Chiral Aziridination of α,β-Unsaturated Esters and Ketones Using *N*-Nitrenes in the Presence of Trifluoroacetic Acid

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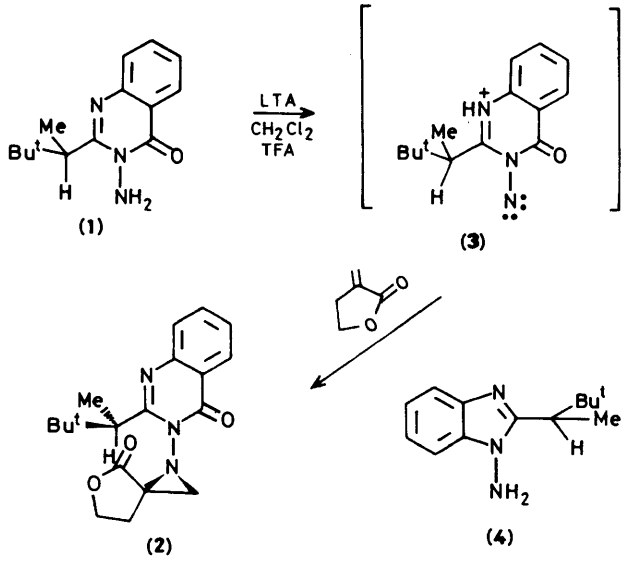
Aziridination of various α,β-unsaturated esters and α,β-unsaturated ketones has been studied using the *N*-nitrene generated by oxidation of 3-amino-2-(1,2,2-trimethylpropyl)quinazolin-4(3*H*)-one (**1**) with lead tetra-acetate in dichloromethane at room temperature. The stereoselectivity of this aziridination is greatly increased by the addition of trifluoroacetic acid before the oxidation of the aminoquinazolinone (**1**). The presence of trifluoroacetic acid has two additional advantages in these aziridinations: (a) it allows the reaction to be carried out at −60 °C with the expected increase in stereoselectivity; and (b) the alkene can be used in molar equivalent amounts with little loss of yield of aziridine. For example, aziridination of methyl acrylate (1.1 mol equiv.) at −60 °C with the *N*-nitrene derived from compound (**1**) (1 mol equiv.) gave the aziridine stereoisomers (**5**) (ratio 23:1) in 65% isolated yield.

In the previous paper,[1] oxidative addition of the *N*-aminoquinazolinone (**1**) to α-methylene-γ-butyrolactone was reported to proceed with complete asymmetric induction in the presence of trifluoroacetic acid. The only aziridine stereoisomer obtained was shown to be compound (**2**) by *X*-ray crystallography.[2]

We were encouraged to study the aziridination of a range of alkenes with the *N*-nitrene (**3**) which is presumed to be the intermediate in the oxidation of the *N*-aminoquinazolinone (**1**) because of the ready availability of the latter, particularly by comparison with the analogous *N*-aminobenzimidazole (**4**).[2]



Oxidation of compound (**1**) in the presence of various α,β-unsaturated esters and α,β-unsaturated ketones (4 mol equiv.) was carried out with lead tetra-acetate (LTA) in dichloromethane containing trifluoroacetic acid (3.4 mol equiv.) at room temperature to give, in each case, the mixtures of stereoisomers shown in Table 1. For comparison, Table 1 also shows the ratio of stereoisomers obtained when the oxidation was carried out in the absence of TFA.

The absence of significant stereoselectivity in these additions in the absence of TFA is ascribed to a transition state geometry for reaction of the nitrene with the alkene as shown in Figure 1.[2] In this transition state, the interaction of the chiral substituent

Table 1. Ratios of stereoisomeric aziridines obtained from oxidation of the *N*-aminoquinazolinone (**1**) in the presence of various alkenes (4 mol equiv.) at room temperature (except entry 2) as measured from n.m.r. spectra of the crude oxidation products

Entry	Alkene	Aziridine stereoisomer ratio without TFA	Aziridine stereoisomer ratio with TFA	Yield
1	CH_2=$CHCO_2Me$	(**5**) 2.4:1	(**5**) 1:8.7	(72) 50%
2	CH_2=$CHCO_2Me$		(**5**) 1:23	(72) 64%[a]
3	CH_2=$CHCO_2Bu^t$	(**6**) 2.1:1	(**6**) 14:1	(75) 39%
4	CH_2=$CMeCO_2Me$	(**7**) 1.2:1	(**7**) 1:5.2	(72) 46%
5	MeCH=$CHCO_2Me$	(**8**)	(**8**) 7.0:1	(78) 58%
6	CH_2=CHCOMe	(**9**) 1.25:1	(**9**) 1:6.5	(78) 62%
7	MeCH=CHCOMe	(**10**) 1.2:1	(**10**) 8.6:1	(82) 52%

[a] 1.1 mol equiv. alkene, −60 °C, 6 mol equiv. TFA.

