref. 13) we assigned minor signals in the NMR spectrum of the crude reaction product to the minor *N*-invertomer of **15a** but it appears that these signals were from an impurity since these were not present in the pure diastereoisomer **15a**.

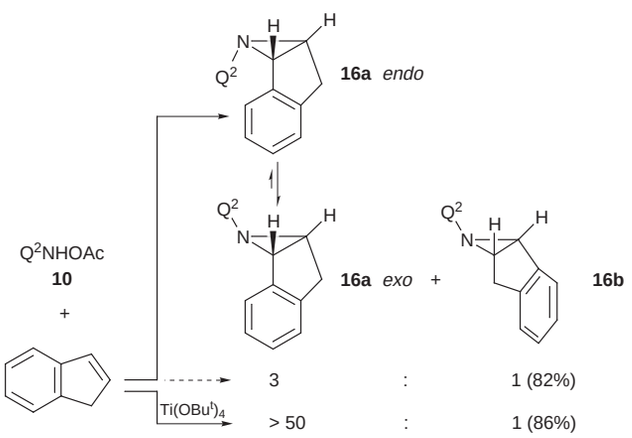
§ X-Ray structure determinations on ring-opened products of aziridines **15a** (unpublished) and **16a**[18] support the stereostructures assigned to them.



Scheme 5



Scheme 6



Scheme 7

butoxide is complete, aziridination of α-methylstyrene was not completely diastereoselective (Scheme 8).

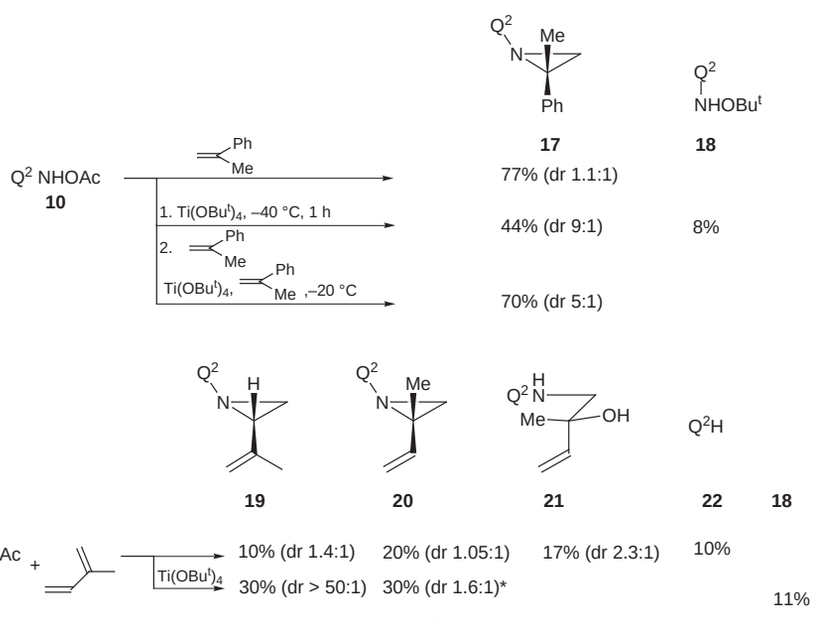
A necessary modification of the work-up procedure for isolation of the product in this case was to pour the reaction mixture into vigorously stirred aqueous sodium carbonate (instead of adding aqueous sodium carbonate to the reaction mixture after aziridination was complete as was done previously). A 5:1 ratio of aziridine diastereoisomers **17** was obtained in 70% yield. We found that this diastereoselectivity could be raised to 9:1 when the titanium(IV) *tert*-butoxide and Q²NHOAc **10** were stirred together for 1 h at −20 °C before addition of the α-methylstyrene. This increase in diastereoselectivity was accompanied by a drop in yield (44%) and by the compensating formation of the 3-*tert*-butoxyaminoquinazolinone (Q²NHOBu^t) **18** as a by-product. A lower yield of aziridine **17** under these conditions is anticipated since, in the absence of the alkene, some reaction between the titanium(IV) *tert*-butoxide and Q²NHOAc **10** to form Q²NHOBu^t **18** will be occurring.

Aziridination of isoprene with Q²NHOAc **10** in the absence of titanium(IV) *tert*-butoxide takes place on both double bonds with preferential addition to the methyl-substituted one (ratio 4.7:1 from NMR spectroscopy on the total reaction product) but with little diastereoselectivity in addition to either: ring-opened alcohol **21** and 3*H*-quinazolinone **22** were also obtained. In the presence of titanium(IV) *tert*-butoxide¶ the regioselectivity changes to 1:1.4 and preferential addition to the *unsubstituted* double bond occurs completely diastereoselectively. Aziridine **19**‖ crystallised directly from the crude reaction product in 30% yield on addition of ethanol. The methyl-substituted double bond, by contrast, gives a 1.6:1 ratio of diastereoisomers of aziridine **20** from examination of the crude reaction mixture by NMR spectroscopy.

Since these 3-acetoxyaminoquinazolinones also aziridinate

¶ Aziridination conditions used here were those giving a single diastereoisomer in the presence of butadiene.

‖ The preferred sense of diastereoselectivity is assumed to be as for styrene/butadiene.



Scheme 8

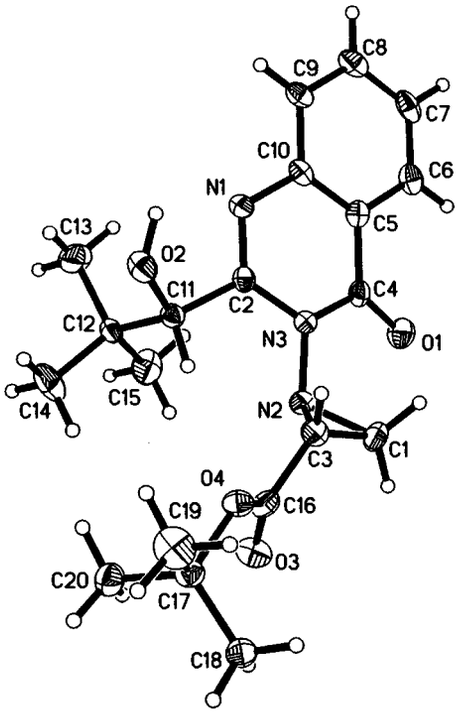
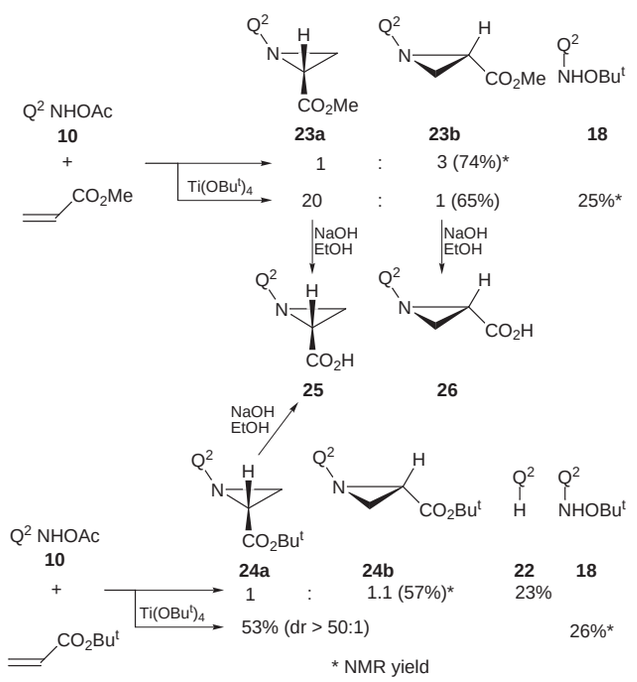


Fig. 1 The molecular structure of **24a** showing the atom numbering scheme and 30% displacement ellipsoids

electron-deficient alkenes (see earlier), we have examined the reaction diastereoselectivity of Q^2NHOAc **10** with acrylates. Using methyl acrylate in the presence of titanium(IV) *tert*-butoxide gave the corresponding aziridine as a ~20:1 ratio of diastereoisomers **23a**:**23b** (Scheme 9), together with



Scheme 9

Q^2NHOBu^t **18** (25%); the major diastereoisomer **23a** (65%) was separated by crystallisation. In the absence of titanium alkoxide the ratio of diastereoisomers **23a**:**23b** obtained was 1:3 *i.e.* the preferred sense of diastereoselectivity is reversed.

In the corresponding titanium(IV) *tert*-butoxide-mediated aziridination of *tert*-butyl acrylate (Scheme 9), the diastereoselectivity was higher (>50:1) but a larger amount of the by-product Q^2NHOBu^t **18** was obtained; in the absence of the

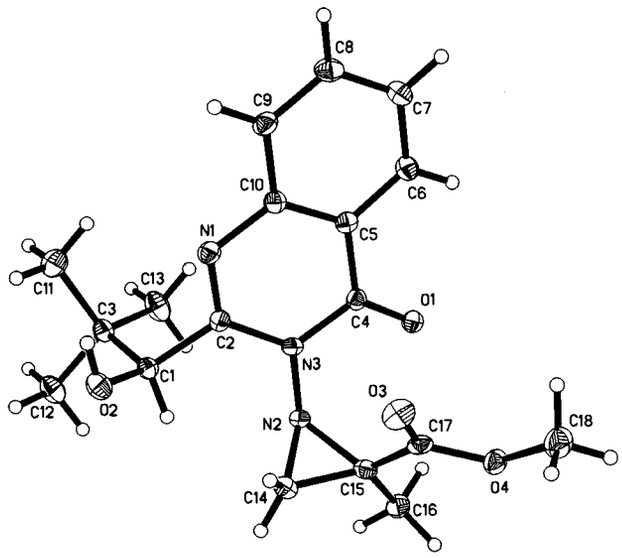
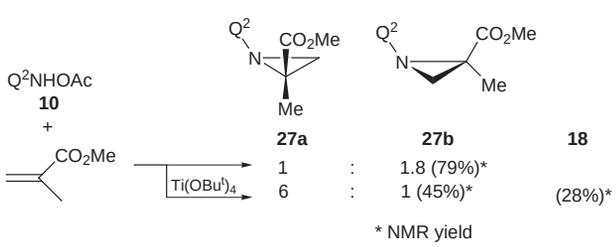


Fig. 2 The molecular structure of **27a** showing the atom numbering scheme and 30% displacement ellipsoids

titanium salt, the diastereoisomer ratio **24a**:**24b** was 1:1.1. An X-ray crystal structure determination carried out on the isolated aziridine diastereoisomer **24a** showed it to have the absolute configuration shown (Fig. 1).

