Aziridination of alkenes using 2-substituted-3-acetoxyamino-quinazolin-4(3*H*)-ones: changes in transition state geometry resulting from addition of trifluoroacetic acid or by an electron-withdrawing 2-substituent

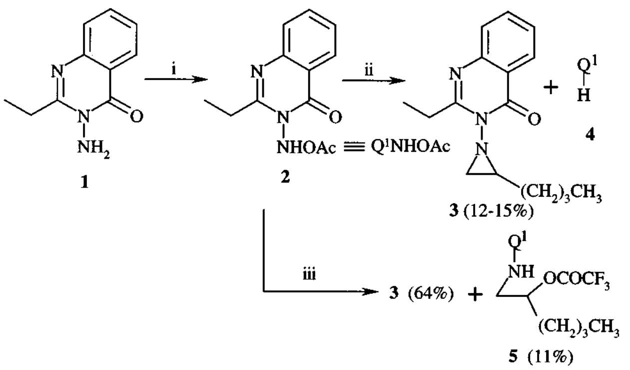
Robert S. Atkinson * and Sabri Ulukanli

Department of Chemistry, The University, Leicester, UK LE1 7RH

Received (in Cambridge) 14th December 1998, Accepted 4th February 1999

The effects of TFA on the competitive reactions of 3-acetoxyaminoquinazolinones **2** and **10** with methyl acrylate and with *tert*-butyl acrylate are interpreted as supporting a change in transition state geometry from one where (Q)*C*=O/(ester)C=*O* overlap **7b** is replaced by (Q)*C*=N$^+$H/(ester)C=*O* overlap **7c** (Q = quinazolinone). Aziridinations of methyl or *tert*-butyl acrylate using 2-trifluoromethyl-substituted 3-acetoxyaminoquinazolinones **20** and **21** take place with (Q)*C*=N/(ester)C=*O* overlap **22** even in the absence of TFA.

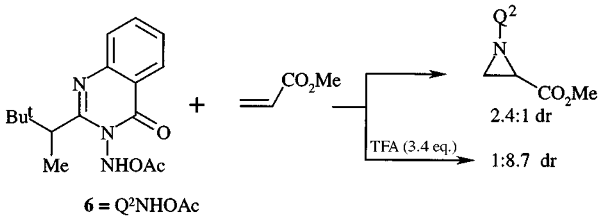
3-Acetoxyaminoquinazolinones *e.g.* **2** (Q^{1}NHOAc), prepared as shown in Scheme 1, are aziridinating agents for alkenes.[1]



Scheme 1 *Reagents*: i, Pb(OAc)$_4$ CH_2Cl_2, 20 °C; ii, hex-1-ene; iii, hex-1-ene, TFA (3.4 equiv.).

The presence of trifluoroacetic acid (TFA) in these aziridinations has a profound effect both upon the yield of aziridine and upon the stereoselectivity of the reaction. Thus, for example, hex-1-ene is a relatively unreactive alkene towards Q^{1}NHOAc **2** and the yield of aziridine **3** is less than 15% even in the presence of excess of alkene: the major product of the reaction is quinazolin-4(3*H*)-one **4**. In the presence of TFA (3 mol equiv.) the combined yield of aziridine **3** and its ring-opened product **5** rises to 75%.[2]

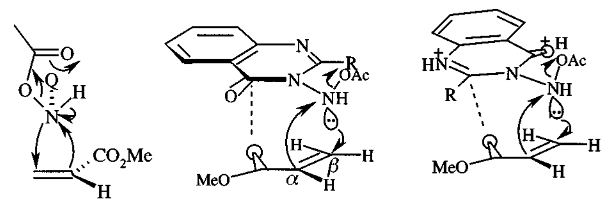
The diastereomer ratio in reagent-controlled aziridination of α,β-unsaturated esters *e.g.* for methyl acrylate with Q^{2}NHOAc **6** is increased from 2.4:1 in the absence of TFA to 1:8.7 in its presence *i.e.* the preferred sense of diastereoselectivity is inverted (Scheme 2).[3]



6 = Q^{2}NHOAc

Scheme 2

These 3-acetoxyaminoquinazolinones **2** and **6** are nitrogen equivalents of peroxyacids and the mechanisms of their reactions with alkenes bearing electron-donating substituents to form the corresponding three-membered rings are presumably similar.[4] However, unlike peroxyacids, compounds **2** and **6** react with *e.g.* α,β-unsaturated esters to give the corresponding aziridines in good yields (see above). We have suggested a mechanism for aziridination in this latter case which involves (a) Michael addition by the acetoxyamino nitrogen to the β-position of the α,β-unsaturated ester followed by (b) S_N2-type substitution of the acetoxy group on the exocyclic nitrogen by the developing negative charge at C_α (see **7b** Scheme 3). Activation of the α,β-unsaturated ester towards Michael addition is brought about by overlap of the ester carbonyl oxygen with the quinazolinone carbonyl carbon: such an overlap requires the s-*cis* conformation of the ester (see **7b**).[5]



7a front view **7b** side view **7c** in the presence of TFA

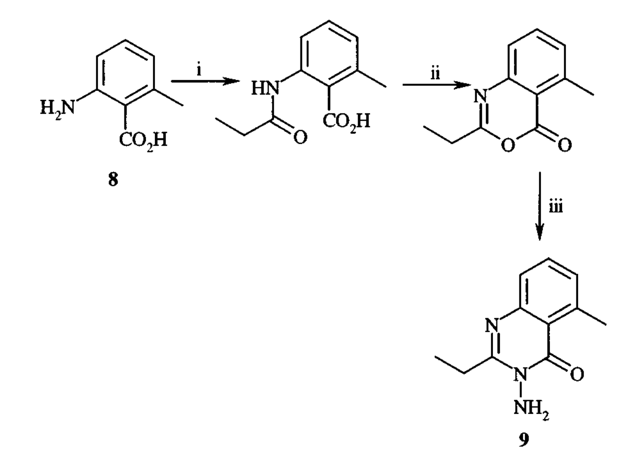
Scheme 3

To account for the increase and the change in the preferred sense of stereoselectivity in Scheme 2 brought about by TFA, we proposed[3] that this acid protonated the (Q)N-1 and changed the transition state geometry from one in which (Q)*C*=O/(ester)C=*O* overlap **7b** is replaced by (Q)*C*=N/(ester)C=*O* overlap **7c** except that at the time the aziridinating species was thought to be the *N*-nitrene. Because a minimum of 3 equiv. of TFA must be used for the effect produced in Scheme 2, it is possible that protonation of the (Q)C=O oxygen also occurs in the aziridinating species in Scheme 3.

In this paper we present evidence which supports this proposed change in transition state geometry from **7b** to **7c** not only in the presence of TFA but also when the quinazolinone 2-substituent is strongly electron-withdrawing, *e.g.* a trifluoromethyl group.

