

# 1-(3,4-Dihydro-4-oxoquinazolin-3-yl)aziridines (Q-substituted aziridines): ring-opening reactions with C–N bond cleavage and preparation of Q-free chirons

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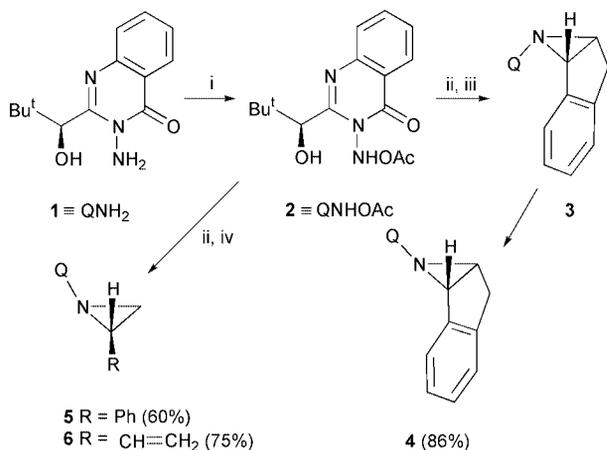
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The presence of the Q group in ring-opening reactions of *N*-(Q)-aziridines **3**, **4**, **5** and **6** has been found to be advantageous in the following ways, (i) nucleophilic ring-opening by cuprate or by azide with inversion of configuration is assisted by the electron-withdrawing character of the Q group, (ii) ring-opening of aziridines **5** or **6** to the corresponding alcohols **36** and **23** with retention of configuration can be accomplished by participation of the Q group: the Q carbonyl oxygen becomes the hydroxy oxygen in the alcohol product, (iii) the combined effects of the electron-withdrawing Q group and ring strain allow preparation of individual aziridine *N*-invertomers **3** and **4** whose ring-opening with hydrogen chloride in dichloromethane proceeds with complementary stereochemistry. The Q group is also believed to be involved in ring-opening of aziridines **5** and **6** mediated by samarium(III) nitrate hexahydrate with predominant retention of configuration. Reductive removal of the Q group from these ring-opened products gave chirons **12**, **19** and **21**.

The dearth of general and stereoselective methods for aziridine synthesis means that these three-membered rings enjoy far less use than epoxides as synthetic relay intermediates.<sup>1,2</sup>

We have shown that enantiopure 3-acetoxyaminoquinazolones e.g. **2** are aziridinating agents for a variety of alkenes.<sup>1</sup> Aziridination of styrene, butadiene and indene with 3-acetoxyaminoquinazolinone **2** (QNHOAc) in the presence of titanium(IV) *tert*-butoxide is highly diastereoselective (Scheme 1).<sup>3</sup>

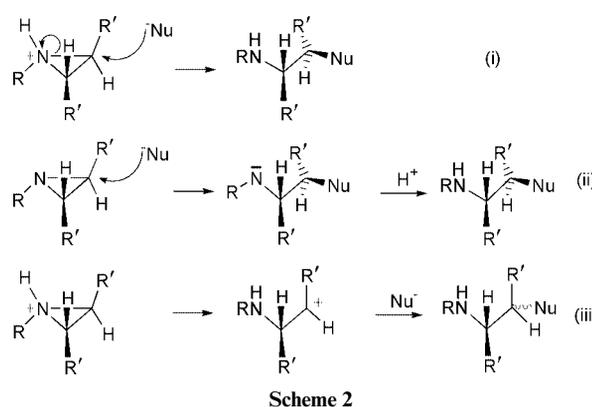


**Scheme 1** (i) LTA, CH<sub>2</sub>Cl<sub>2</sub>, –20 °C; (ii) Ti(O*t*Bu)<sub>4</sub>; (iii) indene; (iv) CH<sub>2</sub>=C(H)R.

To make use of the aziridine products in Scheme 1, removal of the Q substituent is required. Although reductive cleavage of the Q group without ring-opening of the aziridine ring has been accomplished by Coates *et al.*,<sup>4</sup> we were particularly interested in studying ring-opening methods on aziridines **3–6** before N–Q bond cleavage. The expectation here was that the Q group could be used to control or assist in the ring-opening of the 3-membered ring in ways not available using the corresponding NH-aziridines. Three ways in which the Q group might, *a priori*,

influence the ring-opening of the aziridine would be by affecting the rate, the stereochemistry or the regiochemistry.

Ring-opening of aziridines typically involves protonation or Lewis acid coordination of the ring-nitrogen combined with nucleophilic assistance to C–N bond breaking [Scheme 2(i)].



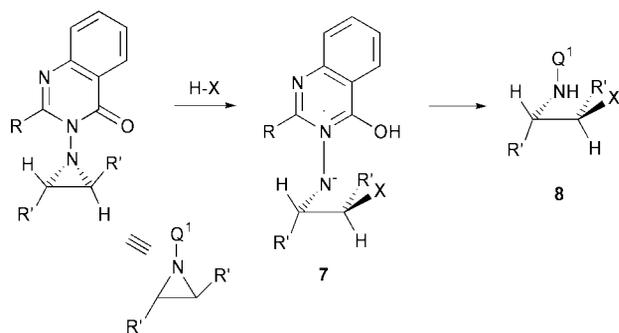
Two variants on this mechanism are ring-opening without prior protonation or activation of the ring nitrogen [Scheme 2(ii)] and ring-opening leading to carbocation formation with only subsequent reaction with the nucleophile [Scheme 2(iii)]. Whereas (i) and (ii) lead to inversion of configuration at the ring carbon, (iii) generally results in some loss in its configurational purity.

Substituents R in Scheme 2(ii) which activate<sup>5</sup> the aziridine towards nucleophilic attack include sulfonyl,<sup>6</sup> alkoxy carbonyl<sup>7</sup> and phosphinyl.<sup>8</sup> However, these groups have no obvious effect on either the stereo- or the regio-chemistry of ring-opening.<sup>9</sup> The barriers to *N*-inversion in these aziridines are relatively low<sup>10</sup> and the geometry at their ring nitrogens, although pyramidal, would be expected to be flatter than *N*-(3,4-dihydro-4-oxoquinazolin-3-yl) substituted (*N*-(Q)-substituted) aziridines. We have some evidence to support this conclusion from a

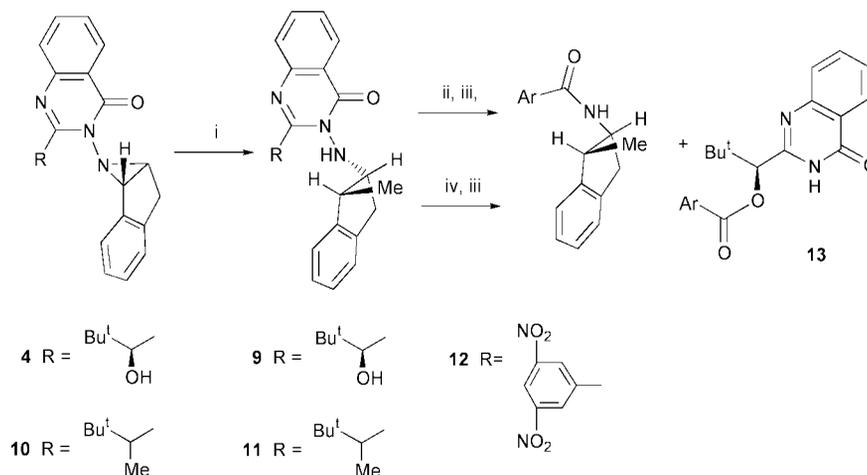
comparison of *N*-sulfonyl-substituted and *N*(*Q'*)-substituted aziridines in the Cambridge Crystallographic Data File. The *N*-sulfonyl-substituted aziridine structures clearly fall into two categories when the pyramidalicity at the ring nitrogen, as measured by the sum of angles ( $\Sigma\phi$ ) at this nitrogen, is considered. One category (13 structures) has the sulfonyl group *cis* to only hydrogens on the 2- and 3-positions of the aziridine ring (2-substituted or 2,3-*cis*-disubstituted) and has an average  $\Sigma\phi$  of 292°. The other category has a substituent *cis* to the sulfonyl group (2,3-*trans* or 2,2-disubstituted) with an average  $\Sigma\phi$  of 300°. Clearly the presence of a substituent *cis* to the sulfonyl group brings about a significant flattening of the nitrogen pyramid. For the 7 *N*(*Q'*-substituted) aziridines in the Data File the corresponding angles were 285° (2 examples) and 291° (7 examples), *i.e.* the *N*(*Q'*-substituted) aziridines have more steeply pyramidal nitrogens than the *N*-sulfonyl-substituted analogues.