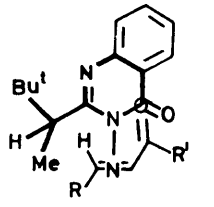


Figure 1.

with HCR= is apparently ineffective in distinguishing between the two faces of the alkene.

The presence of TFA is presumed to bring about a change in this transition state geometry to that shown in Figure 2 by

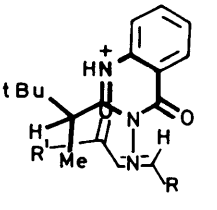


Figure 2.

augmenting the secondary interaction[3] between the carbonyl group on the alkene and the C=N of the quinazolinone through protonation of the latter on N-1 (Figure 2). The isolated yields

Table 2. Ratios of aziridine invertomers as measured from n.m.r. spectra of separated stereoisomers or mixtures of stereoisomers at 300 MHz. *syn/anti* Refers to the ester/ketone—quinazolinone relationship. A value of >30:1 indicates that only a single invertomer was visible. Assignments (*syn/anti*) were based on shielding-deshielding effects described previously*

Aziridine	Major stereoisomer	Minor stereoisomer
(7) CH_2=$CMeCO_2Me$	1.3:1 *syn:anti*	>30:1 *syn:anti*
(8) MeCH=$CHCO_2Me$	*ca.* 16:1 *syn:anti*	5:1 *syn:anti*
(10) MeCH=CH_2COMe	>30:1 *syn:anti*	*ca.* 1.1:1 *anti:syn*

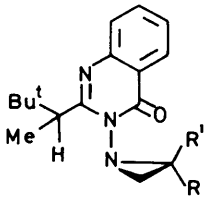
* D. J. Anderson, D. C. Horwell, and R. S. Atkinson, *J. Chem. Soc. C*, 1971, 624.

of products in Table 1 refer to those of the pure major stereoisomer, and the losses which have occurred in some cases by comparison with yields of the crude product (in brackets; includes both stereoisomers) are either the result of neglect of mixed fractions on chromatography (entries 1 and 7) or direct crystallisation of the crude product without any attempt to recover further material from the mother liquor (entries 3 and 4).

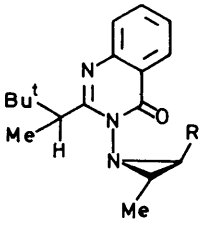
Measurement of these stereoisomer ratios in Table 1 was carried out on the crude reaction product at 300 MHz. Although there was invariably some coincidence of the respective signals from both stereoisomers, there was also, in each case, separated signals from the latter which allowed the ratios of the two to be calculated.

The relative configuration of the two chiral centres is not known for any of the aziridines in Table 1, but there are correlations between stereoisomer ratios which bear on this question. Thus, there is a close correspondence between the stereoisomer ratios produced in the absence of TFA with methyl acrylate and t-butyl acrylate (entries 1 and 3) as would be expected if both proceed *via* transition states analogous to that shown in Figure 1 (R = H, R^1 = OMe, OBu^t). However, whereas for methyl acrylate, the *minor* stereoisomer from the reaction in the absence of TFA becomes the *major* stereoisomer in the presence of TFA, the reverse is the case for t-butyl acrylate. This strongly suggests that the sense of the induction from addition of the protonated *N*-nitrene (**3**) to methyl acrylate is the opposite to that from addition to t-butyl acrylate, *i.e.* that the major stereoisomers produced in the two cases do not have the same relative configurations at both their chiral centres.

Further assistance to assignment of relative configuration to the aziridines (**7**), (**8**), and (**10**) in Table 1 comes from examination of the surprisingly different invertomer ratios for the two stereoisomers of each of the latter (Table 2).

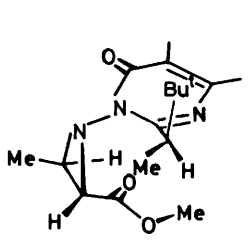


(**5**) R = CO_2Me, R^1 = H
(**6**) R = CO_2Bu^t, R^1 = H
(**7**) R = CO_2Me, R^1 = Me
(**9**) R = COMe, R^1 = H

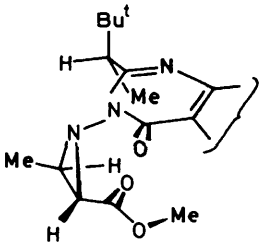


(**8**) R = CO_2Me
(**10**) R = COMe

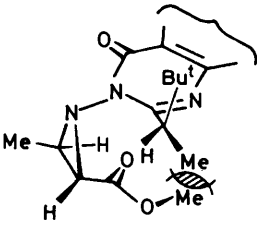
The two preferred rotamers around the N–N bonds in these aziridines may be assumed to be those in which the lone pairs are eclipsed.[1,4] The *syn*-invertomer of *e.g.* compound (**8**), therefore, may be represented as (**8a**)⇌(**8b**) in one stereoisomer and (**8c**)⇌(**8d**) in the other. It is assumed that the preferred conformation of the ester function in structures (**8a**)—(**8d**) is close to that depicted, but the analysis below would also hold for the conformation in which the ester was rotated through 180° around the aziridine–CO bond.