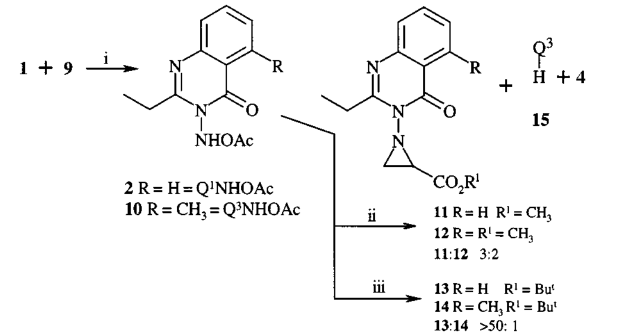
3-Amino-2-ethyl-5-methylquinazolin-4(3*H*)-one **9** is prepared from the commercially available 6-methylanthranilic acid **8** by the route shown in Scheme 4.

Competitive aziridination of methyl acrylate (1 equiv.) by a mixture of 3-acetoxyaminoquinazolinones **2** and **10**, prepared



Scheme 4 *Reagents*: i, $(CH_3CH_2CO)_2O$; ii, Ac_2O; iii, NH_2NH_2, EtOH.

in situ by acetoxylation with lead tetraacetate (LTA) (2.1 mol equiv.) of the corresponding 3-aminoquinazolinones **1** (1 equiv.) and **9** (1 equiv.) gave a 3 : 2 ratio of aziridines **11** and **12** (Scheme 5).



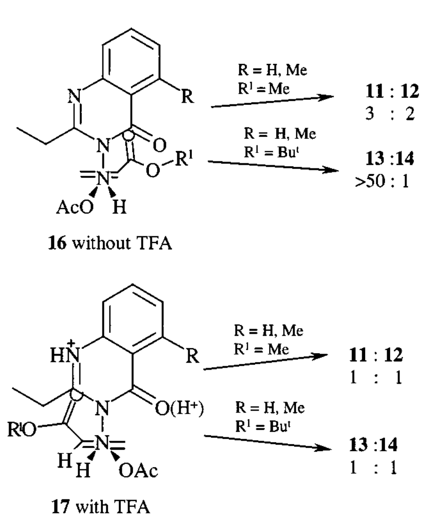
Scheme 5 *Reagents*: i, LTA, CH_2Cl_2, −20 °C; ii, methyl acrylate; iii, *tert*-butyl acrylate.

This ratio of aziridines **11** : **12** was measured directly from the NMR spectrum of the crude reaction product by integration of signals at δ 3.58 and 3.41 from the aziridine ring protons adjacent to the ester groups in **11** and **12** respectively (from comparison with the authentic samples). In contrast, an analogous competitive aziridination of *tert*-butyl acrylate with 3-acetoxyaminoquinazolinones **2** and **10** gave only aziridine **13**: none of the aziridine **14** was detectable when the NMR spectrum of the crude reaction mixture was compared with that from a sample of authentic aziridine **14**. The 3-acetoxyaminoquinazolinone **10** is converted to quinazolin-4(3*H*)-one **15** which was isolated from the reaction mixture in 40% yield.

However, when these competitive reactions of compounds **2** and **10** with either methyl acrylate or with *tert*-butyl acrylate were carried out in the presence of TFA (3 equiv.) a 1 : 1 ratio of aziridines **11** : **12** and **13** : **14** was obtained in each case.

These changes in aziridine ratios are in agreement with those predicted from a change in mechanism from **7b** to **7c** (Scheme 3) and correspond to a change from *endo*(Q)*C*=O/(ester)C=*O* overlap **16** to *endo*(Q)*C*=N/(ester)C=*O* overlap **17** (Scheme 6) mediated by TFA. Thus even with methyl acrylate there is a small steric interaction between the methyl group of the ester and the 5-methyl group which favours formation of aziridine **11**. The augmented interaction of the 5-methyl group with the *tert*-butyl group is responsible for the absence of any aziridine **14** from the reaction of *tert*-butyl acrylate with compound **10**.

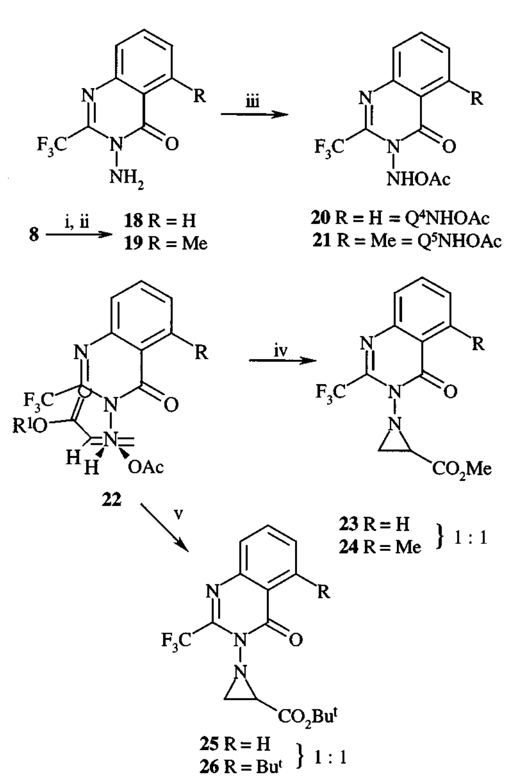
However, in the presence of TFA, the 5-methyl substituent is without effect in competitive aziridination of both methyl acrylate and *tert*-butyl acrylate because *endo* interaction of the ester carbonyl oxygen and the quinazolinone imine carbon



Scheme 6

(Q)*C*=N (as in **17**) removes the methyl or *tert*-butyl group from the vicinity of this 5-methyl substituent.

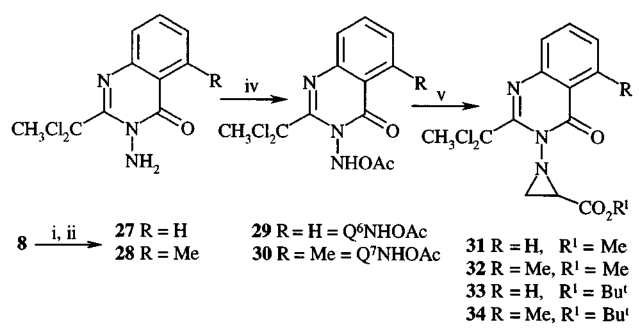
We have also prepared the 3-amino-5-methyl-2-trifluoromethylquinazolinone **19** (Scheme 7) by a route analogous to that in Scheme 4. Its 3-acetoxyamino derivative **21** shows a similar stability at room temperature to that of the previously prepared 5-H analogue **20**.[6] Competitive aziridination of methyl acrylate (1 equiv.) with a mixture of the compounds **20** (1 equiv.) and **21** (1 equiv.) gave a 1 : 1 ratio of the corresponding aziridines **23** and **24** (Scheme 7) from examination of the NMR spectrum of the crude reaction mixture and by comparison with the spectra of authentic samples.