Along with the steeper pyramidal nitrogen of *N*(*Q'*)-substituted aziridines goes a larger barrier to *N*-inversion. For the particular case of the indene-derived aziridine, the rate of *N*-inversion is sufficiently retarded to allow isolation of the kinetically formed *N*-invertomer **3** and to observe its conversion into the thermodynamically more stable *N*-invertomer **4**.<sup>3</sup>

The *Q* substituent is certainly electron-withdrawing and might, therefore, be expected to also activate the aziridine ring towards attack by nucleophiles [Scheme 2(ii)]. At the same time, the inductively electron-withdrawing *Q* group might be expected to further reduce the basicity of the aziridine ring nitrogen and hence discourage ring-opening *via* (i) or (iii) in Scheme 2. On the other hand, the *Q* group itself contains two basic sites available for protonation at N-1 or C=O. The positive charge resulting from protonation at either of these sites can be resonance stabilised by involving N-3 leading to the possibility of ring-opening in the presence of acid *via* an initially formed ylide species, *e.g.* **7**: rapid tautomerism to the more stable isolated product **8** would be anticipated (Scheme 3).



Scheme 3



Scheme 4 Reagents: (i) MeMgBr, CuBrSMe<sub>2</sub>; (ii) SmI<sub>2</sub>, Bu'OH, THF; (iii) 3,5-diNO<sub>2</sub>C<sub>6</sub>H<sub>3</sub>COCl, Et<sub>3</sub>N; (iv) SmI<sub>2</sub> (0.5 eq.), Bu'OH, THF, Mg.

In this paper we examine the ring-opening of aziridines **3**, **4**, **5** and **6** with particular attention to the role played by the *Q* substituent.<sup>11</sup>

## Results and discussion

Aziridine **4** was reacted with excess methylmagnesium bromide in the presence of cuprous bromide–dimethyl sulfide complex to give the ring-opened product **9** in 57% yield (Scheme 4) confirming that this *Q* group was able to stabilise the developing negative charge on nitrogen in the transition state for ring-opening. The presence of the hydroxy group in the *Q* side chain is not vital for the success of the reaction since ring-opening of aziridine **10** which lacks this hydroxy group also takes place under the same conditions to give the corresponding product **11** in 48% yield.

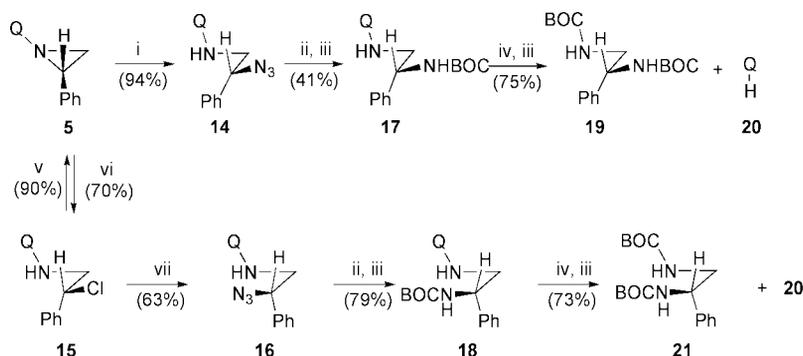
Confirmation that attack of the cuprate took place as expected with inversion of configuration was provided by an X-ray crystal structure of the ring-opened product<sup>11a</sup> **11** and it is assumed that inversion also occurs in ring-opening of aziridine **4**.

Conversion of the ring-opened product **9** to the *Q*-free amide chiron **12** was accomplished by samarium diiodide in the presence of *tert*-butyl alcohol<sup>12</sup> and reaction with its 3,5-dinitrobenzoyl chloride; 4-oxo-3*H*-quinazolin-2-yl 3,5-dinitrobenzoate **13** was also isolated by chromatography.

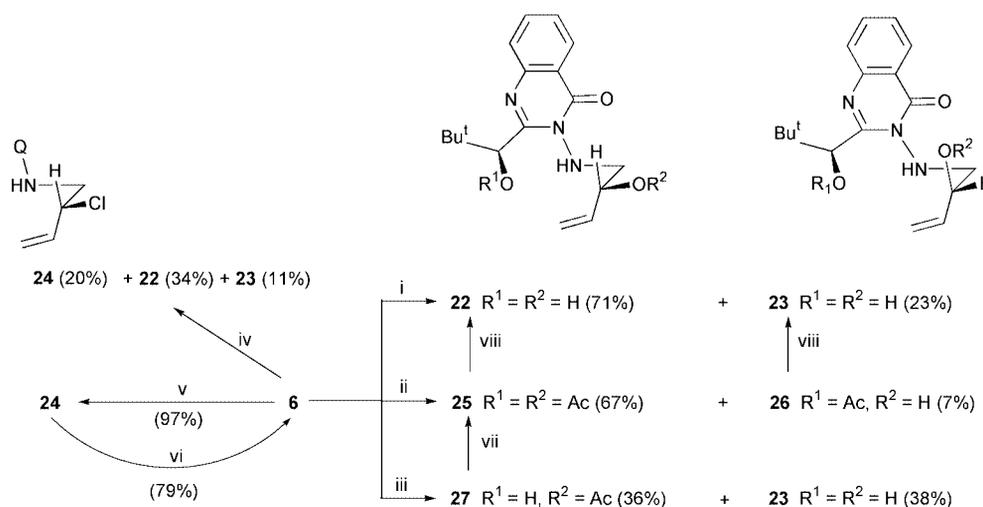
Endo *et al.* have shown<sup>13</sup> that in reductions using samarium diiodide, submolar quantities of this reagent can be used in the presence of magnesium metal which reduces Sm<sup>3+</sup>→Sm<sup>2+</sup> *in situ*. Applying this procedure to the *N*-*Q* bond reduction in conversion of amine **9** to amide **12** was successful with only a small loss in yield by comparison with reduction using excess samarium diiodide (see Scheme 4).

A further example of the ability of the *Q* group to facilitate nucleophilic attack without the necessity for prior protonation [Scheme 2(ii)] was the reaction of aziridine **5** with azide ion. Reaction takes place on heating in dimethyl sulfoxide at 70 °C to give a mixture of products from which the ring-opened azide **14** was separated but in only 9% yield (Scheme 5). Inclusion of acetic acid (1 eq.) in the reaction mixture (**WARNING**)<sup>†</sup> however, resulted in azide **14** as the only product. It appears that the function of the acetic acid is to protonate the anionic nitrogen formed in the rate-determining aziridine ring-opening step since the effect of increased concentration of acetic acid on the rate of disappearance of aziridine **5** was so small (Table 1).

<sup>†</sup> Sodium azide in the presence of acid can give rise to hydrogen azide: this reaction has not been carried out on more than 200 mg of sodium azide.



**Scheme 5** Reagents: (i)  $\text{NaN}_3$ , AcOH, DMSO; (ii) Pd/C,  $\text{H}_2$ ; (iii) BOC-ON,  $\text{Et}_3\text{N}$ ; (iv)  $\text{SmI}_2$ , Bu<sup>t</sup>OH, THF; (v) NaH, THF; (vi) HCl,  $\text{Et}_2\text{O}$ ; (vii)  $\text{NaN}_3$ , DMSO.