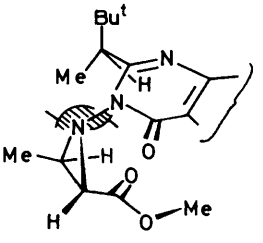
(**8a**)



(**8b**)



(**8c**)



(**8d**)

As indicated in structures (**8c**) and (**8d**), non-bonded interactions are expected to be more severe than in (**8a**) and (**8b**) and consequently, population of the anti-invertomer will be more likely for the former than the latter. On this basis, therefore, the major stereoisomer may be assumed to be that shown in (**8a**)⇌(**8b**) and the same relative configuration would be expected for the major stereoisomer of compound (**5**). Similar arguments may be used to predict the relative configurations in the major stereoisomers of compounds (**7**) and (**10**), but confirmation must await *X*-ray structure determinations.

An obvious means of improving the stereoisomer ratios in Table 1 would be to carry out the reactions at lower temperatures. Lead tetra-acetate is only sparingly soluble in dichloromethane at less than −30 °C and the rate of dissolution at this temperature is also very slow (*i.e.* when the dissolved material is being consumed). This lack of solubility necessitates the use of larger volumes of dichloromethane which results in less efficient trapping of the nitrene for the same number of mole equivalents of the alkene trap. However, we find that LTA is markedly more soluble at room temperature in dichloromethane which contains TFA, and these solutions containing sufficient TFA* are homogeneous at temperatures (−78 °C) where crystallisation takes place in its absence.

The exact nature of the ligands on the lead in dichloromethane solutions of lead tetra-acetate containing TFA is not at present known. Lead tetra(trifluoroacetate) is an isolable material which, not surprisingly, is more powerful as an oxidising agent than lead tetra-acetate.[5] If any exchange of acetate ligands by trifluoroacetate occurs on the addition of trifluoroacetic acid described above then an increase in oxidising ability of the resultant lead(IV) species would be anticipated.† Experiments using starch iodide paper suggest that oxidation of *N*-aminoquinazolinone (**1**) with LTA in dichloromethane [*ca.*

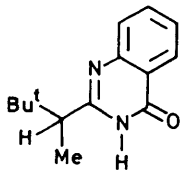
* Minimum 6 mol equiv.

† Protonation of the acetate ligand before or during the oxidation may increase the oxidising ability of the LTA, even in the absence of ligand exchange.

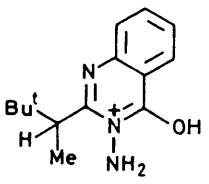
0.5M solutions of LTA and (**1**)] containing TFA proceeds slowly at −60 °C and it is likely that this oxidation will proceed more slowly, if at all, in the absence of TFA at this temperature.*

The variation in stereoselectivity at lower temperature was examined using methyl acrylate as the trap. Simultaneous but slow addition of solutions of LTA, dissolved in TFA–dichloromethane, and the *N*-aminoquinazolinone (**1**) also dissolved in TFA–dichloromethane (6 mol equiv. of TFA in total) to a solution of methyl acrylate (1.1 mol equiv.) in dichloromethane cooled to −60 °C gave a 64% isolated yield of the aziridine (**5**) containing a 20:1 ratio of stereoisomers.

In the above reaction, the solution remains homogeneous at all times. No lead di-acetate is precipitated as is the case in the absence of TFA. However, when a similar oxidation to that above was carried out using 1.1 mol equiv. of methyl acrylate and only 3.4 mol equiv. of TFA (in total) at −60 °C, a substantial amount of solid material was evident in the solution at −60 °C and the latter became homogeneous only on warming above −30 °C: less than 5% of the aziridine (**5**) was obtained and the major product was the deaminated quinazolinone (**11**).



(**11**)



(**12**)

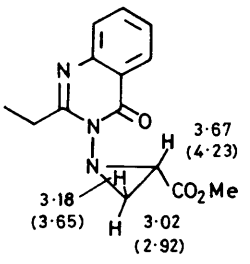
The importance of adding sufficient TFA at these low temperatures was shown by carrying out the same oxidation, adding the aminoquinazolinone (**1**) in dichloromethane to a solution of LTA in the latter containing 10 mol equiv. of TFA. The solution remained homogeneous throughout and the aziridine (**5**) was, from the n.m.r. spectrum of the crude reaction mixture, the only product formed (65% isolated).