Scheme 7 *Reagents*: i, $(CF_3CO)_2O$; ii, NH_2NH_2, EtOH; iii, LTA, CH_2Cl_2, −20 °C; iv, methyl acrylate; v, *tert*-butyl acrylate.

The corresponding competitive reaction of *tert*-butyl acrylate with Q^4NHOAc **20** and Q^5NHOAc **21** likewise gave a 1 : 1 ratio of aziridines **25** and **26**. It appears, therefore, that even in the absence of TFA, the presence of a trifluoromethyl group as the 2-substituent on the quinazolinone favours an aziridination transition state **22** having (Q)*C*=N/(ester)C=*O* overlap as illustrated in Scheme 7. The increase in electrophilicity at the (Q)*C*=N carbon brought about either by protonation of (Q)N-1 or by trifluoromethyl substitution at (Q)C-2 is most likely responsible for the change in transition state geometry.

In an attempt to discover just how electron-withdrawing this quinazolinone 2-substituent needs to be for a transition state resembling **22** to be favoured we synthesised the 2-(1,1-dichloro)ethyl-substituted 3-amino-5-methylquinazolinone **28** (Scheme 8) from 6-methylanthranilic acid **8** by a route analo-



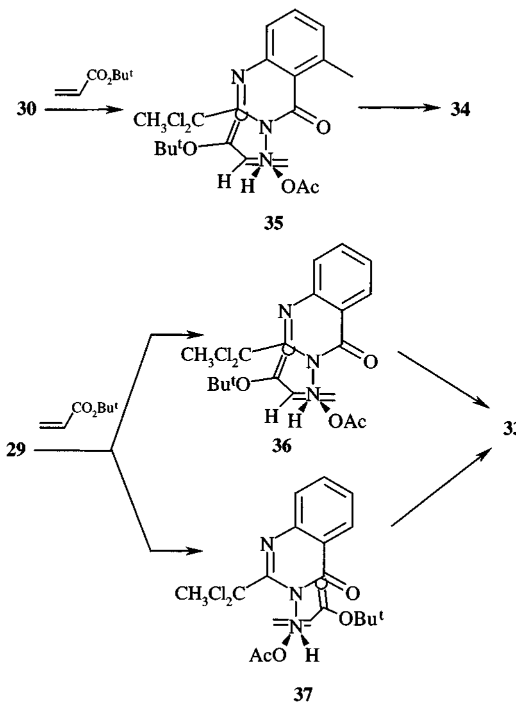
Scheme 8 *Reagents*: i, CH_3CCl_2COCl, pyr; ii, NH_2NH_2, EtOH; iii, heat; iv, LTA, CH_2Cl_2, −20 °C; v, methyl acrylate or *tert*-butyl acrylate.

gous to that in Scheme 4. Competitive reactions of the corresponding 3-acetoxyamino derivative **30** and the known 5-H analogue **29** for methyl acrylate gave aziridines **32** and **31** in a 1 : 1.1 ratio from integration of the respective aziridine H-3 proton signals in the NMR spectrum of the crude reaction product. However, competitive reaction of Q^{6}NHOAc **29** and Q^{7}NHOAc **30** with *tert*-butyl acrylate gave aziridines **33** and **34** in a 3 : 2 ratio respectively from comparison of signals from the corresponding aziridine ring protons.

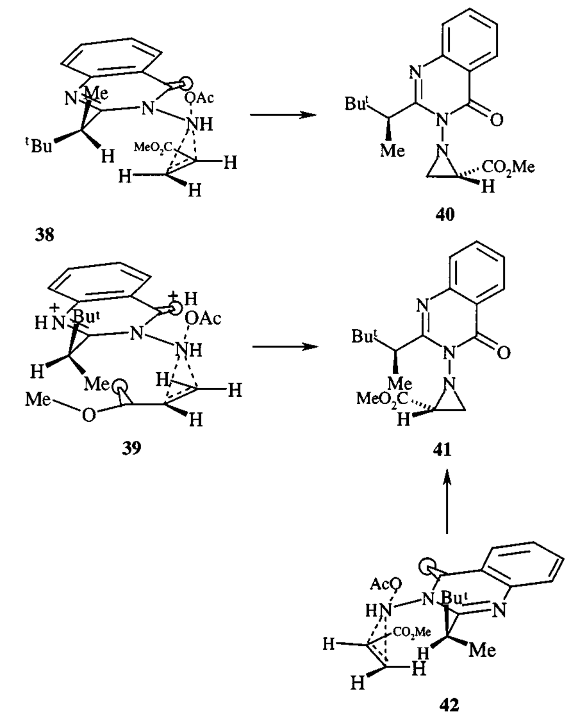
Preferential aziridination of *tert*-butyl acrylate by Q^{6}NHOAc **29** may be the result of the reduced electrophilicity and greater bulk of the dichloroethyl group by comparison with the trifluoromethyl group. Thus, whereas Q^{7}NHOAc **30** reacts *via* a transition state **35** analogous to **22**, competitive reaction by Q^{6}NHOAc **29** occurs by both transition states **36** and **37** leading to more of aziridine **33** than **34** (Scheme 9). If this interpretation is correct, the aziridination of *e.g.* methyl acrylate *via* a transition state resembling **22** may be possible with a *chiral* 2-substituent on the quinazolinone less electron-withdrawing, if also less bulky, than the 1,1-dichloroethyl group. Diastereoselectivity in aziridination *via* the two competing transition states represented by **22** (CF_3 replaced by chiral group) would be expected to be greater than *via* the two transition states represented by **7b** (R the same chiral group).

The effect of addition of TFA on aziridination of methyl acrylate with Q^{2}NHOAc **6** (Scheme 2)[3] can be accounted for by a change in transition state geometry from **38** to **39** (Scheme 10): the acetoxy group on the exocyclic nitrogen is *syn* to the chiral centre in **38** and *anti* in **39** and, we believe, plays an important role in determining the preferred *sense* of diastereoselectivity in the reaction with or without the presence of TFA.

Thus the relative configuration of the major aziridine diastereoisomer formed in the absence of TFA was previously assigned as **40** by analogy with the relative configuration of the preferred diastereoisomer from aziridination of methyl crotonate with Q^{2}NHOAc **6**. The sites occupied by the methyl and *tert*-butyl in transition state **38** presumably reflect the unfavourable interaction between the *tert*-butyl and *N*-acetoxy group which is present in the transition state **42** for formation of the minor aziridine diastereoisomer **41**. There is a change in the preferred sense of diastereoselectivity in the TFA-catalysed reaction giving aziridine **41** because the opposite face of the α,β-unsaturated ester is attacked in transition state **39** by comparison with **38** with the same configuration at the (Q)C-2



Scheme 9



Scheme 10

chiral centre in both cases. The methyl group can be better accommodated "inside" in transition state **39** to avoid unfavourable interaction with the ester OMe and because the *N*-acetoxy group is now *anti* to the chiral centre.