**Scheme 6** Reagents: (i) dil.  $\text{H}_2\text{SO}_4$ , dioxane; (ii) AcOH, 70 °C, 17 h; (iii) AcOH,  $\text{H}_2\text{O}$ , 70 °C, 5 h; (iv) HCl, dioxane; (v) HCl, ether; (vi) NaH–THF; (vii) AcOH, 70 °C, 12 h; (viii) NaOH,  $\text{H}_2\text{O}$ .

**Table 1** Effect of acetic acid on rate of disappearance of aziridine **5** in DMSO containing sodium azide determined by NMR spectroscopy<sup>a</sup>

Entry	AcOH added (eq.)	Unchanged isolated aziridine <b>5</b> (%)
1	0	35
2	1	31
3	2	31

<sup>a</sup> See Experimental for conditions.

Azide **14** is very likely formed with complete inversion of configuration since it was found to be different from, and not contaminated with, the diastereoisomeric azide **16** prepared from aziridine **5** by ring-opening with hydrogen chloride followed by displacement of the chloride in **15** by azide. Proof that chloride **15** was formed from aziridine **5** with inversion of configuration came from its reconversion back to aziridine **5** in high yield by the action of sodium hydride in tetrahydrofuran (THF).

Conversion of diastereoisomeric azides **14** and **16** into their respective Q-free, BOC-protected diamine enantiomers **19** and **21**, was accomplished as shown in Scheme 5 by reagents not affecting the configuration at the chiral centres. The almost equal but opposite optical rotations for **19** and **21**, separated by chromatography from QH **20** in each case, support stereospecific inversion in each of the three substitution steps in Scheme 5 and the absolute configurations assigned follow from the known absolute configuration of aziridine **5**.<sup>3</sup>

#### Involvement of the Q group in the stereochemistry of aziridine ring-opening

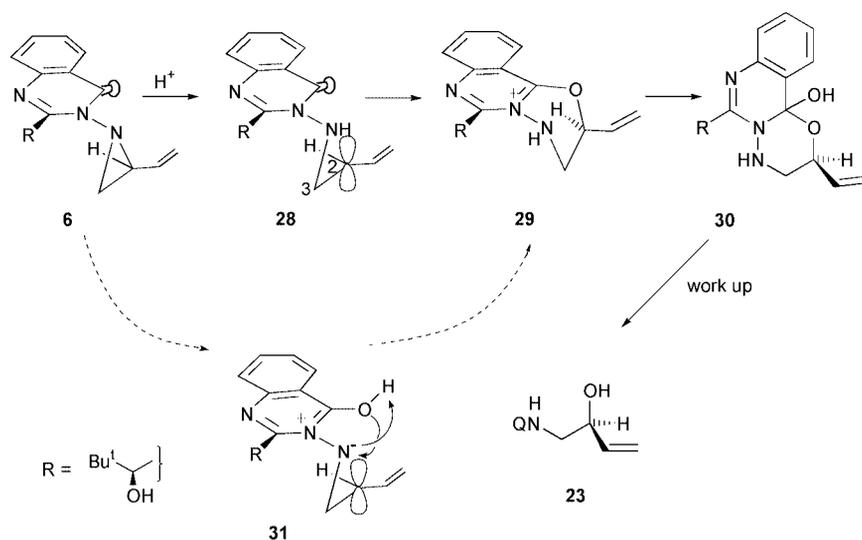
Reaction of aziridine **6** with sulfuric acid in dioxane gives a

separable mixture of diol stereoisomers **22** and **23** (Scheme 6). The same 3 : 1 ratio of diols **22** and **23** was obtained by reaction of aziridine **6** with hydrochloric acid in dioxane but, in addition, the chloride **24** (20%) was isolated, which appeared to be a single diastereoisomer. The same chloride **24** was obtained in quantitative yield when aziridine **6** was treated with hydrogen chloride gas in ether and was shown to be formed with inversion of configuration by its reconversion to aziridine **6** (79%) on treatment with sodium hydride in THF.

Reaction of aziridine **6** with glacial acetic acid at 70 °C overnight gave diacetate **25** (67%) and monoacetate **26** (7%). Reaction of aziridine **6** with glacial acetic acid containing water (20 eq.) and for a shorter time (5 h) resulted in the formation of diol **23** (38%) together with the allylic monoacetate **27** (36%) showing that acetylation of the Q side-chain hydroxy group occurs after aziridine ring-opening. Further treatment of allylic acetate **27** with the hot acetic acid solution above yielded diacetate **25** but no monoacetate **26**, showing that the latter was not formed from **25** or **27** *in situ*.

Diacetate **25**, monoacetates **26** and **27** and the two diols **22** and **23** were interrelated and their stereostructures identified by the chemical correlations in Scheme 6 together with an X-ray crystal structure determination on diacetate **25**.<sup>11b</sup> Thus diacetate **25** and the major diol **22** are formed with inversion of configuration and monoacetate **26** and diol **23** with retention of configuration. The proportion of diacetate **25** (inversion) to monoacetate **26** (retention) was increased to 38 : 1 by carrying out the reaction of aziridine **6** with glacial acetic acid in the presence of molecular sieves to scavenge any water.

A mechanism to account for the retention of configuration in formation of diol **23** and hence monoacetate **26** in the reaction of aziridine **6** with acetic acid–water involves participation by the quinazolinone ring as outlined in Scheme 7.

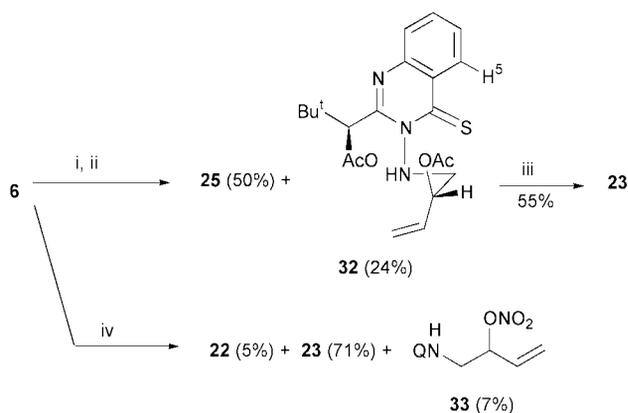


Scheme 7

In Scheme 7, the allylic cation **28** formed by ring-opening, possibly *via* the Q-protonated intermediate **31** (see Scheme 3) must be trapped by the quinazolinone carbonyl oxygen from the *syn*-face, *i.e.* before rotation around the C2–C3 bond can occur. This C2–C3 bond rotation might be more retarded in carbocation **31** as a result of the formal negative charge on the exocyclic nitrogen than in carbocation **28** with its neutral exocyclic NH.‡ Further acetylation of only the more hindered hydroxy group in the Q side-chain on heating for 17 h (Scheme 6) is assumed to result from ‘protection’ of the allylic hydroxy group as the cyclic amide hemiacetal **30** and liberation of the free hydroxy group only on aqueous work up.

The acetate **27** and hence diacetate **25**, formed from aziridine **6** with inversion of configuration, could arise from capture of allylic carbocation **28** by acetic acid.

In this mechanism in Scheme 7, the allylic oxygen in diol **23** is derived from the quinazolinone carbonyl oxygen. As a test for this mechanism we repeated the reaction in acetic acid saturated with hydrogen sulfide. Further acetylation of the crude product with acetic anhydride and pyridine gave a separable mixture of diacetate **25** and the quinazolinone-4-thione **32** (Scheme 8).



**Scheme 8** Reagents: (i) AcOH, H<sub>2</sub>S, 70 °C, 17 h; (ii) Ac<sub>2</sub>O, pyr.; (iii) H<sub>2</sub>O<sub>2</sub>, NaOH, EtOH; (iv) Sm(NO<sub>3</sub>)<sub>3</sub>·6H<sub>2</sub>O, CH<sub>3</sub>CN.

The lowest field aromatic proton in the NMR spectrum of the quinazolinone ring is H-5 at  $\delta$  8.2 and the replacement of the carbonyl group by a thione causes a downfield shift of this H-5 proton to  $\delta$  8.6–8.7. As expected, this product **32** was formed with retention of configuration as shown by its con-

‡ We cannot exclude the possibility that this aziridine ring-opening in fact proceeds by a route analogous to that in Scheme 7 but involving the *cis*-*N*-invertomer of aziridine **6**.