Hydrolysis of aziridine **24a** by sodium hydroxide in ethanol required five days at room temperature and the acid **25** formed proved to be identical to that obtained by hydrolysis of the major diastereoisomer **23a** from aziridination of methyl acrylate. Hydrolysis of the aziridine diastereoisomer **23b** gave an acid **26** which was *not* identical to aziridine acid **25**. Accordingly, the preferred sense of diastereoselectivity in aziridination of methyl and of *tert*-butyl acrylate is the same.

Aziridination of methyl methacrylate gave a 6:1 mixture of diastereoisomeric aziridines **27a**:**27b** in the presence of titanium(IV) *tert*-butoxide (1:1.8 in its absence) together with Q^2NHOBu^t **18** (25%) (Scheme 10). The preferred sense of



Scheme 10

diastereoselectivity was again determined by an X-ray crystal structure determination on the major diastereoisomer (Fig. 2).

Thus, as in aziridination of electron-rich alkenes described earlier, the presence of an additional methyl group on the double bond undergoing reaction lowers the diastereoselectivity of aziridine formation.

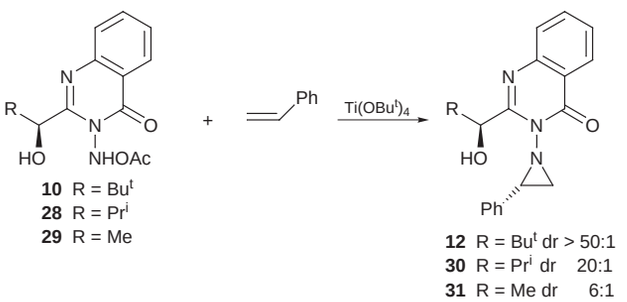
High diastereoselectivity in these aziridinations using Q^2NHOAc **10** has only been obtained in the presence of titanium alkoxides: using zirconium(IV) *tert*-butoxide instead, gave only the *tert*-butoxyaminoquinazolinone **18** (50%) and triisopropyl borate gave only the isopropyloxyquinazolinone **13** (75%) and no aziridine was detectable in either case.

A reduction in the number of mol equiv. of titanium(IV) *tert*-butoxide (TTB) used resulted in some loss of diastereoselectivity (Table 1) but (with 1.5 mol equiv.) in an increased yield (86%). At least some of this increased yield may be accounted for by the easier work-up with the need to separate lesser amounts of titanium residues.

Table 1

Reaction	No. of TTB equivalents	Ratio of aziridine diastereoisomers **12a** : **12b**	Yield of aziridine (%)
a	1.0	6.8 : 1	73
b	1.5	34 : 1	86

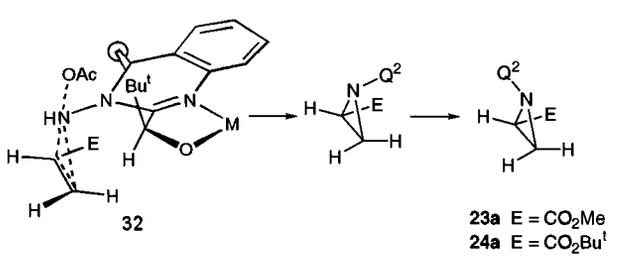
Reaction of the related 3-acetoxyaminoquinazolinones **28**** and **29** with styrene in the presence of titanium(IV) *tert*-butoxide under the same conditions used for Q²NHOAc **10** gave the aziridines **30** and **31** respectively in the diastereoisomer ratios (dr) shown in Scheme 11.



Scheme 11

A summary of chemical shifts for aziridine ring protons and the RC*H*OH protons in the NMR spectra of major and minor aziridine diastereoisomers of **12a**, **30** and **31** is given in Table 2. The good correlation between chemical shifts for major and minor diastereoisomers of these aziridines (Table 2) coupled with the decline in diastereoisomer ratios for aziridines **12**→**30**→**31** (Scheme 11) suggest that similar transition states (*cf*. **14**) are involved in each case.

In the aziridination of methyl acrylate and of *tert*-butyl acrylate, the absolute configurations of the major diastereoisomers **23a** and **24a** also correspond to those anticipated from a transition state model analogous to **14**, *i.e.* **32** (in which the configuration at the sp³-hybridised nitrogen has been inverted [14] (Scheme 12).



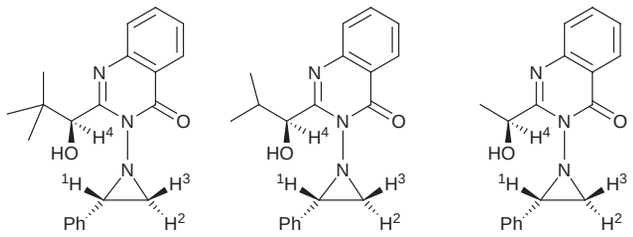
Scheme 12

However, aziridination of methyl acrylate in the presence of titanium(IV) *tert*-butoxide using the 3-acetoxyaminoquinazolinones **10**, **28** and **29**, gives aziridines **21a**, **33** and **34** with the respective diastereoisomer ratios shown (Scheme 13).

The preferred sense of diastereoselectivity in formation of aziridine **34** is assumed to be opposite to that for formation of **21a** because it seems unlikely that the diastereoisomer ratio for **34** would exceed that of **33** which would be the case if **21a**, **33** and **34** were all formed *via* analogous transition states and with the same preferred sense of diastereoselectivity. It seems unlikely, therefore, that model **32** holds for aziridination of methyl acrylate with **10**, **28** and **29** and conceivably it does not hold for any of them.

** 3-Acetoxyaminoquinazolinone **28** and the derived aziridine **30** were prepared by Mr A. G. Al-Sehemi in these laboratories to whom we offer our thanks.

Table 2

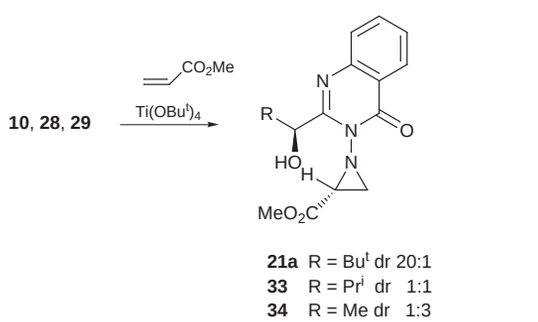


	12a		**30**		**31**	
	Major	Minor	Major	Minor	Major	Minor
H¹	3.84	4.29	3.73	4.47	3.96	4.39
H²	2.91	2.74	2.90	2.63	2.68	2.58
H³	3.50	3.20	3.55	3.45	3.62	3.40
H⁴	4.99	5.22	4.91	5.15	5.08	5.28

Table 3

Mol equiv. HOAc present initially	**23a**/**23b** (dr)	Yield **23a**	Yield Q²NHOBu^t **18**
0*	3 : 1	28	8
1	>20 : 1	65	25
2	>20 : 1	57	17
3	3 : 1	34	37
4	1 : 1	17	50

* The solution of Q²NHOAc was base-washed (see Experimental section).



Scheme 13

Since in transition state **32** the departing acetoxy group is *syn* to the quinazolinone 2-substituent severe steric interaction between this acetoxy group and the *tert*-butyl group can be anticipated. Furthermore, the interaction between N-1 and titanium in the chelated Q²NHOAc is likely to reduce the nucleophilicity of the lone pair of electrons on the exocyclic nitrogen *N*HOAc by a relay effect and thus decrease its reactivity towards α,β-unsaturated esters.†† (This same effect is expected to *increase* the reactivity of the chelated Q²NHOAc **10** towards the electron-rich alkenes in Scheme 2.)

As indicated in Table 3, in the reaction of Q²NHOAc **10** with methyl acrylate, both the diastereoselectivity and the yield in formation of aziridines **23a**/**23b** are dependent upon the number of mol. equiv. of acetic acid present initially before addition of titanium(IV) *tert*-butoxide. The results suggest that for high diastereoselectivity and yield in these reactions, the coordinated titanium must contain at least one acetate group.

To summarise: the sense of diastereoselectivity in aziridination of styrene using Q²NHOAc **10** in the presence of titanium(IV) *tert*-butoxide is satisfactorily accounted for using

†† Aziridination of α,β-unsaturated esters (by Ti-free Q²NHOAc) is believed to involve N–C_β bond formation running ahead of C_α–N bond formation (ref. 11).

transition state model **14**. The same model **14** can be used to predict the sense of diastereoselectivity in aziridination of butadiene, indene, and the unsubstituted double bond of isoprene. The preferred sense of diastereoselectivity in the corresponding aziridinations of methyl acrylate and of *tert*-butyl acrylate with Q^2NHOAc **10** is also in agreement with an analogous transition state model **32**. However, this conclusion is not supported from the diastereoselectivities of aziridination of methyl acrylate using 3-acetoxyaminoquinazolinones **28** and **29**, congeners of Q^2NHOAc **10**.

The lesser diastereoselectivities obtained in aziridinations of α-methylstyrene and of the more substituted double bond of isoprene remain to be explained as does the remarkable change in regioselectivity of isoprene aziridination in brought about by the presence of titanium(IV) *tert*-butoxide.

Experimental

General

250 and 300 MHz ^{1}H NMR spectra were recorded on Bruker ARX 250 and DRX 300 NMR spectrometers respectively. ^{13}C NMR spectra were recorded on a Bruker ARX 250 spectrometer at 75 MHz. NMR spectra were recorded at room temperature in deuterated chloroform unless otherwise stated. *J* Values are given in Hz. IR spectra of crystalline compounds were recorded as solutions in dichloromethane and of liquids as thin films using a Perkin-Elmer 298 spectrometer. Standard mass spectra were recorded on a Kratos Concept 1H Magnetic Sector Mass Spectrometer with fast atomic bombardment (FAB) ionisation in all cases. Except for the molecular ion MH^+ only peaks ≥20% of the base peak are given. Elemental analysis was carried out by CHN analysis, Wigston, Leicester. Melting points were determined on a Kofler hot stage and are uncorrected. Optical rotations were determined on a Perkin-Elmer 341 Polarimeter at 589 nm and are given in units of 10^{-1} deg cm^2 g^{-1}. Flash chromatography was carried out on silica gel C60 (35–70 mesh) (from Prolabo). TLC was conducted on silica gel 60 f_{254} (Merck 5554) on aluminium strips.