Experimental

^{1}H NMR spectra were recorded on a Bruker ARX 250 NMR spectrometer. Chemical shifts are reported as δ in units of parts per million (ppm) relative to tetramethylsilane (δ 0.00 singlet) in deuterated chloroform ($CDCl_3$); *J* values are given in Hz. Melting points were obtained on a Kofler hot stage and are uncorrected. Infrared spectra (IR) of all compounds were recorded in dichloromethane (CH_2Cl_2) using a Perkin-Elmer

PE 298 spectrometer. Mass spectra were recorded on a Kratos Concept 1H Magnetic Sector Mass spectrometer and all spectra were determined in units of mass relative to charge (*m*/*z*) with electron impact (EI) ionisation or fast atomic bombardment (FAB); only peaks ≥20% of the base peak are given. Dichloromethane was distilled from CaH_2 and stored over 4 Å molecular sieves. Lead tetraacetate was freed from acetic acid under reduced pressure prior to use. All other reactants were reagent grade and were used as received.

General procedure (1) for the aziridination of α,β-unsaturated esters

3-Aminoquinazolinone (1 equiv.) and acetic acid-free lead tetraacetate (LTA) (1.1 mol equiv.) were added alternately and continuously in very small portions over 15 min to a vigorously stirred solution of dry dichloromethane (1 cm^3/100 mg of 3-aminoquinazolinone) cooled with a dry ice–acetone bath held at −20 to −25 °C. The mixture was then stirred for a further 5 min before dropwise addition of the α,β-unsaturated ester (1.5–3.5 equiv.) as a solution in dichloromethane (1 cm^3/500 mg) over 2 min and the temperature of the solution was then allowed to rise to ambient over 20–25 min with stirring throughout. Lead diacetate was separated, dichloromethane (15 cm^3) added, the organic solution washed successively with saturated aqueous sodium hydrogen carbonate and water, dried with magnesium sulfate and the solvent removed by evaporation under reduced pressure.

General procedure (2) for the aziridination of α,β-unsaturated esters in the presence of TFA

A solution of 3-acetoxyaminoquinazolinone at −20 °C was prepared as described above, separated from lead diacetate at this temperature (on a small scale a Pasteur pipette can be used) and the cold solution added dropwise over 2 min to a stirred solution of the alkene (1.5–3.5 equiv.) in dichloromethane (1 cm^3/50 mg) containing TFA (3 equiv.) and held at −20 °C (bath temp.). The temperature of the stirred solution was allowed to rise to room temperature over 20–25 mins. After addition of dichloromethane (15 cm^3), the solution was washed successively with aqueous saturated sodium hydrogen carbonate and water, dried with magnesium sulfate and the solvent removed by evaporation under reduced pressure.

Preparation of 3-amino-2-ethyl-5-methylquinazolin-4(3*H*)-one 9

To 6-methylanthranilic acid **8** (Aldrich) (12.5 g, 82 mmol) was added propionic anhydride (10.7 g, 82 mmol) and the mixture was heated at 100 °C with stirring for 1 h. After cooling the mixture was poured into water, dichloromethane (100 cm^3) was added and the organic layer separated, dried and concentrated under reduced pressure to give an oil which was then cyclised by heating under reflux in acetic anhydride (35 cm^3) for 2.5 h. The bulk of the acetic anhydride was removed by distillation under reduced pressure (Kugelrohr) using a water pump. *2-Ethyl-5-methyl-4H-3,1-benz[d]oxazin-4-one* was obtained as a colourless solid by crystallisation of the residue from light petroleum (13.4 g, 86%) mp 84–85 °C (Found: M^+ 189.0789. $C_{11}H_{11}NO_2$ requires *M* 189.0789); δ_H 1.54 (t, *J* 7.5, CH_2CH_3), 2.87 (q, *J* 7.5, CH_2CH_3), 2.98 (s, 5-CH_3), 7.45 (d, *J* 7.2, H-6), 7.58 (dd, *J* 7.5 and 0.6, H-8) and 7.80 (dd, *J* ~7.0 and 7.5, H-7); ν_{max}/cm^{-1} 2950w, 1750s, 1655s and 1600s; *m*/*z* (%) 189 (M^+, 71), 160 (100) and 104 (22). 2-Ethyl-5-methyl-4*H*-3,1-benz[*d*]oxazinone (6.7 g, 35 mmol) and hydrazine hydrate (12.3 g, 246 mmol) were heated under reflux for 6 h with ethanol (100 cm^3) as solvent under nitrogen. After cooling, the bulk of the ethanol was removed under reduced pressure and the residue dissolved in dichloromethane (100 cm^3) which was then washed with water (100 cm^3), dried and concentrated to give *3-amino-2-ethyl-5-methylquinazolin-4(3H)-one* **9** as colourless crystals (4.36 g, 61%) mp 142–144 °C (from ethanol) (Found: C, 65.25; H, 6.45; N, 20.65. $C_{11}H_{13}N_3O$ requires C, 65.0; H, 6.45; N, 20.65%); δ_H 1.29 (t, *J* 7.2, CH_2CH_3), 2.83 [s, 5-CH_3 (Q)], 2.96 (q, *J* 7.2, CH_2CH_3), 4.72 (s, NH_2) and 7.55–7.11 [m, H-6, H-7 and H-8 (Q)]; ν_{max}/cm^{-1} 3320w, 2965w, 1665s, 1595s and 1570m; *m*/*z* (%) 204 (MH^+, 100), 154 (58), 137 (29) and 136 (43).

Aziridination of methyl acrylate using Q^1NHOAc 2

The general procedure 1 was followed using **1** (0.1 g, 0.53 mmol), LTA (0.26 g, 0.58 mmol) and methyl acrylate (0.05 g, 0.63 mmol) in dichloromethane (2 cm^3). An NMR spectrum of the crude product showed that a mixture of aziridine **11** and quinazolin-4(3*H*)-one **4** was present in a ratio 4.4 : 1 from the integration of signals at δ 8.15 and 8.22 ppm respectively. The crude product crystallised on addition of ethanol to give aziridine **11** as a colourless solid (0.1 g, 71%) mp 116–118 °C (from ethanol) (lit.[1] mp 116–118 °C) δ_H 1.42 (t, *J* 6.9, CH_2CH_3), 2.85 (d, *J* 5.0, azir. H-3 *trans* to Q), 3.02 (m, CH_2CH_3), 3.12 (d, *J* 7.5, azir. H-3 *cis* to Q), 3.58 (dd, *J* 7.5 and 5.0 azir. H-2), 3.80 (s, OCH_3), 7.32–7.76 [m, 6-H, 7-H, 8-H (Q)] and 8.15 [d, *J* 8.2, 5-H (Q)].