Experiments carried out at room temperature using 1.1 mol equiv. of the alkene, with and without TFA, but using otherwise identical conditions strongly suggest that protonation of the quinazolinone stabilised this ring towards intramolecular attack by its attached nitrene. Thus the yield of aziridine drops from 65% to <20% when TFA is omitted from the oxidation. (The stereoselectivity also decreases, see Table 1.)

The isolation of the aziridine (**5**) (65%) from a reaction using *ca.* equimolar quantities of trap (methyl acrylate) and nitrene precursor [the aminoquinazolinone (**1**)] is without precedent in nitrene chemistry (including that of *N*-nitrenes) and is of obvious importance if aziridination of scarce or expensive alkenes and/or ease of isolation of product is taken into account.

Our rationalisation of the superior induction brought about by addition of TFA in these aziridinations (Table 1) has assumed protonation on the quinazolinone N-1 (Figure 2). Protonation of the aminoquinazolinone (**1**) and thus the derived *N*-nitrene (**3**) on the amide carbonyl oxygen might also have come into consideration since this would produce the aromatic quinazolinium species (**12**).

The different sense of induction brought about in the addition of the nitrene from the oxidation of compound (**4**) (without TFA present) and compound (**1**) (with TFA present) in the presence of α-methylene-γ-butyrolactone was interpreted in terms of protonation at N-1.[1] However, the n.m.r. spectrum of the aziridine (**13**) in deuteriochloroform containing TFA suggested that protonation on the amide carbonyl oxygen in this molecule is at least competitive with that at N-1. Thus the chemical shifts of the aziridine ring protons shown in structure (**13**) are shifted downfield to the positions indicated in brackets on addition of TFA. It is clear that the two aziridine ring hydrogens *cis* to the quinazolinone ring experience significantly greater deshielding than the one which is *anti*. This is in agreement with the presence of a ring current in the quinazolinone ring [*cf.* (**12**)] bringing about selective deshielding of the two *cis*-aziridine ring protons. Although the relative basicities of the quinazolinone *N*-1 and carbonyl oxygen would not be expected to differ significantly in the axiridine (**13**) and the *N*-aminoquinazolinone (**1**), it is not clear that this will necessarily be the case in the *N*-nitrene (**3**) derived from the latter. Thus it is conceivable that, even if the *N*-aminoquinazolinone were protonated on oxygen, deprotonation and reprotonation at N-1 could occur after formation of the nitrene but before its addition to the alkene.



(**13**)

Experimental

For general experimental details see references 1 and 2. N.m.r. spectra were measured at 300 MHz in $CDCl_3$ solutions unless otherwise indicated. t-Butyl acrylate (FLUKA) was used as received.

Oxidation of 3-Amino-2-(1,2,2-trimethylpropyl)quinazolin-4(3H)-one (**1**) *in the Presence of Alkenes.*—This was carried out at room temperature (a) in the absence of trifluoroacetic acid (TFA) and (b) in the presence of trifluoroacetic acid, using the conditions described previously in each case.[1]

(i) *Using t-butyl acrylate.* Procedure (b) was followed using the *N*-aminoquinazolinone (**1**) (0.17 g), LTA (0.34 g), t-butyl acrylate (0.36 g), and TFA (0.27 g) in dry dichloromethane (1.7 ml). Crystallisation of the crude product from ethanol gave the major stereoisomer of 3-(2-*t-butoxycarbonylaziridin*-1-*yl*)-2-(1,2,2-*trimethylpropyl*)*quinazolin*-4(3H)-*one* (**6**) as a colourless solid (0.1 g, 39%), m.p. 124—125 °C (Found: C, 67.75; H, 7.85; N, 11.15. $C_{21}H_{29}N_3O_3$ requires C, 67.9; H, 7.85; N, 11.3%); δ (major stereoisomer: major invertomer with ester/quinazolinone *trans*) 8.17 (ddd, *J* 8, 1.5 and 0.6 Hz, 5-H), 7.68 (ddd, *J* 8.3, 6.8, and 1.5 Hz, 7-H), 7.63 (ddd, *J* 8.3, 1.5, and 0.6 Hz, 8-H), 7.39 (ddd, *J* 8, 6.8, and 1.5 Hz, 6-H), 3.55 (q, *J* 7 Hz, C*H*Me), 3.23—3.00 (m, 3 aziridine H), 1.54 (s, CO_2Bu^t), 1.41 (d, *J* 7 Hz, CH*Me*), and 1.01 (s, Bu^t); signals assigned to the major invertomer with ester/quinazolinone *cis* were present at δ 3.36 (q, *J* 7 Hz, C*H*Me), 1.32 (s, CO_2Bu^t), and 0.99 (s, Bu^t): the ratio of invertomers was *ca.* 16:1; $\nu_{max.}$ 1 725s, 1 670s, 1 590s cm^{-1}; *m/z* (%) 371 (M^+) (5), 315 (88), 259 (26), 187 (21), 174 (100), 173 (53), 159 (48), 131 (30), and 117 (40).