Dichloromethane was distilled from calcium hydride. Light petroleum refers to the 40–60 °C fraction. Routine drying of organic solutions was carried out using magnesium sulfate. Ether refers to diethyl ether.

Commercially available lead tetraacetate was freed from acetic acid prior to use using an oil pump (~1 mmHg) for 15 min. Titanium(IV) *tert*-butoxide was initially prepared by a literature method[16] but subsequently purchased from Merck and used as received. (*S*)-*tert*-Leucine was purchased from Degussa Ltd and generously donated by Roche Products. All other reactants were reagent grade and used as received unless stated otherwise. All reaction products were dried under vacuum (~1 mmHg) prior to spectroscopic analysis and further use. Removal of solvent under reduced pressure was accomplished by using a rotary evaporator (Buchi) at ~15 mmHg (water pump) unless otherwise indicated.

Preparation of 3-amino-2-(1-hydroxy-2,2-dimethylpropyl)-quinazolin-4(3*H*)-one 9

To a stirred solution of (*S*)-*tert*-leucine (25.0 g, 0.191 mol) in glacial acetic acid (600 cm^3) at room temperature was added solid sodium nitrite (52.64 g, 0.763 mol) slowly over a period of 1 h. After addition the solution was left for a further 1 h before the bulk of the acetic acid was removed under reduced pressure. Water (50 cm^3) was added and the aqueous solution extracted with ether (3 × 70 cm^3). The combined ethereal extracts were then washed with brine (50 cm^3), dried, and the solvent removed under reduced pressure. Trituration of the resulting greenish solid with light petroleum gave (*S*)-2-acetoxy-3,3-dimethylbutyric acid (20.10 g, 60.5%), $[a]_D$ −23.7 (*c* 9.93, ethanol) [lit.,[17] −22.8 (*c* 1.6, ethanol)].

(*S*)-2-Acetoxy-3,3-dimethylbutyric acid (16 g, 91.9 mmol) was dissolved in sodium-dried ether and two drops of *N*,*N*-dimethylformamide added followed by slow dropwise addition of thionyl chloride (19 cm^3, 260 mmol) to the stirred solution. The solution was left to stand overnight at room temperature and then unreacted thionyl chloride removed under reduced pressure using a water pump. The resulting cloudy oil was dissolved in sodium-dried ether (300 cm^3) and methyl anthranilate (24 cm^3, 185 mmol) was added dropwise briskly with stirring; a thick white precipitate was formed over the following hour. After setting aside overnight the solid was filtered off, washed with ether, and the combined filtrates washed successively with hydrochloric acid (2 M, 5 × 50 cm^3), saturated aqueous sodium hydrogen carbonate and brine (3 × 25 cm^3), then dried and the solvent removed by evaporation under reduced pressure. Crystallisation of the crude product gave the *anthranilate* **8** (26.3 g, 93%), mp 61–63 °C (from ethanol) (Found: C, 62.35; H, 6.85; N, 4.55. $C_{16}H_{21}NO_5$ requires C, 62.55; H, 6.9; N, 4.55%), $[a]_D$ −151 (*c* 1.0, ethanol); ν_{max}/cm^{-1} 3290 w, 1750 s, 1695 s, 1590 s, 1525 s and 1450 s; δ_H 1.02 [9H, s, C(C*H*$_3$)$_3$], 2.21 (3H, s, OCOC*H*$_3$), 3.84 (3H, s, OC*H*$_3$), 4.85 (1H, s, C*H*OAc), 7.01 (1H, dd, *J* 7.2 and 8.2, Ar*H*), 7.46 (1H, ddd, *J* 1.6, 7.2 and 8.5, Ar*H*), 7.95 (1H, dd, *J* 1.6 and 8.2, Ar*H*), 8.66 (1H, d, *J* 8.5, Ar*H*) and 11.46 (1H, br s, N*H*); δ_C 20.5 (*C*H$_3$CO), 26.1 [(*C*H$_3$)$_3$], 34.1 [*C*(CH$_3$)$_3$], 52.0 (CO$_2$*C*H$_3$), 81.1 [*C*HC(CH$_3$)$_3$], 115.1 [*C*(Ar)], 120.1, 122.6, 130.6, 134.3 [4 × *C*H(Ar)], 140.4 [*C*(Ar)] and 167.6, 168.2, 169.8 (3 × *C*=O); *m*/*z* 330 (MNa^+, 16%), 308 (MH^+, 100), 216 (23), 178 (28) and 157 (83).

The foregoing amide **8** (16.26 g, 53.04 mmol) was dissolved in ethanol (10 cm^3) and heated with hydrazine monohydrate (10 cm^3, 206.15 mmol) in a steel bomb at 140 °C for 17 h. After removing the bulk of the solvent under reduced pressure, water (50 cm^3) was added and the solution extracted with ether (3 × 50 cm^3). The combined organic layers were washed with water (50 cm^3), dried, and the solvent removed by evaporation under reduced pressure. Crystallisation of the residual white solid gave 3-*amino*-2-(1-*hydroxy*-2,2-*dimethylpropyl*)*quinazolin*-4(3H)-*one* **9** (10.97 g, 84%), mp 135–136 °C (from ethanol) (Found: C, 62.85; H, 6.85; N, 17.0; O, 12.95. $C_{13}H_{17}N_3O_2$ requires C, 63.15; H, 6.95; N, 17.0; O, 12.95%); $[a]_D$ 20.2 (*c* 1.04, ethanol); ν_{max}/cm^{-1} 3500 w, 1680 s, 1595 s and 1475 s; δ_H 1.11 [9H, s, C(C*H*$_3$)$_3$], 3.87 (1H, d, *J* 10, O*H*), 4.78 (2H, s, N*H*$_2$), 5.25 (1H, d, *J* 10, C*H*OH), 7.54 [1H, ddd, *J* 1.6, 8.2 and 8.2, 6-*H*(Q)], 7.74 [1H, d, *J* ~7, 8-*H*(Q)], 7.82 [1H, ddd, *J* ~1, ~7 and 8.2, 7-*H*(Q)] and 8.31 [1H, dd, *J* 1 and 8.2, 5-*H*(Q)]; δ_C 26.3 [C(*C*H$_3$)$_3$], 37.4 [*C*(CH$_3$)$_3$], 74.6 (*C*HOH), 119.9 [*C*CO(Q)], 126.2, 126.5, 126.9, 134.1 [4 × *C*H(Q)], 145.6 [*C*N=C(Q)], 158.2 [*C*=N(Q)] and 161.9 [*C*O(Q)]; *m*/*z* 248.1399 (MH^+, 100%) and 230 (25).

Low temperature NMR spectrum of 3-acetoxyamino-2-(1-hydroxy-2,2-dimethylpropyl)quinazolin-4(3*H*)-one 10

To $CDCl_3$ (2 cm^3) stirred at −12 °C (bath temp.) was added powdered LTA (180 mg, 0.406 mmol). After dissolution the reaction mixture was cooled to −20 °C and a solution of 3-aminoquinazolinone **9** (100 mg, 0.404 mmol in $CDCl_3$ (2 cm^3) added dropwise with stirring over 1 min. After stirring at this temperature for a further 20 min the cold solution was separated from the lead salts (Pasteur pipette), washed with cold (0 °C) saturated aqueous sodium hydrogen carbonate, dried, and then filtered rapidly through a cooled Pasteur pipette containing a cotton wool plug directly into a cooled (−12 °C) NMR tube and the spectrum recorded at −20 °C without any intermediate warming of the solution. The title compound appeared to consist of at least a 14:1 ratio of diastereoisomers, by comparison of two NHOAc singlets at 10.73 and 10.85 ppm (no other signals corresponding to the minor diastereoisomer were visible). δ_H (major diastereoisomer) ($CDCl_3$, 300 MHz) 1.03 [9H, s, C(C*H*$_3$)$_3$], 2.11 (3H, s, OCOC*H*$_3$), 3.68 (1H, d, *J* 10, O*H*), 5.13 [1H, d, *J* 10, C*H*C(CH$_3$)$_3$], 7.56 [1H, dd, *J* 7.0 and

8.0, 6-*H*(Q)], 7.76 [1H, d, *J* 8.1, 8-*H*(Q)], 7.87 [1H, dd, *J* 7.0 and 8.1, 7-*H*(Q)], 8.25 [1H, dd, *J* 8.0, 5-*H*(Q)] and 10.85 (1H, s, N*H*).

Aziridination of styrene

(a) With Q²NHOAc 10. *General aziridination procedure A.*—To dry dichloromethane (2 cm^3) stirred at −12 °C (bath temp. given throughout) was added powdered LTA (377 mg, 0.85 mmol) in one portion. After dissolution the reaction mixture was cooled to −20 °C and 3-aminoquinazolinone **9** (200 mg, 0.81 mmol) in dry dichloromethane (2 cm^3) added dropwise over 1 min. Stirring was continued for a further 20 min, the solution filtered rapidly through a cotton wool-plugged Pasteur pipette (end of general procedure A) and styrene (0.11 cm^3, 0.96 mmol) added. The reaction mixture was stirred for 2 min at −20 °C before its temperature was allowed to reach ambient by removal of the cooling bath.

General work-up procedure B.—The solution obtained above was filtered, washed successively with saturated aqueous sodium hydrogen carbonate and brine (2 × 5 cm^3) and then dried. Removal of solvent by evaporation under reduced pressure (end of general procedure B) gave two diastereoisomeric aziridines **12b** and **12a** (253 mg, 90%) in a 3:2 ratio [by integration of the signals at 2.74 and 2.91 ppm respectively (see below)]. Crystallisation gave the major *aziridine diastereoisomer* **12b** as colourless crystals, mp 124–127 °C (from ethanol); δ_H 0.98 [9H, s, C(C*H*$_3$)$_3$], 2.74 (1H, dd, *J* 2.0 and 5.0, C*H*H *cis* to Ph), 3.20 (1H, dd, *J* 2.0 and 8.0, CH*H trans* to Ph), 3.76 (1H, d, *J* 10.0, O*H*), 4.29 (1H, dd, *J* 5.0 and 8.0, C*H*Ph), 5.22 (1H, d, *J* 10.0, C*H*OH), 7.32–7.50 [6H, structured m, 6-*H*(Q), 5 × *H*(Ph)], 7.60–7.78 [2H, structured m, 7-*H*, 8-*H*(Q)] and 8.22 [1H, dd, *J* 1.0 and 7.5, 5-*H*(Q)].