Aziridination of methyl acrylate using Q^3NHOAc 10

The general procedure 1 was followed using **9** (0.1 g, 0.49 mmol), LTA (0.24 g, 0.54 mmol), methyl acrylate (0.05 g, 0.59 mmol) and, in addition, HMDS (0.16 g, 0.98 mmol)[7] in dichloromethane (2 cm^3) was added. An NMR spectrum of the crude product showed a mixture of aziridine **12** and quinazolin-4(3*H*)-one **15** present in a 3.5 : 1 ratio from the integration of signals at δ 3.50 and 10.72 ppm respectively. The crude product crystallised on addition of ethanol to give *aziridine* **12** as a colourless solid (0.11 g, 78%) mp 132–134 °C (from ethanol) (Found: M^+ 287.126. $C_{15}H_{17}N_3O_3$ requires *M* 287.126); δ_H 1.40 (t, *J* 7.2, CH_2CH_3), 2.81 (s, 5-CH_3), 2.92 (dd, *J* 5.0 and 1, azir. H-3 *trans* to Q), 3.03 (m, CH_2CH_3 and azir. H-3 *cis* to Q), 3.41 (dd, *J* 7.5 and 5.0, azir. H-2), 3.85 (s, OCH_3), 7.13 [d, *J* 7.2, 6-H (Q)] and 7.49 [m, 7-H and 8-H (Q)]; ν_{max}/cm^{-1} 1750s, 1675s and 1600m; *m*/*z* (%) 287 (M^+, 85), 145 (100), 90 (24) and 89 (22).

Aziridination of *tert*-butyl acrylate using Q^1NHOAc 2

General procedure 1 was followed using **1** (0.1 g, 0.53 mmol), LTA (0.26 g, 0.58 mmol) and *tert*-butyl acrylate (0.1 g, 0.79 mmol) in dichloromethane (2 cm^3). An NMR spectrum of the crude product showed a mixture of aziridine **13** and its corresponding quinazolin-4(3*H*)-one **4** were present in a ratio 5.3 : 1 from integration of signals at δ 8.15 and 8.22 ppm respectively. The crude product crystallised on addition of ethanol to give *aziridine* **13** as a colourless solid (0.1 g, 70%) mp 88–89 °C (from ethanol) (Found: M^+ 315.158. $C_{17}H_{21}N_3O_3$ requires *M* 315.158); δ_H 1.42 (t, *J* 7.5, CH_2CH_3), 1.53 (s, Bu^t), 2.87 (dd, *J* 5.0 and 1.3, azir. H-3 *trans* to Q), 3.09 (q, *J* 7.5, CH_2CH_3), 3.26 (dd, *J* 7.5 and 1.3, azir. H-3 *cis* to Q), 3.51 (dd, *J* 7.5 and 5.0 azir. H-2), 7.37–7.72 [m, 6-H, 7-H, 8-H (Q)] and 8.15 [ddd, *J* 7.2, 1.3 and 0.6, 5-H (Q)]; ν_{max}/cm^{-1} 1725s, 1670s and 1595m; *m*/*z* (%) 315 (M^+, 33), 259 (100), 175 (23), 174 (42), 173 (32), 131 (90) and 130 (48).

Aziridination of *tert*-butyl acrylate using Q^3NHOAc 10

The general procedure 1 was followed using **9** (0.1 g, 0.49 mmol), LTA (0.24 g, 0.54 mmol) and *tert*-butyl acrylate (0.09 g, 0.74 mmol) in dichloromethane (2 cm^3). The crude product crystallised on addition of ethanol to give *aziridine* **14** as a colourless solid (0.12 g, 74%) mp 121–123 °C (from ethanol) (Found: C, 65.6; H, 7.0; N, 12.7. $C_{18}H_{23}N_3O_3$ requires C, 65.65; H, 7.05; N, 12.75%); δ_H 1.47 (t, *J* 7.2, CH_2CH_3), 1.60 (s, Bu^t), 2.88 [s, 5-CH_3 (Q)], 2.97 (dd, *J* 4.7 and 1.3, azir. H-3 *trans* to Q), 3.11 (q, *J* 7.2, CH_2CH_3), 3.21 (dd, *J* 7.5 and 1.3, azir. H-3 *cis* to Q), 3.35 (dd, *J* 7.5 and 4.7 azir. H-2), 7.22 [d, *J* 7.2, 6-H (Q)] and

7.56 [m, 7-H and 8-H (Q)]; ν_{max}/cm^{-1} 1735s, 1675s and 1595m; *m*/*z* (%) 329 (M$^+$, 22), 273 (64), 188 (24) and 145 (100).

Preparation of 3-amino-2-trifluoromethyl-5-methylquinazolin-4(3*H*)-one 19

To a suspension of 6-methylanthranilic acid (10.3 g, 68 mmol) in $CHCl_3$ (200 cm^3) was added trifluoroacetic anhydride (43 g, 205 mmol) dropwise with stirring. The mixture was heated under reflux for 1 h, then cooled and the excess trifluoroacetic anhydride removed under reduced pressure to give a yellow solid. *2-Trifluoromethyl-5-methyl-4H-3,1-benz[d]oxazin-4-one* was obtained as a colourless solid (13.4 g, 86%) mp 86–88 °C (from light petroleum) (Found: C, 52.2; H, 2.7; N, 6.05. $C_{10}H_6NO_2F_3$ requires C, 52.4; H, 2.65; N, 6.1%); δ_H 2.83 (s, 5-C*H*$_3$), 7.48 (d, *J* 7.9, 6-H), 7.60 (d, *J* 7.5, 8-H) and 7.76 (app. t, *J* ~7.5, 7-H); ν_{max}/cm^{-1} 1780s, 1680m and 1600m; *m*/*z* (%) 229 (M$^+$, 32), 160 (100) and 104 (38). 2-Trifluoromethyl-5-methyl-4*H*-3,1-benz[*d*]oxazin-4-one (9.5 g, 41.5 mmol) and hydrazine hydrate (12.3 g, 246 mmol) were stirred for 1 h at room temperature in ethanol (50 cm^3). The bulk of the ethanol was removed under reduced pressure and the residue dissolved in ethyl acetate (100 cm^3) which was washed successively with hydrochloric acid (2 M, 100 cm^3) and brine (100 cm^3), dried with magnesium sulfate and evaporated to give *3-amino-2-trifluoromethylquinazolin-4(3H)-one* **19** as colourless crystals (6.4 g, 63%) mp 154–156 °C (from ethanol) (Found: C, 49.55; H, 3.4; N, 17.1. $C_{10}H_8N_3OF_3$ requires C, 49.4; H, 3.3; N, 17.3%); δ_H 2.83 [s, 5-C*H*$_3$ (Q)], 4.83 (s, N*H*$_2$) and 7.55–7.11 [m, H-6, H-7 and H-8 (Q)]; ν_{max}/cm^{-1} 3320w, 1680s, 1640s and 1600m; *m*/*z* (%) 243 (M$^+$, 100), 227 (32), 214 (61) and 144 (38).