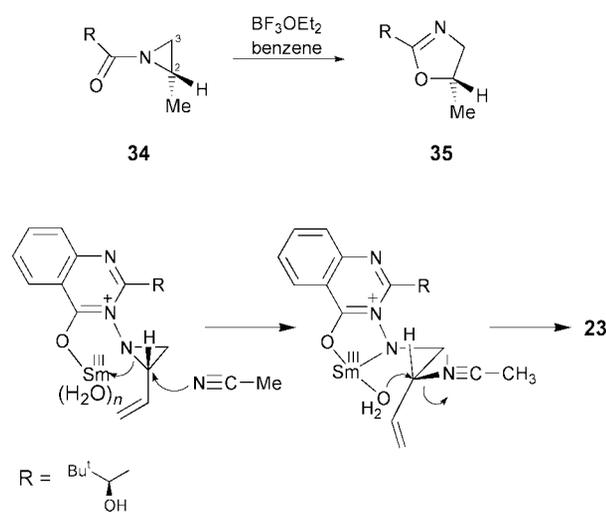
version to the diol **23** by treatment with basic hydrogen peroxide. The isolation of quinazolinone diacetate **25** in the reaction in Scheme 8 is important because it shows that without the intervention of the amide hemiacetal **30**, exchange of the Q-carbonyl oxygen for sulfur in diol **23** or monoacetate **26** as a route to quinazolinone-4-thione **32**, is not occurring.

The formation of quinazolinone-4-thione **32** is consistent with the mechanism in Scheme 7 with interception of the quinazolinium species **29** by hydrogen sulfide.

Aziridine ring-opening with retention of configuration at the ring carbon has been reported in the conversion of *N*-acylaziridine **34** into oxazoline **35** by boron trifluoride–diethyl ether: theoretical results support an S<sub>N</sub><sup>1</sup> mechanism.<sup>14</sup>

#### Aziridine ring-opening mediated by samarium(III) salts

We have found that the ring-opening of these Q-substituted aziridines is catalysed by samarium(III) salts. Treatment of aziridine **6** with samarium trinitrate hexahydrate (1 eq.) in acetonitrile (Scheme 8) gave the diols **23** and **22** in a ratio of 13:1. A by-product (7%) in this reaction was the nitrate ester **33** (of unknown relative configuration). A mechanism involving coordination of the highly oxophilic Sm(III) to the Q-carbonyl group and double inversion as shown in Scheme 9 could account for the predominant overall retention of configuration.

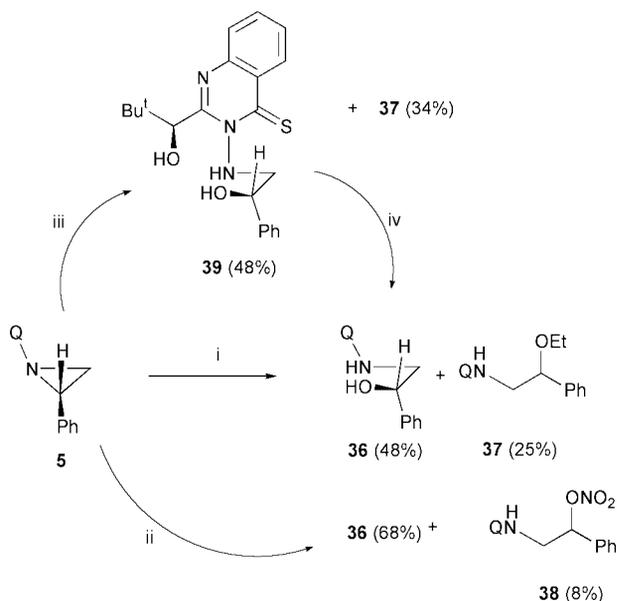


Scheme 9

Thus, overall since the diacetate **25** is efficiently converted into the diol **22** by hydrolysis (see Scheme 6), methods for ring-opening of aziridine **6**, formally by water, either with inversion or with retention of configuration are available.

### Ring-opening of aziridine **5** with ethanol

When aziridine **5** was heated in boiling ethanol containing two drops of water for 34 h, ring-opening occurred to give benzyl alcohol **36** and a benzylic ethyl ether **37** of unknown configuration (Scheme 10).



**Scheme 10** Reagents: (i) EtOH, H<sub>2</sub>O, 78 °C, 34 h; (ii) Sm(NO<sub>3</sub>)<sub>3</sub>·6H<sub>2</sub>O, CH<sub>3</sub>CN; (iii) EtOH, H<sub>2</sub>S, 78 °C; (iv) H<sub>2</sub>O<sub>2</sub>, NaOH, EtOH.

Evidence for the benzylic alcohol **36** having been formed with retention of configuration came from the ring-opening of aziridine **5** with samarium(III) nitrate hexahydrate. In a reaction analogous to that described previously (Scheme 8), benzyl alcohol **36** together with nitrate ester **38** were isolated § (Scheme 10) in comparable yields to the corresponding products from ring-opening of vinylaziridine **6**. Since the allylic alcohol **23** from this latter reaction is formed with retention of configuration, the configuration of benzyl alcohol **36** is assigned accordingly.

Since aziridine **5** was not affected by heating in wet propan-2-ol or wet dioxane, it appeared that the ring-opening in Scheme 10 was probably catalysed by ethanol acting as an acid

§ None of the ring-opened alcohol with inversion of configuration was identified in this reaction.

[propan-2-ol ( $pK_a$  16.5) is less acidic than ethanol ( $pK_a$  16)] with a reaction mechanism analogous to that for conversion of aziridine **6** into allylic alcohol **23** (Scheme 7). To test this mechanism we heated aziridine **5** in a Young's tube with hydrogen sulfide-saturated ethanol for 94 h at 78 °C. The *N*-(4-thiocarbonylquinazolin-3-yl)-substituted benzyl alcohol **39** (46%) was separated from ether **37** (34%) by chromatography. As expected, treatment of this alcohol **39** with basic hydrogen peroxide gave the corresponding *N*-(oxoquinazolinyl) analogue **36**. Benzyl ether **37** had not undergone any (Q)-carbonyl→(Q)-thione conversion ¶ which excludes a mechanism for formation of alcohol **39** by direct attack on the Q-carbonyl of **36** by hydrogen sulfide followed by oxygen/sulfur exchange *via* a hemithioacetal.

### Ring-opening of indene-derived aziridines **3** and **4** with hydrogen chloride

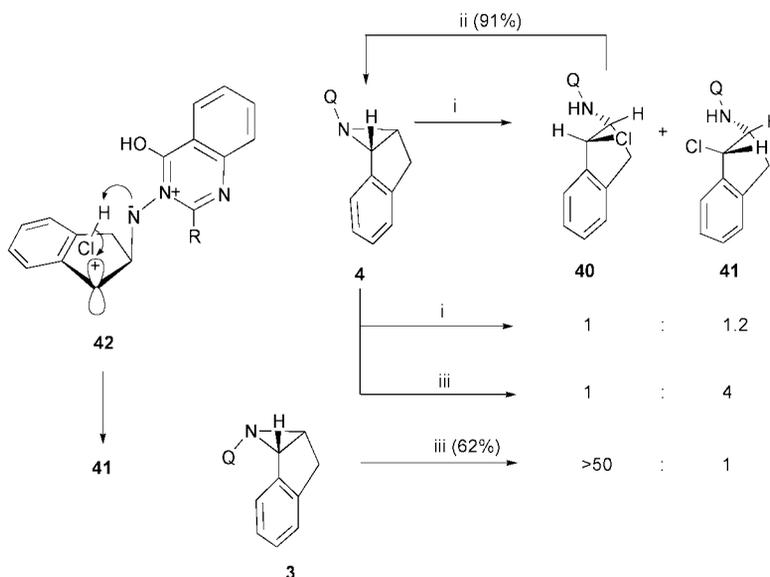
In contrast to the ring-opening of styrene- and butadiene-derived aziridines **5** and **6** with hydrogen chloride, reaction of the thermodynamically more stable *N*-invertomer of indene-derived aziridine **4** with a solution of hydrogen chloride gas in ether yielded a ~1:1 mixture of chlorides **40** and **41** (Scheme 11). This loss of stereospecificity could be ascribed to the presence of a longer-lived carbocation intermediate [Scheme 2(iii)] which is trapped from both faces by chloride anion.