The ratio of major:minor stereoisomers in the n.m.r. spectrum of the crude reaction product was 14:1. An identical oxidation with that above carried out in the absence of TFA [procedure (a)] gave a 2.1:1 ratio of the respective stereoisomers with unobscured signals from the minor stereoisomer at δ 3.83 (q, *J* Hz, C*H*Me), 3.78 (dd, *J* 7.4 and 7.4 Hz, aziridine C*H*CO_2Bu^t, *cis* to quinaz.), 3.27 (d, *J* 7.5 Hz, aziridine C*H*H, *cis*

* There are a number of complications which have prevented unambiguous confirmation of this likelihood.

to quinaz.), 2.71 (d, *J* 4.7 Hz, CH*H trans* to quinaz.), 1.53 (s, CO_2Bu^t), 1.37 (d, *J* 7 Hz, CH*Me*), and 1.04 (s, Bu^t).

(ii) *Using methyl methacrylate.* Procedure (b) was followed using the *N*-aminoquinazolinone (**1**) (0.308 g), LTA (0.613 g), methyl methacrylate (0.503 g), and TFA (0.49 g) in dry dichloromethane (3 ml). Crystallisation of the crude product from ethanol gave the major stereoisomer of 3-(2-*methoxycarbonyl*-2-*methylaziridin*-1-*yl*)-2-(1,2,2-*trimethylpropyl*)*quinazolin*-4(3H)-*one* (**7**) as a colourless solid (0.2 g, 46%), m.p. 123—125 °C (Found: C, 66.5; H, 7.3; N, 12.25. $C_{19}H_{25}N_3O_3$ requires C, 66.45; H, 7.35; N, 12.25%); δ (major stereoisomer, major invertomer with ester/quinazolinone *cis*) 8.25—7.34 (m, 5-, 6-, 7-, and 8-H), 3.52 (s, CO_2Me), 3.32 (q, *J* 7 Hz, C*H*Me), 2.96 (d, *J* 0.7 Hz, aziridine C*H*H, *cis* to quinaz.), 2.84 (d, *J* 0.7 Hz, aziridine CH*H*, *trans* to quinaz.), 1.82 (s, aziridine Me), 1.45 (d, *J* 7 Hz, CH*Me*), and 1.01 (s, Bu^t); δ (major stereoisomer, minor invertomer with ester/quinazolinone *trans*) 8.25—7.34 (m, 5-, 6-, 7-, and 8-H), 3.84 (s, CO_2Me), 3.47 (d, *J* 3 Hz, aziridine C*H*H, *cis* to quinaz.), 3.20 (d, *J* 3 Hz, aziridine CH*H*, *trans* to quinaz.), 3.17 (q, *J* 6.9 Hz, C*H*Me), 1.42 (d, *J* 6.9 Hz, CH*Me*), 1.36 (s, aziridine Me), and 0.95 (s, Bu^t); $\nu_{max.}$ 1 730s, 1 660s, and 1 610 cm^{-1}; *m/z* (%) 343 (M^+) (4), 287 (100), 174 (54), 159 (94), 131 (70), 130 (41), 117 (79), and 77 (22). The ratio of major:minor stereoisomers in the n.m.r. spectrum of the crude reaction product was 5.2:1.

An identical oxidation carried out in the absence of TFA [procedure (a)] gave a 1:1.2 ratio of the respective stereoisomers with δ (minor stereoisomer, single invertomer with ester/quinazolinone *cis*) 8.25—7.34 (m, 5-, 6-, 7-, and 8-H), 3.58 (d, *J* 2.6 Hz, aziridine C*H*H *cis* to quinaz.), 3.55 (s, CO_2Me), 3.18 (q, *J* 7 Hz, C*H*Me), 3.03 (d, *J* 2.6 Hz, aziridine CH*H*, *trans* to quinaz.), 1.75 (s, aziridine Me), 1.24 (d, *J* 7 Hz, CH*Me*), and 1.02 (s, Bu^t).