Aziridination of methyl acrylate using Q^{4}NHOAc 20

The general procedure 1 was followed using **18** (0.1 g, 0.87 mmol), LTA (0.43 g, 0.96 mmol) and methyl acrylate (0.15 g, 1.74 mmol) in dichloromethane (3 cm^3) to give *aziridine* **23** which crystallised on addition of ethanol as a colourless solid (0.15 g, 56%) mp 105–107 °C (from ethanol) (Found: M$^+$ 313.067. $C_{13}H_{10}F_3N_3O_3$ requires *M* 313.067); δ_H 2.63 (d, *J* 4.4, azir. H-3 *trans* to Q), 3.74 (s, OMe), 3.93 (d, *J* 7.2, azir. H-3 *cis* to Q), 4.26 (dd, *J* 4.4 and 7.2 azir. H-2), 7.81–7.52 [m, 6-H, 7-H, 8-H (Q)] and 8.13 [dd, *J* 7.9 and 1, 5-H (Q)]; ν_{max}/cm^{-1} 1750s, 1690s and 1605m; *m*/*z* (%) 313 (M$^+$, 62), 214 (100), 171 (27), 145 (46), 104 (88), 90 (39), 76 (51) and 55 (27).

Aziridination of methyl acrylate using Q^{5}NHOAc 21

The general procedure 1 was followed using **19** (0.2 g, 0.87 mmol), LTA (0.43 g, 0.96 mmol) and methyl acrylate (0.15 g, 1.74 mmol) in dichloromethane (3 cm^3) to afford *aziridine* **24** which crystallised on addition of ethanol as a colourless solid (0.16 g, 58%) mp 130–132 °C (from ethanol) (Found: C, 51.45; H, 3.75; N, 12.75. $C_{14}H_{12}N_3O_3F_3$ requires C, 51.4; H, 3.7; N, 12.85%); δ_H 2.52 (d, *J* 4.4, azir. H-3 *trans* to Q), 2.64 (s, 5-C*H*$_3$), 3.64 (s, OC*H*$_3$), 3.74 (d, *J* 7.2, azir. H-3 *cis* to Q), 4.08 (dd, *J* 7.2 and 4.4, azir. H-2) and 7.16–7.60 [m, 6-H, 7-H, 8-H (Q)]; ν_{max}/cm^{-1} 1750s, 1690s and 1605m; *m*/*z* (%) 355 (M$^+$, 8), 299 (45), 214 (56), 84 (100) and 57 (40).

Aziridination of *tert*-butyl acrylate using Q^{4}NHOAc 20

The general procedure 1 was followed using **18** (0.2 g, 0.87 mmol), LTA (0.43 g, 0.96 mmol) and *tert*-butyl acrylate (0.22 g, 1.74 mmol) in dichloromethane (3 cm^3) to afford *aziridine* **25** which crystallised on addition of ethanol to give a colourless solid (0.2 g, 63%) mp 118–120 °C (from ethanol) (Found: C, 54.0; H, 4.55; N, 11.8. $C_{16}H_{16}N_3O_3F_3$ requires C, 54.1; H, 4.55; N, 11.85%); δ_H 1.50 (s, Bu^t), 2.60 (d, *J* 4.7, azir. H-3 *trans* to Q), 3.99 (d, *J* 7.2, azir. H-3 *cis* to Q), 4.20 (dd, *J* 7.2 and 4.4, azir. H-2), 7.56–7.83 [m, 6-H, 7-H, 8-H (Q)] and 8.20 [d, *J* 8.2, 5-H (Q)]; ν_{max}/cm^{-1} 1735s, 1690s and 1605m; *m*/*z* (%) 355 (M$^+$, 8), 299 (45), 214 (56), 84 (100) and 57 (40).

Aziridination of *tert*-butyl acrylate using Q^{5}NHOAc 21

The general procedure 1 was followed using **19** (0.1 g, 0.41 mmol), LTA (0.2 g, 0.45 mmol) and *tert*-butyl acrylate (0.11 g, 0.82 mmol) in dichloromethane (2 cm^3) to afford *aziridine* **26** which crystallised on addition of ethanol as a colourless solid (0.09 g, 57%) mp 164–165 °C (from ethanol) (Found: C, 55.2; H, 4.95; N, 11.35. $C_{16}H_{16}N_3O_3F_3$ requires C, 55.3; H, 4.9; N, 11.35%); δ_H 1.49 (s, Bu^t), 2.58 (d, *J* 4.4, azir. H-3 *trans* to Q), 2.79 (s, 5-C*H*$_3$), 3.92 (d, *J* 7.2, azir. H-3 *cis* to Q), 4.16 (dd, *J* 7.2 and 4.4, azir. H-2) and 7.26–7.77 [m, 6-H, 7-H, 8-H (Q)]; ν_{max}/cm^{-1} 1745s, 1690s and 1605m; *m*/*z* (%) 369 (M$^+$, 24), 313 (100), 296 (30), 229 (20), 228 (74), 144 (39), 118 (96), 90 (30), 89 (22), 69 (21), 57 (93) and 55 (54).