(b) With Q²NHOAc 10 and titanium(IV) isopropoxide. A cold (−20 °C) solution of 3-acetoxyaminoquinazolinone **10** in dichloromethane (4 cm^3) was prepared as described (general procedure A) from **9** (200 mg, 0.81 mmol) and LTA (377 mg, 0.85 mmol) and added to a stirred solution of titanium(IV) isopropoxide (460 mg, 1.62 mmol) and styrene (0.11 cm^3, 0.96 mmol) in dry dichloromethane (1 cm^3) held at −20 °C (bath temp.). After stirring for 2 min the temperature of the reaction mixture was allowed to reach ambient by removal of the cooling bath.

General work-up procedure C.—Saturated aqueous sodium hydrogen carbonate (5 cm^3) was added to the above reaction mixture followed by vigorous stirring until a white gelatinous precipitate formed. The solution was filtered and the organic layer separated, washed with brine (2 × 5 cm^3), dried, and the solvent evaporated under reduced pressure (end of general procedure C) to give a pale yellow residue containing aziridine **12a** (14%) and 3-isopropoxyaminoquinazolinone **13** 59% by NMR comparison of this mixture with those of authentic samples of **12a** and **13** (see below).

(c) with Q²NHOAc 10 and titanium(IV) *tert*-butoxide (2 equiv.). A cold (−20 °C) solution of 3-acetoxyaminoquinazolinone **10** in dichloromethane (40 cm^3) was prepared as described previously (general procedure A) from **9** (2.8 g, 11.34 mmol) and LTA (5.52 g, 12.45 mmol) and added to a stirred mixture of titanium(IV) *tert*-butoxide (7.70 g, 22.7 mmol), styrene (1.6 cm^3, 13.6 mmol) and dry dichloromethane (10 cm^3) maintained at −20 °C (bath temp.). After stirring for 2 min the temperature of the reaction mixture was allowed to reach ambient. Work-up (general procedure C) gave a pale yellow solid and crystallisation gave *aziridine* **12a** (2.56 g, 65%), mp 127–128 °C (from ethanol) (Found: C, 72.2; H, 6.7; N, 12.0. $C_{21}H_{23}N_3O_2$ requires C, 72.2; H, 6.65; N, 12.0%); $[\alpha]_D$ 403.0 (*c* 1.00, ethanol); ν_{max}/cm^{-1} 3450 w, 1675 s and 1585 s; δ_H 0.88 [9H, s, C(C*H*$_3$)$_3$], 2.91 (1H, dd, *J* 2.5 and 5.0, C*H*H *cis* to Ph), 3.50 (1H, dd, *J* 2.5 and 7.9, CH*H trans* to Ph), 3.67 (1H, d, *J* 10.4, O*H*), 3.84 (1H, dd, *J* 5.0 and 7.9, C*H*Ph), 4.99 (1H, d, *J* 10.4, C*H*OH), 7.37 [5H structured m, 5 × *H*(Ph)], 7.48 [1H, ddd, *J* 1.0, 6.9 and 8.2, 6-*H*(Q)], 7.66 [1H, dd, *J* 1.0 and 8.5, 8-*H*(Q)], 7.75 [1H, ddd, *J* 1.6, 6.9 and 8.5 7-*H*(Q)] and 8.24 [1H, dd, *J* 1.6 and 8.2, 5-*H*(Q)]; δ_C 25.7 [C(*C*H$_3$)$_3$], 37.8 [*C*(CH$_3$)$_3$], 42.1 (*C*H$_2$), 47.3 (*C*HPh), 74.4 (*C*HOH), 121.4 [*C*CO(Q)], 126.3, 126.8, 126.9, 128.3, 128.7, 134.0 [4 × CH(Q), 3 × CH(Ph)], 136.1 [*C*(Ph)], 144.8 (*C*N=C), 158.1 [*C*=N(Q)] and 159.6 [*C*O(Q)]; *m*/*z* 350 (MH^+, 100%) and 215 (20). A crystal was grown from light petroleum–ethyl acetate for X-ray structure determination which showed that the major diastereoisomer has the *S* configuration at the aziridine ring C-2. Examination of the crude reaction product above by NMR spectroscopy showed the absence of signals from aziridine diastereoisomer **12b**.

(d) With Q²NHOAc 10 and titanium(IV) *tert*-butoxide (1 and 1.5 equiv.). Two cold (−20 °C) solutions of 3-acetoxyaminoquinazolinone **10**, a and b, in dichloromethane (4 cm^3) were prepared as described previously (general procedure A) from **9** (200 mg, 0.81 mmol) and LTA (377 mg, 0.85 mmol) at −20 °C. The two solutions, a and b, were each added to separate stirred solutions of styrene (0.11 cm^3, 0.96 mmol) in dichloromethane (2 cm^3) maintained at −20 °C (bath temp.) containing titanium(IV) *tert*-butoxide (274 mg, 0.81 mmol and 411 mg, 1.21 mmol respectively). After stirring for 2 min the cooling baths were removed and the temperature of each reaction mixture allowed to reach ambient. Each reaction was worked-up as described previously (general procedure C), the results are given in Table 1.

Aziridination of buta-1,3-diene

(a) With Q²NHOAc 10. Dichloromethane (4 cm^3) was cooled to −20 °C (bath temp.), saturated with buta-1,3-diene (>10 equiv.) and a cold (−20 °C) solution of 3-acetoxyaminoquinazolinone **10** in dichloromethane (4 cm^3), prepared as described previously (general procedure A) from **9** (200 mg, 0.81 mmol) and LTA (377 mg, 0.85 mmol) added with stirring. After 2 min the cooling bath was removed and the temperature of the solution allowed to reach ambient. Standard work-up (general procedure B) gave a colourless residue (185 mg) whose NMR spectrum showed it to comprise a 1:1.3 mixture of aziridine diastereoisomers **14a** and **14b** (76%) by integration comparison of signals at δ 2.70 and 2.51 respectively. Signals for the major diastereoisomer **14b** were visible at δ 1.03 [9H, s, C(C*H*$_3$)$_3$], 2.52 (1H, dd, *J* 1.3 and 5.3, C*H*H *cis* to vinyl), 2.95 (1H, dd, *J* 1.3 and 7.9, CH*H trans* to vinyl), 3.75 (2H, structured m, C*H* aziridine, OH), 5.11 (1H, d, *J* 10.4, C*H*OH), 5.38 (1H, dd, *J* 1.6 and 10.1, CH_CH$_T$=), 5.53 (1H, dd, *J* 1.6 and 17.3, CH$_C$$H_T$=) and 5.82 (1H, ddd, *J* 6.9, 10.1 and 17.3, C*H*=).

(b) With Q²NHOAc 10 and titanium(IV) *tert*-butoxide. A solution of titanium(IV) *tert*-butoxide (5.50 g, 16.22 mmol) and dichloromethane (5 cm^3) was cooled to −20 °C and saturated with buta-1,3-diene (>10 equiv.). A lead diacetate-free cold (−20 °C) solution of 3-acetoxyaminoquinazolinone **10** in dichloromethane (25 cm^3), prepared as described previously (general procedure A) from **9** (2.0 g, 8.1 mmol) and LTA (3.77 g, 8.5 mmol) at −20 °C was then added and the resulting mixture stirred for 2 min before its temperature was allowed to rise to ambient by removal of the cooling bath. General work-up procedure C gave a white crystalline solid which NMR spectroscopy showed to be a single aziridine diastereoisomer **15a**. Crystallisation yielded 2-*vinylaziridine* **15a** (2.05 g, 85%), mp 131–133 °C (from ethanol) (Found: C, 68.0; H, 7.1; N, 13.9. $C_{17}H_{21}N_3O_2$ requires C, 68.2; H, 7.05; N, 14.05%); $[\alpha]_D$ 330.0 (*c* 1, ethanol); ν_{max}/cm^{-1} 3450 w, 1680 s, 1595 s and 1475 s; δ_H 1.01 [9H, s, C(C*H*$_3$)$_3$], 2.70 (1H, dd, *J* 2.6 and 5.5, C*H*H *cis* to vinyl), 3.14 (1H, dd, *J* 2.6 and 7.8, CH*H trans* to vinyl), 3.27 (1H, ddd, *J* 5.5, 7.6 and 7.8, aziridine C*H*), 3.72 (1H, d, *J* 10.3, O*H*), 5.10 (1H, d, *J* 10.3, C*H*OH), 5.41 (1H, dd, *J* 1.7 and 9.4, CH_CH$_T$=), 5.61 (1H, dd, *J* 1.7 and 17.2, CH$_C$$H_T$=), 5.72 (1H, ddd, *J* 7.6, 9.4 and 17.2, C*H*=), 7.46 [1H, ddd, *J* 1.3, 7.0 and 8.1, 6-*H*(Q)], 7.64 [1H, structured m, 8-*H*(Q)], 7.73 [1H, ddd, *J* 1.5, 7.0 and 8.3, 7-*H*(Q)] and 8.22 [1H, d (further split) *J* 8, 5-*H*(Q)]; δ_C 26.3 [C(*C*H$_3$)$_3$], 38.5 [*C*(CH$_3$)$_3$], 41.0 (*C*H$_2$), 48.3 (*C*HC=C), 74.8

(*C*HOH), 120.6 (*C*H_2=), 121.7 [*C*CO(Q)], 126.9, 127.1, 127.2, 134.4, 134.8 [4 × *C*H(Q), *C*H=], 145.1 [*C*N=C(Q)], 158.2 [*C*=N(Q)] and 159.8 [*C*O(Q)]; *m*/*z* 300 (MH^+, 100%) and 215 (20).

Aziridination of indene

(a) With Q²NHOAc 10. A cold (−20 °C) solution (bath temp.) of 3-acetoxyaminoquinazolinone **10** in dry dichloromethane (4 cm^3) was prepared as described previously (general procedure A) from **9** (200 mg, 0.81 mmol) and LTA (377 mg, 0.85 mmol) and indene (0.13 cm^3, 1.11 mmol) added to the stirred solution. After 2 min the cooling bath was removed and the temperature of the solution was allowed to reach ambient. Standard work-up, described previously (general procedure B) gave a white solid (239 mg, 82%) which by NMR spectroscopy comprised a 3:1 ratio of aziridines **16a** and **16b** by comparison of signals at 4.09 and 4.71 ppm respectively. Signals assignable to the minor diastereoisomer were visible at δ_H 0.98 [9H, s, C(CH_3)$_3$], 3.29 [1H, d, *J* ~5, azir. C*H*(Ar)] and 3.88 [1H, t, *J* ~5, azir. C*H*(CH_2)]. Signals for the major diastereoisomer were identical to those given below.