However, when hydrogen chloride gas was bubbled into an ice-cold dichloromethane solution of aziridine **3** (prepared directly by aziridination of indene, see Scheme 1) only chloride **40** was isolated in 62% yield from indene. The *trans*-configuration of chloride **40** was confirmed by its re-conversion to aziridine **4** in excellent yield by treatment with sodium hydride–THF; in contrast, reaction of chloride **41** under the same conditions gave a mixture of unidentified products.

To confirm that the change in stereochemistry in reactions of the two aziridine *N*-invertomers **3** and **4** with hydrogen chloride was not the result of the difference in solvent used (dichloromethane and ether), aziridine **4** was ring-opened with hydrogen chloride in dichloromethane using the same conditions applied to aziridine **3** above. Unexpectedly, this ring-opening gave a 4:1 mixture of chloride diastereoisomers **41** and **40** *i.e.* the major product is formed with retention of configuration.

It is possible that the inversion of configuration which accompanies ring-opening of aziridine **3** may be the result of

¶ This result suggests that ether **37** is very likely formed with inversion of configuration.



**Scheme 11** Reagents: (i) HCl, ether; (ii) NaH, THF; (iii) HCl, CH<sub>2</sub>Cl<sub>2</sub>, 0 °C.

shielding of one face of the carbocation by the Q group. The retention of configuration in reaction of aziridine **4** with hydrogen chloride may arise *via* a transition state resembling **42** where an un-ionised hydrogen chloride molecule suffers deprotonation leaving the chloride to attack from the *syn* face. In ether solution, the concentration of chloride anions will be higher and *syn* and *anti* attack will become competitive.

The lower barriers for *cis*→*trans* *N*-inversion in other *N*-(Q')-aziridines limit the number of pairs of aziridine *N*-invertomers available for further study: the barrier for conversion of aziridine **3** to **4** is abnormally high because of the ring-strain associated with the 5,3-ring-fusion in addition to the effect of the electron-withdrawing Q group.

## Summary

The Q group in *N*-(Q)-aziridines **4**, **5** and **6** activates the ring towards nucleophilic attack by cuprates and by azide.

Involvement of the Q group in ring-opening of aziridines **5** and **6** gives the corresponding alcohols **23** (in acetic acid) and **36** (in ethanol) respectively, with retention of configuration. The carbonyl oxygen of the Q ring becomes the oxygen of the hydroxy group. Better yields of ring-opened alcohols **23** and **36** are obtained by ring-opening using samarium(III) nitrate hexahydrate in acetonitrile. Since ring-opening of aziridine **6** by acetic acid can be accomplished with inversion of configuration and the derived acetate **25** can be hydrolysed to the alcohol **22**, access to either alcohol stereoisomers **22** or **23** is possible starting from a single stereoisomer of the aziridine **6**.

Aziridine *N*-invertomers **3** and **4** are isolable because of the enhanced barrier to *N*-inversion: stereochemically complementary modes of ring-opening are obtained by use of hydrogen chloride in dichloromethane giving inversion of configuration (for **3**) and mainly retention (for **4**).

## Experimental

### General

Unless otherwise indicated <sup>1</sup>H NMR spectra were recorded at 250 MHz and <sup>13</sup>C at 63 MHz using a Bruker ARX 250 spectrometer. <sup>1</sup>H NMR spectra at 400 MHz were recorded using a Bruker DRX 400 spectrometer. IR spectra of crystalline compounds were recorded at room temperature in dichloromethane and of liquids as thin films using a Perkin-Elmer 298 spectrometer. Optical rotations were determined on a Perkin-Elmer 341 Polarimeter at 589 nm and are given in 10<sup>-1</sup> deg cm<sup>2</sup> g<sup>-1</sup>.

All NMR spectra were recorded at room temperature in deuterated chloroform unless otherwise indicated. For other general experimental details see ref. 3.

BOC-ON refers to [2-(*tert*-butoxycarbonyloxyimino)-2-phenylacetonitrile and was supplied by Aldrich. LTA refers to lead tetraacetate.

### Ring-opening of aziridine **4** with methylmagnesium bromide–copper(I) bromide–dimethyl sulfide

To a flame-dried 3-necked flask equipped with a stirrer bar and under an argon atmosphere was added a solution of aziridine **4** (100 mg, 0.277 mmol) in freshly distilled THF (2 cm<sup>3</sup>) *via* a septum cap, followed by a solution of methylmagnesium bromide in THF (0.35 cm<sup>3</sup>, 3.0 mol dm<sup>-3</sup>). After effervescence had ceased, copper bromide–dimethyl sulfide complex (57 mg, 0.33 mmol) was quickly added and then the reaction vessel again flushed with argon. The resulting deep red solution was stirred under argon for 4 h at room temperature before being syringed into a stirred aqueous saturated ammonium chloride solution (5 cm<sup>3</sup>) maintained at 0 °C. The resulting deep blue aqueous solution was extracted with ethyl acetate (10 cm<sup>3</sup>) and the organic layer separated, dried and evaporated under

reduced pressure to give a brown residue. Column chromatography (eluent 4:1 light petroleum–ethyl acetate) yielded amine **9** (*R*<sub>f</sub> 0.35) (60 mg, 57%) as a colourless oil (Found: MH<sup>+</sup> 378.2182. C<sub>23</sub>H<sub>27</sub>N<sub>3</sub>O<sub>2</sub> requires MH<sup>+</sup> 378.2182); *a*<sub>D</sub> 177.1 (*c* 3.5, ethanol); *v*<sub>max</sub>/cm<sup>-1</sup> 3480w, 1660s and 1595s; *δ*<sub>H</sub> (400 MHz) 0.89 [9H, s, C(CH<sub>3</sub>)<sub>3</sub>], 1.21 (3H, d, *J* 6.9, CH<sub>3</sub>), 2.91 (1H, dd, *J* 6.2 and 15.8, CHH), 3.13 (1H, struct. m, CHCH<sub>3</sub>), 3.18 (1H, dd, *J* 6.6 and 15.8, CHH), 3.58 (1H, d, *J* 10.2, OH), 3.74 (1H, struct. m, CHNH), 4.94 (1H, d, *J* 10.2, CHOH), 5.60 (1H, d, *J* 5.6, NH), 7.18 [4H, struct. m, 4 × CH(Ar)], 7.50 [1H, ddd, *J* 1.1, 7.0 and 8.0, 6-H(Q)], 7.71 [1H, br d, *J* ~8, 8-H(Q)], 7.78 [1H, ddd, *J* 1.5, 7.0 and 8.2, 7-H(Q)] and 8.28 [1H, dd, *J* 1.5 and 8.0, 5-H(Q)]; *δ*<sub>C</sub> 18.3 (CH<sub>3</sub>), 25.8 [C(CH<sub>3</sub>)<sub>3</sub>], 37.1 (CH<sub>2</sub>), 37.8 [C(CH<sub>3</sub>)<sub>3</sub>], 43.5 (CH), 69.0 (CH), 74.1 (CH), 120.7 [CCO(Q)], 123.5, 124.5, 126.7, 126.9, 127.3, 134.6 [6 × CH(Q), CH(Ar)], 139.9, 145.7, 146.0 [2 × C(Ar), CN=C(Q)], 159.2 [C=N(Q)] and 161.7 [CO(Q)]; *m/z* (%) 378 (100, MH<sup>+</sup>), 248 (83) and 191 (20).