Preparation of 3-amino-2-(1,1-dichloroethyl)-5-methylquinazolin-4(3*H*)-one 28

To a solution of 6-methylanthranilic acid (3 g, 20 mmol) in pyridine (30 cm^3) was added 2,2-dichloropropanoyl chloride (3.2 g, 20 mmol) dropwise with stirring. The mixture was stirred for a further 16 h at room temperature, then ethyl acetate was added (50 cm^3), the solution washed successively with hydrochloric acid (2 M, 3 × 50 cm^3), brine (50 cm^3) and water (50 cm^3), the organic layer was dried with magnesium sulfate and then evaporated under reduced pressure to give 2-(1,1-dichloroethyl)-5-methyl-4*H*-3,1-benz[*d*]oxazin-4-one as a brown solid (2.5 g, 49%). δ_H 2.54 and 2.82 (2 × s, 5-C*H*$_3$ and C*H*$_3$CCl$_2$), 7.38 (d, *J* 7.5, 6-H), 7.52 (d, *J* 7.9, 8-H) and 7.9 (dd, *J* 7.5 and 7.9, 7-H); ν_{max}/cm^{-1} 1770s, 1650s and 1600m. 2-(1,1-Dichloroethyl)-5-methyl-4*H*-3,1-benz[*d*]oxazin-4-one (2.3 g, 8.5 mmol) and hydrazine hydrate (0.5 g, 10 mmol) were heated under reflux for 3 h in ethanol (5 cm^3). The bulk of the ethanol was removed under reduced pressure and the residue dissolved in dichloromethane (30 cm^3) which was washed with water (30 cm^3) and brine (30 cm^3), dried with magnesium sulfate and evaporated to give *N*-2,2-dichloropropanoyl-6-methylanthranilic acid hydrazide as a brown solid (1 g, 40%). δ_H 2.27 and 2.3 (2 × s, 5-C*H*$_3$ and C*H*$_3$CCl$_2$), 4.05 (s, br, NHN*H*$_2$), 6.98 (d, *J* 7.9, 6-H), 7.22 (dd, *J* 8.2 and 7.9, 7-H), 7.34 (s, N*H*NH$_2$), 7.74 (d, *J* 8.2, 8-H) and 9.5 (s, N*H*). The *N*-2,2-dichloropropanoyl-6-methylanthranilic acid hydrazide (1 g, 3.4 mmol) was placed in a Young's tube with ethanol (3 cm^3) and heated at 150 °C for 16 h. Excess ethanol was removed, the residue dissolved in dichloromethane (30 cm^3) which was then washed successively with water (30 cm^3) and brine (30 cm^3), dried with magnesium sulfate and evaporated to give *3-amino-2-(1,1-dichloroethyl)-5-methylquinazolinone* **28** as a colourless solid (0.8 g, 82%) mp 173–175 °C (from ethanol) (Found: M$^+$ 271.027. $C_{11}H_{11}N_3OCl_2$ requires *M* 271.027); δ_H 2.67 and 2.9 [2 × s, 5-C*H*$_3$ (Q) and C*H*$_3$CCl$_2$], 5.15 (s, N*H*$_2$), 7.31 [d, *J* 6.9, 6-H, (Q)] and 7.54–7.65 [m, H-7 and H-8 (Q)]; ν_{max}/cm^{-1} 3320w, 1675s and 1600m; *m*/*z* (%) 271 (M$^+$, 100), 238 (23), 236 (74), 219 (51), 208 (26), 207 (30), 206 (62), 183 (20), 146 (21), 144 (26), 89 (24) and 77 (21).

Aziridination of methyl acrylate using Q^{6}NHOAc 29

General procedure 1 was followed using **27** (0.1 g, 0.39 mmol), LTA (0.19 g, 0.43 mmol) and methyl acrylate (0.07 g, 0.77 mmol) in dichloromethane (2 cm^3). The crude product was purified by chromatography over silica eluting with light petroleum–ethyl acetate (6:1) and *aziridine* **31** (R_f 0.29) was obtained as a colourless oil (0.04 g, 27%) (Found: M$^+$ 341.033. $C_{14}H_{13}N_3O_3Cl_2$ requires *M* 341.033); δ_H 2.53 (d, *J* 3.8, azir. H-3 *trans* to Q), 2.55 (s, C*H*$_3$CCl$_2$), 3.65 (s, OC*H*$_3$), 4.07 (d, *J* 6.6, azir. H-3 *cis* to Q), 4.58 (dd, *J* 6.6 and 3.8 azir. H-2), 7.42 [ddd, *J* 8.2, 6.9 and 1.3, 6-H (Q)], 7.64 [m, 7-H and 8-H (Q)] and 8.05 [dd, *J* 8.2 and 1.3, 5-H (Q)]; ν_{max}/cm^{-1} 1770s, 1680s and 1590s; *m*/*z* (%) 341 (M$^+$, 6), 308 (34), 306 (100) and 207 (20).

Aziridination of methyl acrylate using Q^7NHOAc 30

General procedure 1 was followed using **28** (0.07 g, 0.27 mmol), LTA (0.13 g, 0.3 mmol) and methyl acrylate (0.05 g, 0.55 mmol) in dichloromethane (2 cm^3). The crude product was purified by chromatography over silica eluting with light petroleum–ethyl acetate (5:1) and *aziridine* **32** (R_f 0.35) was obtained as a colourless solid, mp 161–163 °C (0.03 g, 31%) (from ethanol) (Found: M^+ 355.049. $C_{15}H_{15}N_3O_3Cl_2$ requires *M* 355.049); δ_H 2.53 (d, *J* 3.8, azir. H-3 *trans* to Q), 2.56 (s, CH_3CCl_2), 2.70 [s, 5-CH_3 (Q)], 3.68 (s, OCH_3), 4.05 (d, *J* 6.6, azir. H-3 *cis* to Q), 4.58 (dd, *J* 6.6 and 3.8 azir. H-2) and 7.16–7.54 [m, 6-H, 7-H and 8-H (Q)]; ν_{max}/cm^{-1} 1770s, 1665s and 1600m; *m*/*z* (%) 355 (M^+, 13), 322 (30), 320 (88), 208 (32) and 206 (100).

Aziridination of *tert*-butyl acrylate using Q^6NHOAc 29

General procedure 1 was followed using **27** (0.1 g, 0.41 mmol), LTA (0.2 g, 0.45 mmol) and *tert*-butyl acrylate (0.1 g, 0.82 mmol) in dichloromethane (2 cm^3). The crude product was purified by chromatography over silica eluting with light petroleum–ethyl acetate (6:1) and *aziridine* **33** (R_f 0.32) was obtained as a colourless solid (0.04 g, 25%) (Found: M^+ 383.080. $C_{17}H_{19}N_3O_3Cl_2$ requires *M* 383.080); δ_H 1.39 (s, Bu^t), 2.47 (d, *J* 4.1, azir. H-3 *trans* to Q), 2.59 (s, CH_3CCl_2), 3.99 (d, *J* 6.6, azir. H-3 *cis* to Q), 4.49 (dd, *J* 6.6 and 4.1 azir. H-2), 7.43 [ddd, *J* 1.3, 6.9 and 8.2, 6-H (Q)], 7.63 [m, 7-H and 8-H (Q)] and 8.07 [dd, *J* 1.0 and 8.2, 8-H (Q)]; ν_{max}/cm^{-1} 1745s, 1660s and 1595s; *m*/*z* (%) 383 (M^+, 9), 294 (34), 292 (100), 207 (45), 146 (29) and 57 (31).