(b) With Q²NHOAc 10 and titanium(IV) *tert*-butoxide. A cold (−20 °C) solution of 3-acetoxyaminoquinazolinone **10** in dichloromethane (4 cm^3) was prepared as described previously (general procedure A) from **9** (200 mg, 0.81 mmol) and LTA (377 mg, 0.85 mmol) and added to a stirred solution of titanium(IV) *tert*-butoxide (548 mg, 1.62 mmol) and indene (0.13 cm^3, 1.11 mmol) in dry dichloromethane (1 cm^3) maintained at −20 °C. After 2 min the cooling bath was removed and the temperature of the mixture allowed to reach ambient. Standard work-up (general procedure C) gave a white solid and crystallisation yielded *aziridine* **16a** as a colourless solid (251 mg, 86%), mp 178–180 °C (from ethanol) (Found: C, 73.0; H, 6.45; N, 11.6. $C_{22}H_{23}N_3O_2$ requires C, 73.1; H, 6.4; N, 11.6%); $[\alpha]_D$ 228.8 (*c* 1.04, ethanol); ν_{max}/cm^{-1} 3500 w, 2970 m, 1680 s, 1590 s, 1470 s, 1300 m, 1230 m, 1075 m and 1020 m; δ_H (8:1 ratio of *N*-invertomers) major invertomer 0.90 [9H, s, C(CH_3)$_3$], 3.33 (1H, dd, *J* 17.9 and 5.0, C*H*H), 3.59 (1H, d, *J* 17.9, CH*H*), 3.74 (1H, d, *J* 10.6, O*H*), 4.09 [1H, d, *J* 5.7, azir. C*H*(Ar)], 4.19 [1H, pseudo t, *J* ~5.0, azir. C*H*(CH_2)], 5.14 (1H, d, *J* 10.6, C*H*OH), 7.22–7.37 (4H, structured m, Ar*H*), 7.48 [1H, ddd, *J* 1.0, 6.6 and 7.9, 6-*H*(Q)], 7.60–7.80 [2H, structured m, 8-*H*(Q), 7-*H*(Q)] and 8.24 [1H, dd, *J* 1.0 and 7.9 5-*H*(Q)]; minor invertomer (observable signals) δ_H 1.18 [9H, s, C(CH_3)$_3$], 3.38 (1H, br s), 3.98 (1 H, m), 4.08 (1H, d, *J* 10.4, O*H*), 4.87 [1H, d, *J* 4.4, azir. C*H*(Ar)], 4.97 (1H, d, *J* 10.4, C*H*OH), 6.86 (1H, br d, *J* 7.8), 6.99 (1H, td, *J* 1.3, 7.5), 7.16 (1H, br t, *J* 6.9) and 7.36 [1H, structured m, 4 × H (Ar or Q)]; δ_C major invertomer 25.8 [C(*C*H_3)$_3$], 35.4 [*C*(CH_3)$_3$], 38.0 (*C*H_2), 51.6, 58.3 (2 × aziridine *C*H), 75.3 (*C*HOH), 121.5 (*C*CO), 124.6, 125.6, 126.3, 126.6, 126.8, 126.9, 128.8, 133.9 [4 × CH(Q), 4 × CH(Ph)], 138.4, 144.1, 144.8 [2 × *C*(Ph), *C*N=C(Q)], 157.5 [*C*=N(Q)] and 159.3 [*C*O(Q)]; δ_C minor invertomer (observable signals) 32.0 (*C*H_2), 49.7 (*C*H), 55.8 (*C*H), 120.9 [*C*CO(Q)], 122.5, 128.0, 133.0, 135.4, 141.2 and 157.0 (6 × *C*H); *m*/*z* 362 (MH^+ 100%), 307 (56) and 215 (26).

Aziridination of α-methylstyrene

(a) With Q²NHOAc 10. A solution of 3-acetoxyaminoquinazolinone **10** in dry dichloromethane (4 cm^3) was prepared as described previously (general procedure A) from **9** (200 mg, 0.81 mmol) and LTA (377 mg, 0.85 mmol) at −20 °C and α-methylstyrene (0.21 cm^3, 1.61 mmol) added to the stirred solution. After 2 min the cooling bath was removed and the temperature of the reaction mixture allowed to rise to 0 °C before it was added dropwise to vigorously stirred saturated aqueous sodium hydrogen carbonate (5 cm^3). The resulting mixture was filtered, the organic layer separated, washed with brine (2 × 5 cm^3), dried and evaporated under reduced pressure to give a colourless oil (283 mg, 77%). Examination of this crude product by NMR spectroscopy showed it to be composed of a 1.1:1 ratio of aziridines **17** by comparison of the integration of signals at 3.19 and 3.04 respectively.

The minor diastereoisomer consisted of a 3:2 ratio of *N*-invertomers by integral comparison of C*H*H signals at 4.10 and 2.69 ppm respectively; major invertomer δ 0.95 [9H, s, C(CH_3)$_3$], 1.54 (3H, s, CH_3), 3.04 (1H, d, *J* 4.4, CH*H*), 4.10 (1H, d, *J* 4.4, C*H*H), 4.77 (1 H, br s, C*H*OH), 7.10 to 7.72 [8H, structured m, 5 × C*H*(Ph), 3 × C*H*(Q)] and 8.25 [1H, br d, *J* ~8, 5-*H*(Q)]; minor invertomer (observable signals) at 1.00 [9H, s, C(CH_3)$_3$], 1.54 (3H, s, CH_3), 2.69 (1H, br s, CH*H*), 3.03 (1H, br s, C*H*H) and 4.83 (1H, br s, C*H*OH). [For NMR spectrum of the major diastereoisomer see below.]

(b) With Q²NHOAc 10 and titanium(IV) *tert*-butoxide (premixed). A solution of 3-acetoxyaminoquinazolinone **10** in dry dichloromethane (4 cm^3) was prepared as described previously (general procedure A) from **9** (200 mg, 0.81 mmol) and LTA (377 mg, 0.85 mmol) at −20 °C and added to a stirred solution of titanium(IV) *tert*-butoxide (548 mg, 1.62 mmol) in dichloromethane (2 cm^3) maintained at −40 °C (bath temp.). After 1 h at this temperature, α-methylstyrene (0.21 cm^3, 1.61 mmol) was added to the solution whose temperature was then allowed to rise to ambient, stirring throughout. The reaction mixture was then added dropwise to rapidly stirred saturated aqueous sodium carbonate (5 cm^3), the organic layer separated, washed with brine (2 × 5 cm^3), dried and concentrated to give a pale brown residue (179 mg). Examination by NMR spectroscopy showed this residue to consist of a 9:1 ratio of aziridine diastereoisomers **17** (44%) by integration comparison of signals at 3.19 and 3.03 ppm respectively, together with *tert*-butoxyaminoquinazolinone **18** (8%) (for characterisation of **18**, see below).

Chromatography (eluent 4:1 light petroleum-ethyl acetate) yielded the major diastereoisomer of *aziridine* **17** as a colourless oil (Found: MH^+, 364.2025. $C_{22}H_{26}N_3O_2$ requires MH^+, 364.2025); ν_{max}/cm^{-1} 3500 m, 1675 s and 1590 s; δ_H 0.79 [9H, s, C(CH_3)$_3$], 1.59 (3H, s, CH_3), 3.19 (1H, d, *J* 4.0, C*H*H), 3.29 (1H, d, *J* 4.0, CH*H*), 3.57 (1H, d, *J* 10.7, CHO*H*), 4.46 (1H, d, *J* 10.7, C*H*OH), 7.30–7.55 [6H, structured m, 6-*H*(Q) and C*H*(Ph)], 7.67 [1H, dd, *J* 1.0 and 8.2, 8-*H*(Q)], 7.74 [1H, ddd, *J* 1.2, 6.9 and 8.2, 7-*H*(Q)], 8.26 [1H, dd, *J* 1.2 and 7.9, 5-*H*(Q)]; *m*/*z* 364 (MH^+, 100%), 260 (20), 233 (31) and 215 (37).

When this experiment was carried out under conditions previously described for styrene in the presence of titanium(IV) *tert*-butoxide, and with the work-up described above, a 5:1 ratio of diastereoisomers of aziridine **17** was obtained (70%).

Aziridination of isoprene

(a) With Q²NHOAc 10. A solution of 3-acetoxyaminoquinazolinone **10** in dry dichloromethane (4 cm^3) was prepared as described previously (general procedure A) from **9** (200 mg, 0.81 mmol) and LTA (377 mg, 0.85 mmol) at −20 °C, and isoprene (0.16 cm^3, 1.62 mmol) added to the stirred solution. After 2 min the cooling bath was removed and the temperature of the solution was allowed to reach ambient. Standard work-up (general procedure B) gave a colourless residue whose NMR spectrum showed it to consist of a 1:4.7 ratio of aziridine **19** (10%) (1.4:1 mixture of diastereoisomers) and aziridine **20** (48%) (1:1.05 mixture of diastereoisomers) together with allylic alcohol **21** (10%) (2.3:1 mixture of diastereoisomers) and Q*H **22** (12%).

Chromatography (eluent light petroleum–ethyl acetate 2:1) yielded aziridine **20** (R_f 0.35) (84 mg, 33%) as a 1:1.05 mixture of diastereoisomers; major diastereoisomer δ_H 1.00 [9H, s, C(CH_3)$_3$], 1.67 (3H, s, CH_3), 2.99 (1H, d, *J* 3.7, C*H*H), 3.01 (1H, d, *J* 3.7, CH*H*), 3.67 (1H, d, *J* 10.4, CHO*H*), 5.12 (1H, d, *J* 10.4, C*H*OH), 5.32–5.43 (3H, structured m, CH_2=C*H*), 7.46 [1H, structured m, 6-*H*(Q)], 7.60–7.80 [2H, structured m, 8-*H*, 7-*H*(Q)] and 8.22 [1H, structured m, 5-*H*(Q)]; minor diastereoisomer (observable signals) 0.98 [9H, s, C(CH_3)], 1.61 (3H, s,

CH_3), 2.93 (1H, d, 3.4, C*H*H), 3.03 (1H, d, *J* 3.4, CH*H*), 3.64 (1H, d, *J* 10.7, CHO*H*), 5.10 (1H, d, *J* 10.7, C*H*OH), 5.40 (1H, dd, *J* 1.0 and 10.7, CH_CH_T=), 5.50 (1H, dd, *J* 1.0 and 17.3, CH_CH_T=), 5.79 (1H, dd, *J* 10.7 and 17.3, C*H*=).