### Ring-opening of aziridine **10** with methylmagnesium bromide–copper(I) bromide–dimethyl sulfide

To a flame-dried, 3-necked flask equipped with a stirrer bar and under an argon atmosphere a solution of aziridine **10** (163 mg, 0.454 mmol) in THF (3 cm<sup>3</sup>) was added *via* a septum cap, followed by a solution of methylmagnesium bromide in THF (0.4 cm<sup>3</sup>, 3.0 mol dm<sup>-3</sup>). After effervescence had ceased copper bromide–dimethyl sulfide complex (93 mg, 0.45 mmol) was quickly added and the reaction vessel flushed with argon. The resulting deep red solution was stirred at room temperature for 1.5 h under argon before being syringed into a stirred saturated aqueous ammonium chloride solution (5 cm<sup>3</sup>) maintained at 0 °C. The resulting deep blue aqueous solution was extracted with ethyl acetate (10 cm<sup>3</sup>) and the organic layer separated, dried and evaporated under reduced pressure to give a brown oil. Chromatography (eluent 9:1 light petroleum–ethyl acetate) yielded amine **11** (*R*<sub>f</sub> 0.35) (82 mg, 48%) as a colourless crystalline solid; mp 136–137 °C (from light petroleum–ethyl acetate). (Found: MH<sup>+</sup> 376.2389. C<sub>24</sub>H<sub>30</sub>N<sub>3</sub>O requires MH<sup>+</sup> 376.2389); *v*<sub>max</sub>/cm<sup>-1</sup> 3290w, 1665s and 1580s; *δ*<sub>H</sub> (400 MHz) 0.91 [9H, s, C(CH<sub>3</sub>)<sub>3</sub>], 1.30 (6H, 2 × d, *J* 6.9, 2 × CH<sub>3</sub>), 2.96 (1H, dd, *J* 6.7 and 15.7, CHH), 3.08 (1H, br s, CHNH), 3.12 (1H, dd, *J* 6.7 and 15.7, CHH), 3.60 (2H, struct. m, 2 × CHCH<sub>3</sub>), 5.87 (1H, d, *J* 6.6, NH), 7.13–7.22 [4H, struct. m, CH(Ar)], 7.45 [1H, ddd, *J* 1.6, 6.7 and 8.0, 6-H(Q)], 7.67–7.78 [2H, struct. m, 7-H and 8-H(Q)] and 8.26 [1H, dd, *J* 1.2 and 8.0, 5-H(Q)]; *δ*<sub>C</sub> 14.5, 18.0 (2 × CH<sub>3</sub>), 27.4 [C(CH<sub>3</sub>)<sub>3</sub>], 35.4 [C(CH<sub>3</sub>)<sub>3</sub>], 37.2 (CH<sub>2</sub>), 42.1, 43.5, 69.1 [CHNH, CHC(CH<sub>3</sub>)<sub>3</sub>, CHCH<sub>3</sub>], 120.3 [CCO(Q)], 123.2, 124.5, 126.0, 126.4, 126.7, 126.8, 127.5, 134.0 [4 × CH(Ar), 4 × CH(Q)], 140.2, 145.5, 146.8 [2 × C(Ar), CN=C(Q)] and 161.3, 162.0 [CO(Q), C=N(Q)]; *m/z* (%) 376 (MH<sup>+</sup>, 100), 246 (21) and 189 (45). A crystal for X-ray structure determination was grown from light petroleum–ethyl acetate.<sup>11a</sup>

### Q–N bond reduction and 3,5-dinitrobenzoylation of *N*-(Q)-amine **9**

Amine **9** (206 mg, 0.55 mmol) in THF (8 cm<sup>3</sup>) containing *tert*-butyl alcohol (1 cm<sup>3</sup>) was reduced with a solution of samarium diiodide in THF (33 cm<sup>3</sup>, 0.1 mol dm<sup>-3</sup>). After the solution had decolourised (~80 min), triethylamine (1 cm<sup>3</sup>) was added, followed by 3,5-dinitrobenzoyl chloride (264 mg, 1.14 mmol) and the resulting red solution stirred for 2 h. Saturated sodium hydrogen carbonate solution (10 cm<sup>3</sup>) was added, the solution filtered and ethyl acetate (20 cm<sup>3</sup>) added to the filtrate. After shaking, the organic layer was separated, washed with brine (10 cm<sup>3</sup>), dried and evaporated under reduced pressure. Chromatography (eluent 5:1 light petroleum–ethyl acetate) yielded amide **12** (*R*<sub>f</sub> 0.23) (151 mg, 81%) mp 172–174 °C (from light petroleum–ethyl acetate) (Found: C, 60.1; H, 4.5; N, 12.2).

$C_{17}H_{15}N_3O_5$  requires C, 59.8; H, 4.4; N, 12.3%;  $a_D$   $-40.18$  ( $c$  1.12,  $CHCl_3$ );  $\nu_{max}/cm^{-1}$  3430w, 1735m, 1675s and 1545s;  $\delta_H$  1.41 (3H, d,  $J$  6.9,  $CH_3$ ), 2.89 (1H, dd,  $J$  6.3, 16.0,  $CHH$ ), 3.23 (1H, quintet,  $J$  6.9,  $CHCH_3$ ), 3.51 (1H, dd,  $J$  7.5, 16.0,  $CHH$ ), 4.56 (1H, struct. m,  $J$  6.3 and 7.5 visible,  $CHNH$ ), 6.56 (1H, br d,  $J$  7.5,  $NH$ ), 7.24 [4H, s,  $4 \times H(Ph)$ ], 8.94 [2H, d,  $J$  2.2,  $H-2$ ,  $H-6$  ( $(NO_2)_2Ar$ )] and 9.16 [1H, s br,  $H-4$  ( $(NO_2)_2Ar$ )];  $m/z$  (%) 342 ( $MH^+$ , 69), 259 (48) and 147 (33).

Further elution with the same solvent yielded *QH-O*-(3,5-dinitrobenzoate) **13** ( $R_f$  0.10) (72 mg, 31%) (Found:  $MH^+$  427.1254.  $C_{20}H_{19}N_4O_7$  requires  $MH^+$  427.1254);  $\nu_{max}/cm^{-1}$  1740m, 1670s, 1610m and 1550s;  $\delta_H$  1.18 (9H, s,  $C(CH_3)_3$ ), 5.47 (1H, s,  $CHO$ ), 7.39 [1H, ddd,  $J$  1.3, 7.0 and 8.0, 6-H(Q)], 7.63 [1H, dd,  $J$  1.3 and 8.2, 8-H(Q)], 7.72 [1H, ddd,  $J$  1.0, 7.0 and 8.2, 7-H(Q)], 8.08 [1H, dd,  $J$  1.0 and 8.0, 5-H(Q)], 8.98 [1H, t,  $J$  2.2,  $H-4$  ( $(NO_2)_2Ar$ )], 9.21 [2H, d,  $J$  1.9,  $H-2$ ,  $H-6$  ( $(NO_2)_2Ar$ )] and 11.95 (1H, s,  $NH$ );  $\delta_C$  26.5 [ $C(CH_3)_3$ ], 35.7 [ $C(CH_3)_3$ ], 83.9 ( $CHO$ ), 120.7 [ $CCO(Q)$ ], 122.6, 126.0, 127.2, 127.8, 129.7 [ $5 \times CH(Q)$ ,  $CH(Ar)$ ], 132.8 [ $C(Ar)$ ], 135.2 [ $CH(Q)$ ], 148.2, 148.6, 151.5 [ $CN=C(Q)$ ,  $2 \times C(Ar)$ ], 162.4 [ $C=N(Q)$ ] and 163.9 [ $CO(Q)$ ] [ $CO$ ,  $CH(Ar)$  missing];  $m/z$  (%) 427 ( $MH^+$ , 51), 307 (20) and 215 (47).