Aziridination of *tert*-butyl acrylate using Q^7NHOAc 30

General procedure 1 was followed using **28** (0.06 g, 0.22 mmol), LTA (0.11 g, 0.24 mmol) and *tert*-butyl acrylate (0.06 g, 0.44 mmol) in dichloromethane (1 cm^3). The crude product was purified by chromatography over silica eluting with light petroleum–ethyl acetate (6:1) and *aziridine* **34** (R_f 0.34) was obtained as a colourless oil (0.02 g, 20%) (Found: M^+ 397.096. $C_{18}H_{21}N_3O_3Cl_2$ requires *M* 397.096); δ_H 1.40 (s, Bu^t), 2.43 (d, *J* 3.8, azir. H-3 *trans* to Q), 2.56 and 2.7 [2 × s, 5-CH_3 (Q) and CH_3CCl_2], 3.97 (dd, *J* 6.6 and 0.6, azir. H-3 *cis* to Q), 4.47 (dd, *J* 6.6 and 3.8, azir, H-2), 7.15–7.53 [m, 6-H, 7-H and 8-H (Q)]; ν_{max}/cm^{-1} 1760s, 1665s and 1600m; *m*/*z* (%) 397 (M^+, 11), 308 (26), 221 (33), 208 (32) and 206 (100).

Competitive aziridination of methyl acrylate using 2 and 10 with and without addition of TFA

General procedure 1 was followed but using a mixture of 3-aminoquinazolinones **1** (0.1 g, 0.53 mmol) and **9** (0.11 g, 0.53 mmol), LTA (0.52 g, 1.16 mmol) and methyl acrylate (0.045 g, 0.53 mmol) in dichloromethane (4 cm^3). Examination of the NMR spectrum of the crude product mixture after work-up showed the presence of aziridines **11** and **12** in a 1.4:1 ratio from the integration of signals at δ 3.58 and 3.41 ppm. When the above reaction was carried out under the same conditions but with addition of TFA (0.36 g, 3.18 mmol) (see general procedure 2) aziridines **10** and **11** were present in a 1:1 ratio in the crude reaction product determined from the integration of the same signals in the NMR spectrum as indicated above.

Competitive aziridination of *tert*-butyl acrylate using 2 and 10 with and without addition of TFA

The same procedure described above was followed using the same quantities of 3-aminoquinazolinones **1** and **9**, LTA and dichloromethane, but using *tert*-butyl acrylate (0.06 g, 0.53 mmol) instead of methyl acrylate. The NMR spectrum of the crude reaction product showed the presence of aziridine **13** and quinazolin-4(3*H*)-one **15** in a 1:1.7 ratio from integration comparison of signals at δ 3.51 and 2.89 ppm. A pure sample of *5-methylquinazolin-4(3H)-one* **15** was isolated by chromatography over silica gel using light petroleum–ethyl acetate (6:1) as eluent as a colourless solid (0.037 g, 40%) (sublimed above 180 °C) (from light petroleum) (Found: C, 69.7; H, 6.4; N, 14.65. $C_{11}H_{12}N_2O_2$ requires C, 70.2; H, 6.4; N, 14.9%); δ_H 1.44 (t, *J* 7.2, CH_2CH_3), 2.78 (q, *J* 7.2, CH_2CH_3), 2.89 [s, 5-CH_3 (Q)] and 7.19–7.8 [m, 6-H, 7-H and 8-H (Q)], 11.2 (s, NH); ν_{max}/cm^{-1} 3000s, 1665s and 1600m; *m*/*z* (%) 189 (MH^+, 100), 188 (32) and 176 (43).

When this reaction was repeated under the same conditions, but with addition of TFA (361 mg, 3.18 mmol) (general procedure 2), the NMR spectrum of the crude reaction product showed the presence of aziridines **13** and **14** in a 1:1 ratio from the integration of signals at δ 3.51 and 3.35 ppm, respectively.

Competitive aziridination of methyl acrylate and of *tert*-butyl acrylate using 20 and 21

General procedure 1 was followed using 3-aminoquinazolin-4(3*H*)-ones **18** (0.1 g, 0.46 mmol) and **19** (0.106 g, 0.46 mmol), LTA (0.449 g, 0.506 mmol) and methyl acrylate (0.049 g, 0.46 mmol) in dichloromethane (4 cm^3). NMR spectroscopic examination of the crude product mixture showed that a 1:1 ratio of **23** and **24** was present from comparison of the signals at δ 4.26 and 4.08 and at δ 3.93 and 3.74 ppm.

Identical quantities of 3-aminoquinazolin-4(3*H*)-ones **18** and **19**, LTA and dichloromethane were used for the aziridination of *tert*-butyl acrylate (0.06 g, 0.46 mmol) and yielded aziridines **25** and **26**. NMR spectroscopic examination of the crude product mixture confirmed that a 1:1 ratio of **25** and **26** was present from comparison of signals at δ 4.20 and 4.16 and at δ 3.99 and 3.92 ppm.

Competitive aziridination of methyl acrylate and of *tert*-butyl acrylate using 29 and 30

The general procedure 1 was followed using 3-aminoquinazolin-4(3*H*)-ones **27** (0.075 g, 0.30 mmol) and **28** (0.079 g, 0.30 mmol), LTA (0.145 g, 0.33 mmol) and methyl acrylate (0.026 g, 0.30 mmol) in dichloromethane (2 cm^3). NMR spectroscopic examination of the crude product mixture showed that a 1.1:1 ratio of **31** and **32** was present from comparison of signals at δ 4.07 and 4.05 ppm (from cutting and weighing the (overlapping) peaks).

The 3-aminoquinazolin-4(3*H*)-ones **27** (0.1 g, 0.387 mmol) and **28** (0.106 g, 0.387 mmol), LTA (0.361 g, 0.814 mmol) in dichloromethane (3 cm^3) were also used for the aziridination of *tert*-butyl acrylate (0.05 g, 0.387 mmol) and yielded aziridines **33** and **34**. NMR (400 MHz) spectroscopic examination of the crude product mixture confirmed that a 3:2 ratio of **33** and **34** was present from comparison of signals at δ 3.99 and 3.97 ppm.

Acknowledgements

We thank the University of Kafkas (Turkey) for support (to S. U.).

References

1 R. S. Atkinson, *Tetrahedron*, 1999, **55**, 1519; R. S. Atkinson, M. J. Grimshire and B. J. Kelly, *Tetrahedron*, 1989, **45**, 2875.
2 R. S. Atkinson and B. J. Kelly, *J. Chem. Soc.*, *Perkin Trans. 1*, 1989, 1627.
3 R. S. Atkinson and G. Tughan, *J. Chem. Soc.*, *Perkin Trans. 1*, 1987, 2803.
4 R. S. Atkinson and B. J. Kelly, *J. Chem. Soc.*, *Perkin Trans. 1*, 1989, 1515.
5 R. S. Atkinson and P. J. Williams, *J. Chem. Soc.*, *Perkin Trans. 1*, 1996, 1951.
6 R. S. Atkinson, M. P. Coogan and C. L. Cornell, *J. Chem. Soc.*, *Perkin Trans. 1*, 1996, 157.
7 R. S. Atkinson, E. Barker and S. Ulukanli, *J. Chem. Soc.*, *Perkin Trans. 1*, 1998, 584.

Paper 8/09703H