Further elution gave aziridine **19** as a 1.4:1 mixture of diastereoisomers (10%); minor diastereoisomer (observable signals) 2.59 (1H, dd, *J* 1.2 and 7.8, C*H*H) and 2.85 (1 H, dd, *J* 1.2 and 5.3, CH*H*). Signals for the major diastereoisomer were identical to those given below.

Further elution with the same solvent yielded allylic alcohol **21** as 2.3:1 mixture of diastereoisomers (R_f 0.18) (45 mg, 17%) (Found: MH^+, 332.1974. $C_{18}H_{26}N_3O_3$ requires MH^+, 332.1974); ν_{max}/cm^{-1} 3440 m, 3300 m, 1660 s, 1595 s and 1475 s; major diastereoisomer δ_H 1.04 [9H, s, C(CH_3)], 1.42 (3H, s, CH_3), 2.84 (1H, t, *J* 10.4, C*H*H), 2.90 (1H, br s, O*H*), 3.26 (1H, dd, *J* 3.8 and 10.4, CH*H*), 3.73 (1H, br s, O*H*), 4.99 (1H, br s, C*H*OH), 5.14 (1H, dd, *J* 1.0 and 11.0, =CH_CH_T), 5.39 (1H, dd, *J* 1.0 and 17.3, =CH_CH_T), 5.81 (1H, dd, *J* 3.8 and 10.4, N*H*), 5.95 (1H, dd, *J* 11.0 and 17.3, C*H*=), 7.48 [1H, structured m, 6-*H*(Q)], 7.69 [1H, dd, *J* 1.5 and 8.5, 8-*H*(Q)], 7.77 [1H, structured m, 7-*H*(Q)], 8.22 [1H, d, *J* 8.2, 5-*H*(Q)]; *m*/*z* 332 (MH^+, 100%), 260 (31), 233 (20), 215 (58) and 175 (36).

Further elution with the same solvent yielded 3*H*-*quinazolinone* **22** (19 mg, 10%) which crystallised as colourless plates, mp 158–161 °C (from light petroleum–ethyl acetate) (Found: C, 67.3, H, 6.95; N, 12.05. $C_{13}H_{16}N_2O_2$ requires C, 67.2; H, 6.95; N, 12.05%); ν_{max}/cm^{-1} 3475 w, 1680 s, 1630 s and 1470 s; δ_H 0.99 [9H, s, C(CH_3)$_3$], 4.31 (1H, s, C*H*OH), 7.39 [1H, *J* 1.3, 6.9 and 7.9, 6-*H*(Q)], 7.58 [1H, br d, *J* 8.2, 8-*H*(Q)], 7.67 [1H, ddd, *J* ~1, 6.9 and 8.2, 7-*H*(Q)], 8.17 [1H, dd, *J* 1.2 and 7.9, 5-*H*(Q)] and 10.55 (1H, br s, NH); δ_C 25.9 [C(*C*H_3)$_3$], 36.5 [*C*(CH_3)$_3$], 78.8 (*C*HOH), 121.0 [*C*CO(Q)], 126.4, 126.8, 127.2, 134.8 [4 × *C*H(Q)], 148.2 [*C*N=C(Q)], 155.9 [*C*=N(Q)] and 162.4 [*C*O(Q)]; *m*/*z* 233 (MH^+, 100%), 215 (56) and 176 (26).

(b) With Q^{2}NHOAc 10 and titanium(IV) *tert*-butoxide. A cold solution of 3-acetoxyaminoquinazalinone **10** in dichloromethane (4 cm^3) was prepared as described earlier (procedure A) from **9** (200 mg, 0.81 mmol) and LTA (377 mg, 0.85 mmol) and added to a stirred mixture of titanium(IV) *tert*-butoxide (548 mg, 1.62 mmol) and isoprene (0.16 cm^3, 1.62 mmol) in dry dichloromethane (1 cm^3) maintained at −20 °C (bath temp.). After 2 min the cooling bath was removed and the temperature of the reaction mixture allowed to reach ambient. Standard work-up (general procedure C) gave a product whose NMR spectrum showed it to be composed of a 1.4:1 ratio of aziridine **19** (as a single diastereoisomer) and aziridine **20** (as a 1:1.6 ratio of diasteroisomers) together with 3-*tert*-butoxyaminoquinazolinone **18** (11%). Trituration with ethanol gave aziridine **19** (76 mg, 30%) as colourless crystals, mp 112–114 °C (from ethanol) (Found: C, 68.7; H, 7.4; N, 13.3. $C_{18}H_{23}N_3O_2$ requires C, 69.0; H, 7.4; N, 13.4%); ν_{max}/cm^{-1} 3060 s, 1680 s and 1595 s; δ_H 1.01 [9H, s, C(CH_3)], 1.74 (3H, s, CH_3), 2.77 (1H, dd *J* 2.5 and 5.3, azir. C*H*H *cis* to CHMe=CH_2), 3.13 (1H, dd, *J* 2.5 and 7.9, CH*H* *trans* to CHMe=CH_2), 3.39 (1H, dd, *J* 5.3 and 7.9, azir. C*H*), 3.68 (1H, d, *J* 10.4, O*H*), 5.11 (1H, d, *J* 10.4, C*H*OH), 5.17 (1H, s, =C*H*H), 5.30 (1H, s, =CH*H*), 7.46 [1H, unresolved ddd, *J* 1.3 and 8.2 visible, 6-*H*(Q)], 7.64 [1H, dd, *J* 1.3 and 8.2, 8-*H*(Q)], 7.73 [1H, ddd, *J* 1.2, 6.9 and 8.2, 7-*H*(Q)] and 8.20 [1H, dd, *J* 1.2 and 8.2, 5-*H*(Q)].

Aziridination of methyl acrylate

(a) With Q^{2}NHOAc 10. A solution of 3-acetoxyaminoquinazolinone **10** in dichloromethane (4 cm^3) was prepared as described previously (general procedure A) from **9** (200 mg, 0.81 mmol) and LTA (377 mg, 0.85 mmol) at −20 °C. Methyl acrylate (0.1 cm^3, 1.1 mmol) was added and the solution stirred at −20 °C (bath temp.) for 2 min. before the cooling bath was removed and the temperature allowed to reach ambient. Standard work-up (general procedure C) gave a brown residue (199 mg) whose NMR spectrum showed it to consist of a 1:3 mixture of aziridine diastereoisomers **23a** and **23b** respectively (74%) by comparison of the signals at δ 2.55 and 2.68 ppm respectively (see below). Chromatography (eluent 2:1 light petroleum–ethyl acetate) yielded the major *aziridine diastereoisomer* **23b** (R_f 0.3), δ_H 1.03 [9H, s, C(CH_3)$_3$], 2.68 (1H, d, *J* 4.4, C*H*H *cis* to ester), 3.61 (1H, d, *J* 7.2, CH*H* *trans* to ester), 3.83 (3H, s, CO_2CH_3), 3.97 (1H, d, *J* 11.0, O*H*), 4.36 (1H, dd, *J* 4.4 and 7.2, C*H*CO_2CH_3), 5.18 (1H, d, *J* 11.0, C*H*OH), 7.46 [1H, ddd, *J* 1.3, 7.0 and 7.9, 6-*H*(Q)], 7.65 [1H, d, *J* 8.0, 8-*H*(Q)], 7.74 [1H, ddd, *J* 1.3, 7.0 and 8.0, 7-*H*(Q)] and 8.16 (1H, dd, *J* 1.3 and 7.9, 5-*H*(Q)]; (minor diastereoisomer; see below).

(b) With Q^{2}NHOAc 10 and titanium(IV) *tert*-butoxide. A cold (−20 °C) solution of 3-acetoxyaminoquinazolinone **10** in dichloromethane (4 cm^3) was prepared as described previously (general procedure A) from **9** (200 mg, 0.81 mmol) and LTA (377 mg, 0.85 mmol) and added to a stirred solution of titanium(IV) *tert*-butoxide (548 mg, 1.62 mmol) and methyl acrylate (0.1 cm^3, 1.1 mmol) in dry dichloromethane (1 cm^3) maintained at −20 °C (bath temp.). After 2 min the cooling bath was removed and the temperature of the reaction mixture allowed to reach ambient. Standard work-up (general procedure C) gave a pale yellow residue whose NMR spectrum showed it consisted of aziridine **23a**/**23b** as a ~20:1 ratio of diastereoisomers (by comparison of the signals at δ 2.50 and 2.60 ppm respectively) together with 3-*tert*-butoxyaminoquinazolinone **18** (25%). Crystallisation of the crude product gave the *aziridine diastereoisomer* **23a** (174 mg, 65%), mp 130–131 °C (from ethanol) (Found: C, 61.95; H, 6.35; N, 12.55. $C_{17}H_{21}N_3O_4$ requires C, 61.6; H, 6.4; N, 12.7%); $[\alpha]_D$ 320.7 (*c* 1.16, chloroform); ν_{max}/cm^{-1} 3400 w, 1750 s and 1675 s; δ_H 1.00 [9H, s, C(CH_3)$_3$], 2.55 (1H, d, *J* 4.1, C*H*H *cis* to ester), 3.73 (3H, s , CO_2CH_3), 3.80 (1H, d, *J* 10.1, O*H*), 3.91 (1H, d, *J* 7.2, CH*H* *trans* to ester), 4.18 (1H, dd, *J* 4.1 and 7.2, C*H*CO_2CH_3), 5.17 (1H, d, *J* 10.1, C*H*OH), 7.39 [1H, unresolved ddd, *J* 1.6 and 8.2 visible, 6-*H*(Q)], 7.59 [1H, d, *J* 7.0, 8-*H*(Q)], 7.68 [1H, ddd, *J* 1.0, 7.0 and 8.2, 7-*H*(Q)] and 8.07 [1H, dd, *J* 1.0 and 7.9, 5-*H*(Q)]; δ_C 25.8 [C(*C*H_3)$_3$], 33.3 (*C*H_2), 36.9 (*C*HCO_2), 37.6 [*C*(CH_3)$_3$], 52.5 (CO_2CH_3), 74.5 (*C*HOH), 121.4 (*C*CO), 126.2, 126.9, 134.5 [3 × *C*H(Q)], 144.8 (*C*N=C), 159.3 [*C*=N(Q)], 161.1 [*C*O(Q)] and 169.0 (CO_2CH_3) [1 *C*H(Q) missing]; *m*/*z* 332 (MH^+, 100%) and 274 (23).