(iii) *Using methyl crotonate.* Procedure (b) was followed using the *N*-aminoquinazolinone (**1**) (0.32 g), LTA (0.64 g), methyl crotonate (0.523 g), and TFA (0.506 g) in dry dichloromethane (3 ml). Chromatography of the crude product over silica eluting with ethyl acetate–light petroleum (1:1.5) gave the minor stereoisomer of 3-(2-*methoxycarbonyl*-3-*methylaziridin*-1-*yl*)-2-(1,2,2-*trimethylpropyl*)*quinazolin*-4(3H)-*one* (**8**) as an oil (0.015 g); δ (major invertomer, ester/quinazolinone *cis*) 8.26—7.36 (m, 5-, 6-, 7-, and 8-H), 3.64 (s, CO_2Me), 3.61 (dq, *J* 5.7 and 5.0 Hz, aziridine C*H*Me), 3.11 (d, *J* 5 Hz, aziridine C*H*CO_2Me), 3.26 (q, *J* 7 Hz, C*H*MeBu^t), 1.65 (d, *J* 5.7 Hz, aziridine Me), 1.23 (d, *J* 7 Hz, CH*Me*Bu^t), and 0.99 (s, Bu^t); (minor invertomer; unobscured signals) 3.88 (s, CO_2Me), 3.48 (d, *J* 5 Hz, aziridine C*H*CO_2Me), 3.40 (q, *J* 7 Hz, C*H*MeBu^t), 1.32 (d, *J* 5.7 Hz, aziridine Me), 1.45 (d, *J* 7 Hz, CH*Me*Bu^t), and 1.04 (s, Bu^t). The ratio of major:minor invertomers in this minor stereoisomer was 5:1. Further elution with ethyl acetate–light petroleum (1:1.5) gave the major stereoisomer of the *aziridine* (**8**) as colourless crystals (0.26 g, 58%), m.p. 117—119 °C (from ethanol) (Found: C, 66.45; H, 7.4; N, 12.2. $C_{19}H_{25}N_3O_3$ requires C, 66.45; H, 7.35; N, 12.25%); δ (major stereoisomer, major invertomer with ester/quinazolinone *cis*) 8.12 (ddd, *J* 8, 1.5, and 0.7 Hz, 5-H), 7.68 (ddd, *J* 8, 6.3, and 1.5 Hz, 7-H), 7.63 (ddd, *J* 8, 2, and 0.7 Hz, 8-H), 7.38 (ddd, *J* 8, 6.3, and 2 Hz, 6-H), 3.59 (s, CO_2Me), 3.39 (d, *J* 4.7 Hz, aziridine C*H*CO_2Me), 3.22 (q, *J* Hz, C*H*MeBu^t); unobscured signals from the minor invertomer were present at δ 3.86 (s, CO_2Me), 1.34 (d, *J* 5.9 Hz, aziridine Me), 1.40 (d, *J* 7 Hz, CH*Me*Bu^t), and 1.04 (s, Bu^t): the ratio of major:minor invertomers was 16:1; $\nu_{max.}$ 1 735s, 1 665s, and 1 588 cm^{-1}; *m/z* (%) 287 (52), 174 (100), 173 (34), 159 (34), 131 (27), and 117 (33).

The ratio of major:minor stereoisomers in the n.m.r. spectrum of the crude reaction product was 7.0:1.

(iv) *Using methyl vinyl ketone.* Procedure (b) was followed using the *N*-aminoquinazolinone (**1**) (0.102 g), LTA (0.203 g), methyl vinyl ketone (0.146 g), and TFA (0.161 g) in dry dichloromethane (1 ml). Chromatography of the crude product over silica eluting with ethyl acetate–light petroleum (1:1.5) gave the major stereoisomer of 3-(2-*acetylaziridin*-1-*yl*)-2-(1,2,2-*trimethylpropyl*)*quinazolin*-4(3H)-*one* (**9**) as a colourless oil (0.081 g) (Found: M^+ 313.1787. $C_{18}H_{23}N_3O_2$ requires M^+ 313.1790); δ (major stereoisomer) 8.17 (ddd, *J* 8, 1.5 and 0.6 Hz, 5-H), 7.70 (ddd, *J* 8, 6.9, and 1.4 Hz, 7-H), 7.63 (ddd, *J* 8, 1.4, and 0.6 Hz, 8-H), 7.42 (ddd, *J* 8, 6.9, and 1.4 Hz, 6-H), 3.31 (q, *J* 7 Hz, C*H*Me), 3.26 (m, aziridine C*H*–C*H*, *cis* to quinaz.), 3.08 (dd, *J* 3.6 and 0.8 Hz, aziridine C*H*H, *trans* to quinaz.), 2.27 (s, COMe), 1.36 (d, *J* 7 Hz, CH*Me*), and 1.02 (s, Bu^t); $\nu_{max.}$ 1 705s, 1 670s, and 1 590s cm^{-1}. The ratio of major:minor stereoisomers in the n.m.r. spectrum of the crude reaction product was 6.5:1.