### Q–N bond reduction and 3,5-dinitrobenzoylation of *N*-(Q)-amine **9** using samarium(II) iodide and magnesium

Magnesium turnings (305 mg, 12.7 mmol) were stirred vigorously overnight in a flame-dried 3-necked flask under an argon atmosphere. The amine **9** (150 mg, 0.4 mmol) dissolved in freshly distilled THF (2 cm<sup>3</sup>) and *tert*-butyl alcohol (1 cm<sup>3</sup>) was added *via* a septum cap and the solution de-gassed 5 times with argon using a 3-way tap. A solution of samarium diiodide in THF (2 cm<sup>3</sup>, 0.1 mol dm<sup>-3</sup>) was added *via* the septum cap to the vigorously stirred solution and the disappearance of the amine monitored by TLC. After 2.5 h the solution was transferred *via* a cannula into a round-bottom flask under an argon atmosphere and triethylamine (1 cm<sup>3</sup>) and 3,5-dinitrobenzoyl chloride (193 mg, 0.84 mmol) were added aqueous with stirring. After 2 h the solution was filtered, saturated sodium hydrogen carbonate solution (5 cm<sup>3</sup>) added and the mixture extracted with ethyl acetate (20 cm<sup>3</sup>). The organic layer was separated, washed with brine, dried and evaporated under reduced pressure. Chromatography of this residue (eluent 5:1 light-petroleum–ethyl acetate) yielded the amide **12** ( $R_f$  0.23) (94 mg, 69%). Further elution with the same solvent yielded *QH-O*-3,5-dinitrobenzoate **13** ( $R_f$  0.10) (87 mg, 51%).

### Ring-opening of aziridine **5** with sodium azide

To a solution of aziridine **5** (300 mg, 0.86 mmol) in DMSO (3 cm<sup>3</sup>) containing acetic acid (52 mg, 0.87 mmol) was added sodium azide (167 mg, 0.26 mmol) and the mixture heated at 70 °C for 17 h with stirring behind a screen (**WARNING**—hydrogen azide present). Water (5 cm<sup>3</sup>) was then added, the solution extracted with ethyl acetate (3 × 10 cm<sup>3</sup>) and the combined organic extracts were washed with water (3 × 5 cm<sup>3</sup>), then saturated brine (5 cm<sup>3</sup>), dried and the solvent removed under reduced pressure to give *azide* **14** (336 mg, 94%) as a colourless oil (Found:  $MH^+$  393.2039.  $C_{21}H_{25}N_6O_2$  requires  $MH^+$  393.2039);  $\nu_{max}/cm^{-1}$  3490w, 3290w, 2100s, 1675s and 1595s;  $\delta_H$  (400 MHz) 0.88 (9H, s,  $C(CH_3)_3$ ), 3.02 (1H, br m,  $CHH$ ), 3.50 (2H, br d,  $OH$ ,  $CHH$ ), 4.72 (1H, dd,  $J$  5.0 and 7.3,  $CHN_3$ ), 4.78 (1H, d,  $J$  10.2,  $CHOH$ ), 5.49 (1H, dd,  $J$  4.7 and 9.5,  $NH$ ), 7.27–7.38 [5H, struct. m,  $5 \times CH(Ph)$ ], 7.42 [1H, ddd,  $J$  ~1, ~7 and ~8, 6-H(Q)], 7.61 [1H, dd,  $J$  1.0 and ~7, 8-H(Q)], 7.70 [1H, ddd,  $J$  1.5, 7.0 and ~8, 7-H(Q)], 8.17 [1H, dd,  $J$  1.5 and ~7, 5-H(Q)];  $\delta_C$  25.6 [ $C(CH_3)_3$ ], 37.5 [ $C(CH_3)_3$ ], 55.1 ( $CH_2$ ), 64.1 ( $CH$ ), 74.1 ( $CH$ ), 120.4 [ $CCO(Q)$ ], 126.4, 126.7, 126.8, 127.1, 128.6, 128.8, 134.4 [ $CH(Ar)$ ,  $CH(Q)$ ], 136.6 [ $C(Ar)$ ], 145.8 [ $CN=C(Q)$ ], 158.1 [ $C=N(Q)$ ] and 161.1 [ $CO(Q)$ ];  $m/z$  (%) 393 ( $MH^+$ , 100), 260 (28), 215 (32) and 175 (22).

### Effect of acetic acid concentration on ring-opening of aziridine **5** with sodium azide

Three 5 cm<sup>3</sup> round-bottom flasks (a), (b) and (c) were each charged with aziridine **5** (100 mg, 0.286 mmol) and sodium azide (56 mg, 0.86 mmol). To flask (a) was added DMSO (1 cm<sup>3</sup>); to flask (b) 1 cm<sup>3</sup> of a solution of acetic acid (0.164 cm<sup>3</sup>, 2.86 mmol made up to 10 cm<sup>3</sup> with DMSO) and to flask (c) 1 cm<sup>3</sup> of a solution of acetic acid (0.33 cm<sup>3</sup>, 5.76 mmol, made up to 10 cm<sup>3</sup> with DMSO). The flasks were then heated in the same oil bath at 70 °C for 5 h. After this time the oil bath was removed, each reaction poured into saturated aqueous sodium hydrogen carbonate solution (5 cm<sup>3</sup>) and worked up in the following way. The solution was extracted with ethyl acetate (3 × 5 cm<sup>3</sup>) and the combined organic extracts were washed with water (3 × 5 cm<sup>3</sup>), then saturated brine (5 cm<sup>3</sup>), dried and the solvent evaporated under reduced pressure. The NMR spectra of the crude products were recorded and the results shown in Table 1.

### Ring-opening of aziridine **5** with a solution of hydrogen chloride in ether

Hydrogen chloride gas was slowly bubbled into a rapidly stirred solution of aziridine **5** (500 mg, 1.43 mmol) in diethyl ether (10 cm<sup>3</sup>) for 20 s and a white solid was immediately precipitated. The reaction mixture was carefully washed with excess saturated aqueous sodium hydrogen carbonate, the organic layer separated, dried and evaporated under reduced pressure to give *chloride* **15** as a colourless solid (388 mg, 70%), mp 153–155 °C (ethanol) (Found: C, 65.65; H, 6.3; N, 10.9.  $C_{21}H_{24}ClN_3O_2$  requires C, 65.55; H, 6.25 and N, 10.9%);  $a_D$  126.0 ( $c$  1.0, chloroform);  $\nu_{max}/cm^{-1}$  3500w, 3280w, 1640s and 1590s;  $\delta_H$  (400 MHz) 0.95 [9H, s,  $C(CH_3)_3$ ], 3.22 (1H, struct. m,  $CHH$ ), 3.59 (1H, d,  $J$  10.2,  $OH$ ), 3.84 (1H, struct. m,  $CHH$ ), 4.91 (1H, d,  $J$  10.2,  $CHOH$ ), 5.09 (1H, dd,  $J$  6.0 and 7.0,  $CHCl$ ), 5.31 (1H, dd,  $J$  4.6 and 9.8,  $NH$ ), 7.29–7.53 [6H, struct. m, 6-H(Q), 5 ×  $CH(Ph)$ ], 7.67 [1H, br d,  $J$  7.0, 8-H(Q)], 7.75 [1H, ddd,  $J$  1.5, 7.0 and 8.1, 7-H(Q)] and 8.22 [1H, dd,  $J$  1.5 and 8.0, 5-H(Q)];  $m/z$  (%) 386 ( $MH^+$ , 100) and 215 (26).

### Reconversion of chloride **15** to aziridine **5** with sodium hydride

The chloride **15** (100 mg, 0.26 mmol) was dissolved in dry THF (2 cm<sup>3</sup>) and sodium hydride (31 mg of a 60% dispersion in oil, 0.77 mmol) added. After stirring at room temperature for 70 min the reaction was quenched with ice–water and extracted with ethyl acetate (3 × 5 cm<sup>3</sup>). The combined organic fractions were separated, dried and the solvent was evaporated to give aziridine **5** (90 mg, 99%).