(c) With Q^{2}NHOAc 10 (acetic acid-free) and titanium(IV) *tert*-butoxide. A solution of 3-acetoxyaminoquinazolinone **10** in dichloromethane (4 cm^3) was prepared as described previously (general procedure A) from **9** (200 mg, 0.81 mmol) and LTA (377 mg, 0.85 mmol). The cold (−20 °C) solution was then shaken once in a separating funnel with cold (0 °C) saturated aqueous sodium hydrogen carbonate (5 cm^3) and then cold (0 °C) brine (5 cm^3). The cold organic layer was separated and quickly dried, keeping the temperature of the solution at ~0 °C, and then added directly and dropwise to a stirred mixture of titanium(IV) *tert*-butoxide (548 mg, 1.62 mmol) and methyl acrylate (0.1 cm^3, 1.1 mmol) in dry dichloromethane (1 cm^3) maintained at −20 °C (bath temp.). After stirring for 2 min the temperature of the reaction mixture was allowed to reach ambient. Work-up (general procedure C) gave a clear residue (98 mg). Examination of the crude product by NMR spectroscopy showed it to consist of a 3:1 mixture of aziridine diastereoisomers **23a** and **23b** (28%) (by comparison of the signals at δ 2.50 and 2.60 ppm respectively) together with 3-*tert*-butoxyaminoquinazolinone **18** (8%).

(d) With Q^{2}NHOAc 10 and zirconium(IV) *tert*-butoxide. A solution of 3-acetoxyaminoquinazolinone **10** in dry dichloromethane (4 cm^3) was prepared as described previously (general procedure A) from **9** (200 mg, 0.81 mmol) and LTA (377 mg, 0.85 mmol) at −20 °C. The cold solution was added to a solution of zirconium(IV) *tert*-butoxide (0.53 cm^3, 1.62 mmol) and methyl acrylate (0.1 cm^3, 1.1 mmol) in dichloromethane stirred at −20 °C (bath temp.). After stirring the solution for 2 min its temperature was allowed to reach ambient by removal of the

cooling bath before it was shaken with aqueous saturated ammonium chloride (20 cm^3), the organic layer separated from the white gelatinous precipitate and washed successively with saturated aqueous sodium hydrogen carbonate and brine (2 × 5 cm^3) and then dried. Evaporation of solvent under reduced pressure gave **18** (144 mg, 56%). Crystallization yielded 3-*tert*-*butoxyaminoquinazolinone* **18** as a colourless solid (from light petroleum), mp 112–114 °C (Found MH^+, 320.1974. $C_{17}H_{26}N_3O_3$ requires MH^+, 320.1974); ν_{max}/cm^{-1} 2960 m, 1690 s and 1600 s; δ_H 0.91 [9H, s, C(CH_3)$_3$], 1.27 [9H, s, OC(CH_3)$_3$], 3.65 (1H, d, *J* 9.8, O*H*), 5.05 (1H, d, *J* 9.8, C*H*OH), 7.37 [1H, unresolved ddd, *J* 1.3 and 8.2 visible, 6-*H*(Q)], 7.58 [1H, dd, *J* 1.3 and 7.6, 8-*H*(Q)], 7.66 [1H, unresolved ddd, *J* 1.3 and 8.2 visible, 7-*H*(Q)], 8.16 [1H, d, *J* 7.9, H-5(Q)] and 8.78 (1H, s, N*H*); δ_C 25.8, 27.2 [2 × C(*C*H_3)$_3$], 37.4 [*C*(CH$_3$)$_3$], 73.9 (*C*HOH), 77.8 [O*C*(CH$_3$)$_3$], 120.4 [*C*CO(Q)], 127.0, 127.1, 127.3, 134.9 [4 × *C*H(Q)], 163.9 (*C*N=C), 157.5 (*C*N) and 160.8 (*C*O); *m*/*z* 320 (MH^+, 22%), 233 (100), 215 (31) and 160 (46).

(e) With Q^{2}NHOAc 10 and triisopropyl borate. A solution of 3-acetoxyaminoquinazolinone **10** in dry dichloromethane (4 cm^3) was prepared as described previously (general procedure A) from **9** (200 mg, 0.81 mmol) and LTA (377 mg, 0.85 mmol) at −20 °C and added to a solution of triisopropyl borate (304 mg, 1.62 mmol) and methyl acrylate (0.1 cm^3, 1.1 mmol) in dichloromethane (1 cm^3) stirred at −20 °C (bath temp.). After stirring the solution for 2 min its temperature was allowed to reach ambient by removal of the cooling bath before it was shaken with saturated aqueous ammonium chloride (20 cm^3), the organic layer separated from the white gelatinous precipitate and washed successively with saturated aqueous sodium hydrogen carbonate and brine (2 × 5 cm^3) and then dried. Evaporation of solvent under reduced pressure gave 3-*isopropoxyaminoquinazolinone* **13** as a colourless gum which was not purified further (186 mg, 75%) (Found MH^+, 306.1818. $C_{16}H_{24}N_3O_3$ requires MH^+, 306.1818); ν_{max}/cm^{-1} 3480 m, 3230 m, 1690 s and 1600 s; δ_H 0.92 [9H, s, C(CH_3)$_3$], 1.06 (3H, d, *J* 6.0, CH_3CHCH$_3$), 1.26 (3H, d, *J* 6.0, CH$_3$CH*C*H$_3$), 3.61 (1H, d, *J* 10.0, O*H*), 4.17 [1H, septet, *J* 6.0, C*H*(CH$_3$)$_2$], 5.00 (1H, d, *J* 10.0, C*H*OH), 7.42 [1H, unresolved ddd, *J* 1.0 and 8.0 visible, 6-*H*(Q)], 7.62 [1H, dd, *J* 1.0 and 8.0, 8-*H*(Q)], 7.71 [1H, unresolved dd, *J* 1.0 and 8.0 visible, 7-*H*(Q)], 8.21 [1H, dd, *J* 1.0 and 8.0, 5-*H*(Q)] and 8.85 (1H, s, N*H*); δ_C 21.2, 21.3 (*C*H$_3$CH*C*H$_3$), 25.8 [C(*C*H$_3$)$_3$(Q)], 36.2 [*C*(CH$_3$)$_3$], 73.7, 74.2 [*C*HOH, O*C*H(CH$_3$)$_2$], 120.4 [*C*CO(Q)], 127.0, 126.9, 126.4, 134.9 [4 × *C*H(Q), 145.8 [*C*N=C(Q)], 157.3 [*C*=N(Q)] and 160.6 [*C*O(Q)]; *m*/*z* 306 (MH^+, 18%), 233 (100), 215 (31) and 160 (41).

Aziridination of *tert*-butyl acrylate

(a) With Q^{2}NHOAc 10. A solution of 3-acetoxyaminoquinazolinone **10** in dichloromethane (4 cm^3) was prepared as described previously (general procedure A) from **9** (200 mg, 0.81 mmol) and LTA (377 mg, 0.85 mmol) at −20 °C and *tert*-butyl acrylate (0.14 cm^3, 0.96 mmol) added. The solution was stirred for 2 min at −20 °C (bath temp.) before the cooling bath was removed and the temperature allowed to reach ambient. Standard work-up (general procedure B) gave a brown residue (241 mg) whose ^{1}H NMR spectrum showed it to consist of a 1:1.1 mixture of aziridine diastereoisomers **24a** and **24b** (51%) (by integral comparison of signals at δ 2.60 and 2.50 respectively) and 3*H*-quinazolinone **22** (23%). For **24b** (observable signals) δ_H 1.06 [9H, s, C(CH_3)$_3$], 1.49 [9H, s, OC(CH_3)$_3$], 2.50 (1H, d, *J* 4.1, C*H*H *cis* to ester), 3.76 (1H, d, *J* 7.3, CH*H trans* to ester) and 4.44 (1H, dd, *J* 4.1 and 7.3, C*H*CO$_2$).

(b) With Q^{2}NHOAc 10 and titanium(IV) *tert*-butoxide. A cold (−20 °C) solution of 3-acetoxyaminoquinazolinone **10** in dichloromethane (4 cm^3) was prepared as described previously (general procedure A) from **9** (200 mg, 0.81 mmol) and LTA (377 mg, 0.85 mmol) and added to a stirred solution of titanium(IV) *tert*-butoxide (548 mg, 1.62 mmol) and *tert*-butyl acrylate (0.14 cm^3, 0.96 mmol) in dry dichloromethane (1 cm^3) maintained at −20 °C (bath temp.). After stirring for 2 min the cooling bath was removed and the temperature of the reaction mixture allowed to reach ambient. Standard work-up (general procedure C) gave a brown residue (251 mg) whose NMR spectrum showed it to consist of a single aziridine diastereoisomer **24a** together with 3-*tert*-butoxyaminoquinazolinone **18** (26%). Crystallization of the crude product gave the *aziridine* **24a** (160 mg, 53%) as colourless needles, mp 156–157 °C (from ethanol) (Found: C, 64.25; H, 7.3; N, 11.15. $C_{20}H_{27}N_3O_4$ requires C, 64.35; H, 7.3; N, 11.25%); $[a]_D$ 262.9 (*c* 1.2, chloroform); ν_{max}/cm^{-1} 3480 w, 1735 s, 1680 s and 1600 s; δ_H 1.07 [9H, s, C(CH_3)$_3$], 1.52 [9H, s, CO$_2$C(CH_3)$_3$], 2.60 (1H, d, *J* 4.4 C*H*H *cis* to ester), 3.83 (1H, d, 7.5, CH*H trans* to ester), 4.04 [1H, dd, *J* 4.4 and 7.5, C*H*CO$_2$C(CH$_3$)$_3$], 5.22 (1H, s, C*H*OH), 7.45 [1H, structured m, 6-*H*(Q)], 7.70 [2H, structured m, 8-*H*, 7-*H*(Q)], 8.15 [1H, d, *J* 7.8, 5-*H*(Q)]; δ_C 26.2, 28.0 [2 × C(*C*H$_3$)$_3$], 33.7 (*C*H$_2$), 37.7 [*C*(CH$_3$)$_3$], 38.8 (*C*HCO$_2$), 74.7 (*C*HOH), 82.5 [O*C*(CH$_3$)$_3$], 121.5 [*C*CO(Q)], 126.3, 127.0, 127.1, 134.5 [4 × *C*H(Q)], 144.8 (*C*N=C), 159.2 [*C*=N(Q)], 161.0 [*C*O(Q)] and 167.6 (*C*O$_2$Bu^t); *m*/*z* 374 (MH^+ 100%), 318 (72), 260 (28), 215 (22) and 175 (48). A crystal suitable for X-ray structure determination was grown from ethanol and showed the absolute configuration at the aziridine ring centre to be *R* (Fig. 1).