An identical oxidation carried out in the absence of TFA [procedure (a)] gave a ratio 1:1.25 for the respective stereoisomers with δ (minor stereoisomer) 8.30—7.38 (m, 5-, 6-, 7-, and 8-H), 3.56 (dd, *J* 8 and 5.4 Hz, aziridine C*H*$COCH_3$), 3.54 (q, *J* 7 Hz, C*H*Me), 2.93 (dd, *J* 5.4 and 1 Hz, aziridine C*H*H *trans* to quinaz.), 2.71 (dd, *J* 8 and 1 Hz, aziridine CH*H cis* to quinaz.), 2.46 (s, CO*Me*) 1.41 (d, *J* 7 Hz, CH*Me*), and 1.01 (s, Bu^t).

(v) *Using pent-3-en-2-one.* Procedure (b) was followed using the *N*-aminoquinazolinone (**1**) (0.103 g), LTA (0.205 g), pent-3-en-2-one (0.141 g), and TFA (0.163 g) in dry dichloromethane (1 ml). Chromatography of the product over silica eluting with ethyl acetate–light petroleum (1:1.5) gave the major stereoisomer of 3-(trans-2-*acetyl*-3-*methylaziridin*-1-*yl*)-2-(1,2,2-*trimethylpropyl*)*quinazolin*-4(3H)-*one* (**10**) as colourless crystals (0.071 g, 52%), m.p. 147—149 °C (from ethanol) (Found: C, 69.6; H, 7.7; N, 12.8. $C_{19}H_{25}N_3O_2$ requires C, 69.7; H, 7.7; N, 12.85%); δ (major stereoisomer, $COCH_3$ and quinazolinone *cis*) 8.08 (ddd, *J* 8, 1.4, and 0.7 Hz, 5-H), 7.80—7.58 (m, 7- and 8-H), 7.36 (ddd, *J* 8, 5.6, 1.4 Hz, 6-H), 3.57 (d, *J* 4.7 Hz, C*H*$COCH_3$), 3.23 (q, *J* 7 Hz, C*H*MeBu^t), 2.92 (dq, *J* 5.7 and 4.7 Hz, aziridine C*H*Me), 2.48 (s, $COCH_3$), 1.60 (d, *J* 5.7 Hz, aziridine Me), 1.46 (d, *J* 7 Hz, C*H*MeBu^t), and 1.00 (s, Bu^t); $\nu_{max.}$ 1 705s, 1 665s, and 1 610 cm^{-1}; *m/z* (%) 284 (15), 271 (56), 228 (22), 174 (100), 159 (43), 131 (37), 117 (42), and 77 (16). The ratio of major:minor stereoisomers in the n.m.r. spectrum of the crude reaction product was 8.6:1.

An identical oxidation carried out in the absence of TFA [procedure (a)] gave a ratio of 1.2:1 for the respective stereoisomers with δ (minor stereoisomer; major invertomer) 8.25—7.32 (m, 5-, 6-, 7-, and 8-H), 3.47—3.33 (m, aziridine C*H*CO_2Me, C*H*MeBu^t); 3.05 (dq, *J* 5.3 and 4.7 Hz, aziridine ring C*H*CH_3, *trans* to quinaz.), 2.42 (s, $COCH_3$), 1.46 (d, *J* 7.2 Hz, CH*Me*Bu^t), *ca.* 1.25 (d, aziridine CH*Me*, *cis* to quinaz.), and 0.99 (s, Bu^t): (minor invertomer) 3.47—3.33 (m, aziridine C*H*CO_2Me, C*H*Me), 3.14 (q, *J* 7 Hz, C*H*MeBu^t), 2.41 (s, $COCH_3$), 1.64 (d, *J* 5.3 Hz, aziridine CH*Me trans* to quinaz.), *ca.* 1.25 (d, CH*Me*Bu^t), and 1.04 (s, Bu^t). The ratio of major:minor invertomers in this minor stereoisomer was *ca.* 1.1:1.

(vi) *Using methyl acrylate.* Procedure (b) was followed using the *N*-aminoquinazolinone (**1**) (0.114 g), LTA (0.227 g), methyl acrylate (0.16 g), TFA (0.18 g) in dry dichloromethane (1 ml). Chromatography of the product over silica, eluting with ethyl acetate–light petroleum (1:2) with combination of those fractions containing the faster running spot of two on t.l.c. at R_F 0.43 gave the major stereoisomer of 3-(2-*methoxycarbonyl*-*aziridin*-1-*yl*)-2-(1,2,2-*trimethylpropyl*)*quinazolin*-4(3H)-*one* (**5**) as a colourless oil (77 mg, 50%) (Found: M^+ 329.1743. $C_{18}H_{23}N_3O_3$ requires M^+ 329.1739); δ (major stereoisomer) 8.15 (ddd, *J* 8, 1.5 and 0.5 Hz, 5-H), 7.68 (ddd, *J* 8, 7, and 1.5 Hz, 7-H), 7.62 (ddd, *J* 8, 1.5, and 0.5 Hz, 8-H), 7.41 (ddd, *J* 8, 7, and 1.5 Hz, 6-H), 3.84 (s, CO_2Me), 3.55 (q, *J* 7 Hz, C*H*Me), 3.40 (dd, *J* 7.7 and 4.8 Hz, aziridine C*H*CO_2Me), 3.33 (dd, *J* 7.6 and 1.4 Hz, aziridine C*H*H *cis* to quinaz.), 3.03 (dd, *J* 4.7 and 1.4 Hz,