Aziridination of methyl methacrylate

(a) With Q^{2}NHOAc 10. Methyl methacrylate (0.11 cm^3, 1.03 mmol) was added to a solution of 3-acetoxyaminoquinazolinone **10** in dichloromethane (4 cm^3), prepared as described previously (general procedure A) from **9** (200 mg, 0.81 mmol) and LTA (377 mg, 0.85 mmol) at −20 °C. The solution was stirred at this temperature for a further 2 min before being allowed to reach ambient temperature. Standard work-up (general procedure B) gave a brown residue (231 mg) whose ^{1}H NMR spectrum showed it to consist of a 1:1.8 mixture of aziridine diastereoisomers **27a** and **27b** (79%), by comparison of signals at δ 3.05 and 2.94 ppm respectively (see below). δ_H major diastereoisomer **27b** 0.93 [9H, s, C(CH_3)$_3$], 1.68 (3H, s, CH_3), 2.94 (1H, d, *J* 3.0, C*H*H), 3.47 (1H, d, *J* 3.0, CH*H*), 3.51 (1H, d, *J* 10.1, O*H*), 3.56 (3H, s, CO$_2$CH_3), 4.49 (1H, d, *J* 10.1, C*H*OH), 7.38 [1H, structured m, 6-*H*(Q)], 7.61 [2H, structured m, 7-*H*, 8-*H*(Q)] and 8.16 [1H, dd, *J* 1 and 7.9, 5-*H*(Q)].

(b) With Q^{2}NHOAc 10 and titanium(IV) *tert*-butoxide. A cold (−20 °C) solution of 3-acetoxyaminoquinazolinone **10** in dichloromethane (4 cm^3) was prepared as described above from **9** (200 mg, 0.81 mmol) and LTA (377 mg, 0.85 mmol) and added to a stirred solution of titanium(IV) *tert*-butoxide (548 mg, 1.62 mmol) and methyl methacrylate (0.11 cm^3, 1.03 mmol) in dry dichloromethane (1 cm^3) held at −20 °C (bath temp.). After stirring for 2 min the cooling bath was removed and the temperature of the reaction mixture allowed to reach ambient. Standard work-up (general procedure C) gave a pale brown residue (193 mg) whose NMR spectrum showed it to consist of a 5.9:1 ratio of aziridine diastereoisomers **27a** and **27b** (43%) together with 3-*tert*-butoxyaminoquinazolinone **18** (28%). Crystallization of the crude product gave the major *aziridine diastereoisomer* **27a** as colourless crystals, mp 169–171 °C (from ethanol) (Found: C, 62.5; H, 6.7; N, 12.1. $C_{18}H_{23}N_3O_4$ requires C, 62.6; H, 6.7; N, 12.2%); $[a]_D$ 262.1 (*c* 1.03, ethanol); ν_{max}/cm^{-1} 3400 w, 1740 s, 1675 s and 1590 s; δ_H (1.3:1 ratio of *N*-invertomers) major *N*-invertomer 0.91 [9H, s, C(CH_3)$_3$], 1.35 (3H, s, CH_3), 3.06 (1H, d, *J* 3.1, C*H*H), 3.35 (1H, d, *J* 3.1, CH*H*), 3.66 (1H, d, *J* 10.4, O*H*), 3.77 (3H, s, CO$_2$CH_3), 4.57 (1H, d, *J* 10.4, C*H*OH), 7.74–7.14 [3H, structured m, 6-*H*, 8-*H*, 7-*H*(Q)] and 8.13 [1H, dd, *J* 1.2 and 8.5, 5-*H*(Q)]; *m*/*z* 346 (MH^+, 100%), 288 (20) and 259 (20). A crystal suitable for X-ray structure determination was grown from ethanol and showed the absolute configuration at the aziridine ring centre to be *R* (Fig. 2).

Table 4

Molecule	**24a**	**27a**
Molecular formula	$C_{20}H_{26}N_3O_4$	$C_{18}H_{23}N_3O_4$
Molecular weight	372.44	345.39
Crystal size	0.75 × 0.53 × 0.08	0.72 × 0.26 × 0.24
Crystal system	orthorhombic	orthorhombic
Space group	$P2_12_12_1$	$P2_12_12_1$
a/Å	9.568(2)	8.787(1)
b/Å	10.047(2)	10.615(1)
c/Å	20.745(2)	18.735(4)
U/Å	1994.2(6)	1747.5
Z	4	4
D_c/g cm^{-3}	1.240	1.313
F(000)	796	736
μ/mm^{-1}	0.087	0.094
2θ range (°)	5.6 to 45	5 to 48
No. reflections:		
measured	2053	2106
observed	1546	1686
R_1	0.0445	0.0347
wR_2 (all data)	0.1119	0.0882
No. parameters refined	244	229
$\Delta\rho$/e A^{-3}	+0.274, −0.161	+0.126, −0.151

Hydrolysis of aziridine methyl ester 23a

Aziridine **23a** (150 mg, 0.45 mmol) was suspended in a rapidly stirred solution of 1:1 ethanol–water (4 cm^3) and sodium hydroxide (18 mg, 0.45 mmol) in water (1 cm^3) added. The aziridine gradually dissolved and after 15 min the clear solution was extracted with ethyl acetate (3 × 5 cm^3), the aqueous solution acidified with dilute sulfuric acid and the resulting white suspension extracted with ethyl acetate (3 × 5 cm^3). The combined organic extracts from the acidified solution were dried and the solvent removed under reduced pressure to give the *aziridine* 2-*carboxylic acid* **25** (126 mg, 88%) as a colourless oil (Found: MH$^+$, 318.1454. $C_{16}H_{20}N_3O_4$ requires MH^+, 318.1453); ν_{max}/cm^{-1} 3450 w, 1670 s and 1595 s; δ_H 1.08 [9H, s, C(CH_3)$_3$], 2.63 (1H, d, J 3.8, CHH *cis* to CO_2H), 4.05 (1H, d, J 7.5, CHH *trans* to CO_2H), 4.09 (1H, dd, J 3.8 and 7.5, CHCO$_2$H), 5.38 (1H, s, CHOH), 6.70 (2H, br s, CO_2H, OH), 7.45 [1H, br. ddd, J 7 and 8 visible, 6-H(Q)], 7.70 [2H, structured m, 7-H, 8-H(Q)] and 8.14 [1H, br d, J 7.8, 5-H(Q)]; m/z 635 [(2MH$^+$)$^+$, 49%], 318 (MH$^+$, 100), 215 (34) and 175 (45).

Hydrolysis of aziridine *tert*-butyl ester 24a

Aziridine **24a** (150 mg, 4.02 mmol) was suspended in a solution of 1:1 ethanol–water (4 cm^3) and a solution of sodium hydroxide (16 mg, 4.02 mmol) in water (1 cm^3) added. After stirring for 5 days at room temperature the solution was extracted with ethyl acetate (3 × 5 cm^3), the aqueous solution acidified with dilute sulfuric acid and re-extracted with ethyl acetate (3 × 5 cm^3). The combined organic extracts from the acidified solution were dried and solvent removed under reduced pressure to give acid **25** (72 mg, 56%) identical with that prepared previously by comparison of their NMR spectra.

The diastereoisomeric aziridine methyl ester **23b** (150 mg, 0.45 mmol) was hydrolysed under identical conditions to those conditions above to give *aziridine* 2-*carboxylic acid* **26** (127 mg, 88%) (Found: MH$^+$, 318.1454. $C_{16}H_{20}N_3O_4$ requires MH^+, 318.1454); δ_H 1.04 [9H, s, C(CH_3)$_3$], 2.74 (1H, br d, J 3.5, CHH *cis* to CO_2H), 3.59 (1H, d, J 7.3, CHH *trans* to CO_2H), 4.23 (1H, br s, CHCO$_2$H), 5.12 (1H, br s, CHOH), 6.52 (2H, br s, 2 × OH), 7.48 [1H, br dd, J ~7.5 and 7.5, 6-H(Q)], 7.66 [1H, br d, J ~7.5, 8-H(Q)], 7.75 [1H, br dd, J ~7.5 and 7.5, 7-H(Q)] and 8.17 [1H, d, J 7.6, 5-H(Q)]; δ_C 26.0 [C(CH_3)$_3$], 35.3 (CH_2), 37.4 [C(CH$_3$)$_3$], 38.0 (CHCO$_2$H), 76.6 (CHOH), 120.9 [CCO(Q)], 126.1, 126.6, 127.0, 134.4 [4 × CH(Q)], 144.5 [CN=C(Q)], 157.5 [C=N(Q)], 160.8 [CO(Q)] and 171.2 (CO$_2$H); m/z 635 [(2M + H)$^+$, 9%], 318 (MH$^+$, 100) and 260 (20).

X-Ray analysis

Crystals of **24a** and **27a** were obtained by crystallisation from ethanol.

Data for **24a** and **27a** were measured on a Siemens P4 diffractometer with ω-scan technique, graphite monochromated Mo-Kα radiation at 190 K. Crystal data and a summary of the experimental details are listed in Table 4. The structures were solved by direct methods and refined by full-matrix least squares on F^2 using the program SHELXTL/PC.[19] Hydrogen atoms were included in calculated positions (C–H = 0.96 Å) for carbon-bonded H atoms; the hydroxy H atoms for both **24a** and **27a** were located from difference Fourier maps. The H atom displacement parameters were set to 1.2 U_{eq}(C) or 1.5 U_{eq} for methyl and hydroxy H. All non-hydrogen atoms were refined with anisotropic displacement parameters.

Full crystallographic details, excluding structure factor tables, have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc.*, *Perkin Trans. 1*, available *via* the RSC Web page (http://www.rsc.org/authors). Any request to the CCDC for this material should quote the full literature citation and the reference number 207/245.

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