aziridine CH*H* trans to quinaz.), 1.37 (d, *J* 7 Hz, CH*Me*), and 1.02 (s, Bu^t); $\nu_{max.}$(film) 1 745s, 1 675s, and 1 590s cm^{-1}; *m/z* (%) 274 (18), 273 (100), 187 (19), 174 (44), 159 (40), 131 (31), 117 (36), and 77 (15). The ratio of major : minor stereoisomers in the above experiment from non-superimposed signals in the n.m.r. spectrum of the crude reaction product was 8.7 : 1.

An identical oxidation carried out in the absence of TFA [procedure (a)] gave a 1 : 2.4 ratio of these same stereoisomers with δ (minor stereoisomer) 8.30—7.36 (m, 5-, 6-, 7-, and 8-H), 3.87 (s, CO_2Me), 3.76 (dd, *J* 8 and 5 Hz, aziridine C*H*CO_2Me, *cis* to quinaz.), 3.72 (q, *J* 7 Hz, C*H*Me), 3.04 (dd, *J* 8 and 1.5 Hz, aziridine C*H*H *cis* to quinaz.), 2.86 (dd, *J* 5 and 1.5 Hz, aziridine CH*H trans* to quinaz.), 1.39 (d, *J* 7 Hz, CH*Me*), and 1.01 (s, Bu^t).

Oxidation of the N-*Aminoquinazolinone* (**1**) *in the Presence of Methyl Acrylate and TFA at* −60 °C.—(i) LTA (2.29 g) was dissolved in dichloromethane (10 ml) containing TFA (5.35 g, 10 mol equiv.) and methyl acrylate (0.44 g, 1.1 mol equiv.) and this solution was cooled to −60 °C. A solution of the *N*-aminoquinazolinone (**1**) (1.15 g) in dichloromethane (8 ml) was then added during 30 min by continuous dropwise addition to the solution above, keeping the temperature at −60 °C. After the solution had been stirred for a further 30 min at this temperature and worked up as usual, an n.m.r. spectrum of the crude product showed signals from the aziridine (**5**) only. Chromatography as described above gave compound (**5**) (1.01 g, 65%) as a mixture (23 : 1) of stereoisomers.

(ii) LTA (4.25 g) was dissolved in dichloromethane (5 ml) containing TFA (1.69 g) and the *N*-aminoquinazolinone (**1**) (2.14 g) was dissolved in dichloromethane (5 ml) containing TFA (1.69 g). Both these solutions were added slowly but continuously dropwise *via* different dropping funnels during 30 min at −60 ° (to methyl acrylate (0.82 g, 1.1 mol equiv.) in dichloromethane (10 ml), ensuring that at all times addition of the LTA solution was ahead of that of the *N*-aminoquinazolone solution. A solid was observable during the addition and the solution only became homogeneous on warming above −30 °C. After the usual work-up, the only product obtained was the de-aminated 2-(1,2,2-*trimethylpropyl*)*quinazolin*-4(3H)-*one* (**11**) (90%), m.p. 147—150 °C (from ethanol) (Found: C, 73.0; H, 8.15; N, 11.95. $C_{14}H_{18}N_2O$ requires C, 73.0; H, 7.9; N, 12.15%); δ (90 MHz) 10.48 (br s, NH), 8.35—7.15 (m, 5-, 6-, 7-, and 8-H), 2.69 (q, *J* 7 Hz, C*H*MeBu^t), 1.40 (d, *J* 7 Hz, CH*Me*), and 1.03 (s, Bu^t); $\nu_{max.}$ 3 180m, 3 120m, and 1 675s cm^{-1}.

(iii) LTA (0.203 g) was dissolved in dry dichloromethane (0.25 ml) containing TFA (0.143 g) and the *N*-aminoquinazolinone (**1**) (0.102 g) was dissolved in dry dichloromethane (0.25 ml) containing TFA (0.143 g) (6 mol equiv. TFA in total). Both these solutions were added dropwise continuously during 15 min to stirred solution of methyl acrylate (0.039 g) in dichloromethane (0.5 ml) at −60 °C ensuring that at all times addition of the LTA solution was slightly ahead of that of the *N*-aminoquinazolinone. The mixture was stirred for a further 15 min at −60 °C, the solution remaining homogeneous throughout, and then allowed to warm to room temperature and worked up in the usual way to give the aziridine (**5**) in 64% yield after chromatography as described above. The ratio of stereoisomers was *ca.* 20 : 1.

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