### Displacement of chloride in **15** by azide

A solution of chloride **15** (381 mg, 0.99 mmol) in DMSO (3 cm<sup>3</sup>) was stirred rapidly with sodium azide (193 mg, 2.97 mmol) overnight at room temperature. The reaction mixture was then diluted with water (5 cm<sup>3</sup>), extracted with ethyl acetate (3 × 5 cm<sup>3</sup>), the combined organic extracts were washed with water (3 × 5 cm<sup>3</sup>) then brine (5 cm<sup>3</sup>), dried and the solvent was removed under reduced pressure to give a crystalline solid. Recrystallisation gave *azide* **16** as a colourless solid (246 mg, 63%), mp 110–112 °C (from 4:1 light petroleum–ethyl acetate) (Found: C, 64.35; H, 6.25; N, 21.15.  $C_{21}H_{24}N_6O_2$  requires C, 64.25; H, 6.15; N, 21.15%);  $a_D$  262.0 ( $c$  1.0, ethanol);  $\nu_{max}/cm^{-1}$  3480w, 3270m, 2095s, 1675s and 1590s;  $\delta_H$  (400 MHz) 0.90 [9H, s,  $C(CH_3)_3$ ], 2.94 (1H, br s,  $CHH$ ), 3.78 (2H, br m,  $CHH$ ,  $OH$ ), 4.69 (1H, dd,  $J$  4.7 and 8.9,  $CHN_3$ ), 4.83 (1H, d,  $J$  10,  $CHOH$ ), 5.64 (1H, dd,  $J$  3.9 and 10.0,  $NH$ ), 7.25–7.34 (5H, struct. m,  $ArH$ ), 7.40 [1H, ddd,  $J$  1.0, ~8 and ~8, 6-H(Q)], 7.59 [1H, br d,  $J$  7.5, 8-H(Q)], 7.68 [1H, ddd,  $J$  1.5, 7.5 and ~8, 7-H(Q)] and 8.17 [1H, dd,  $J$  1.5 and 8.1, 5-H(Q)];  $m/z$  (%) 393 ( $MH^+$ , 100), 260 (32) and 215 (20).

### Conversion of azide **14** to *N*-BOC,*N'*-(*Q*)-diamine **17**

Azide **14** (418 mg, 1.06 mmol) was dissolved in ethyl acetate (10 cm<sup>3</sup>), 5% palladium on charcoal (40 mg) added and the mixture stirred rapidly for 48 h under an atmosphere of hydrogen. The solution was then filtered through a plug of Celite, the solvent removed under reduced pressure and the residue dissolved in a mixture of 1:1 THF–water (10 cm<sup>3</sup>). To the stirred solution was then added triethylamine (0.2 cm<sup>3</sup>) and BOC-ON (Aldrich) (289 mg, 1.17 mmol). After stirring at room temperature for 45 min a solid had precipitated and was filtered off and washed with cold ethanol. Crystallisation yielded *N*-BOC, *N'*-(*Q*)-diamine **17** (206 mg, 41%), mp 225–227 °C (from ethanol–dichloromethane) (Found: C, 66.5; H, 7.25; N, 12.2. C<sub>26</sub>H<sub>34</sub>N<sub>4</sub>O<sub>4</sub> requires C, 66.9; H, 7.35; N, 12.0%);  $a_D$  105.5 (*c* 0.36, CHCl<sub>3</sub>);  $\nu_{\max}/\text{cm}^{-1}$  1710s, 1680s and 1595s;  $\delta_H$  1.00 [9H, s, C(CH<sub>3</sub>)<sub>3</sub>], 1.44 [9H, s, OC(CH<sub>3</sub>)<sub>3</sub>], 3.11 (1H, struct. m, CHH), 3.57 (1H, struct. m, CHH), 3.62 (1H, d, *J* 10.1, OH), 4.94 (1H, d, *J* 10.1, CHOH), 4.98–5.08 (2H, br m, CHNH, NHCO), 5.40 (1H, dd, *J* 4.1 and 10.0, NH), 7.27–7.41 [5H, struct. m, 5 × *H*(Ph)], 7.47 [1H, ddd, *J* 1.2, 6.9 and 7.9, 6-H(Q)], 7.67 [1H, br d, *J* 8.2, 8-H(Q)], 7.76 [1H, ddd, *J* 1.2, 6.9 and 8.2, 7-H(Q)] and 8.23 [1H, dd, *J* 1.2 and 7.9, 5-H(Q)]; *m/z* (%) 467 (MH<sup>+</sup>, 49), 260 (39) and 215 (20).

### Conversion of azide **16** to *N*-BOC,*N'*-(*Q*)-diamine **18**

Azide **16** (246 mg, 0.63 mmol) was dissolved in ethyl acetate (10 cm<sup>3</sup>), 5% palladium on charcoal (25 mg) added and reduction with hydrogen effected as described above. After the same work-up, the residue was dissolved in a mixture of 1:1 THF–water (10 cm<sup>3</sup>) and triethylamine (0.13 cm<sup>3</sup>) and BOC-ON (185 mg, 0.75 mmol) were added to the stirred solution. After stirring at room temperature for 2 h the solution was extracted with ethyl acetate (3 × 10 cm<sup>3</sup>), the combined extracts were washed with brine (10 cm<sup>3</sup>), dried and the solvent was evaporated under reduced pressure. Chromatography (eluent 4:1 light petroleum–ethyl acetate) yielded *N*-BOC,*N'*-(*Q*)-diamine **18** (*R*<sub>f</sub> 0.26) (230 mg, 79%) which crystallised as colourless needles, mp 183–187 °C (from ethanol) (Found: MH<sup>+</sup> 467.2658. C<sub>26</sub>H<sub>35</sub>N<sub>4</sub>O<sub>4</sub> requires MH<sup>+</sup> 467.2658);  $a_D$  151.5 (*c* 0.68, CHCl<sub>3</sub>);  $\nu_{\max}/\text{cm}^{-1}$  3450m, 3300w, 1720s and 1680s;  $\delta_H$  0.99 [9H, s, C(CH<sub>3</sub>)<sub>3</sub>], 1.46 [9H, s, OC(CH<sub>3</sub>)<sub>3</sub>], 3.15 (1H, ddd, *J* 5.0, 5.0 and 10.5, CHH), 3.47 (1H, br m, CHH), 3.57 (1H, d, *J* 10.0, OH), 4.89 (1H, d, *J* 10.0, CHOH), 4.99 (1H, br s, CHPh), 5.43 (1H, br d, *J* 7.5, NHCO), 5.57 (1H, dd, *J* 3.1 and 10.5, NH), 7.30–7.37 [5H, struct. m, 5 × *CH*(Ph)], 7.48 [1H, ddd, *J* 1.2, 6.9 and 8.0, 6-H(Q)], 7.67 [1H, br d, *J* 8.1, 8-H(Q)], 7.76 [1H, ddd, *J* 1.2, 6.9 and 8.1, 7-H(Q)] and 8.23 [1H, dd, *J* 1.2 and 8.0, 5-H(Q)];  $\delta_C$  25.9, 28.3 [2 × C(CH<sub>3</sub>)<sub>3</sub>], 37.8 [C(CH<sub>3</sub>)<sub>3</sub>], 55.3 (CH<sub>2</sub>), 74.4 (CHOH), 80.1 (OC(CH<sub>3</sub>)<sub>3</sub>), 120.6 (CCO(Q)), 126.1, 126.6, 126.9, 127.4, 127.8, 128.9, 134.6 (7 × CH), 146.0 [CN=C(Q)], 155.4, 158.3 and 161.2 [C=N(Q), CO(Q), CO] (CH, C missing); *m/z* (%) 467 (MH<sup>+</sup>, 100), 411 (32), 260 (50), 215 (42) and 175 (30).

### Q–N bond reduction of *N*-BOC,*N'*-(*Q*)-diamine **18** using samarium(II) iodide

A flame-dried 3-necked flask equipped with stirrer bar under an argon atmosphere was charged with amine **18** (184 mg, 0.30 mmol) dissolved in freshly distilled and dried THF (3 cm<sup>3</sup>) containing *tert*-butyl alcohol (1 cm<sup>3</sup>) via septum cap and the solution de-gassed 5 times with argon using a 3-way tap. A solution of samarium diiodide in THF (9 cm<sup>3</sup>, 0.1 mol dm<sup>-3</sup>) was added slowly dropwise using a syringe via the septum cap with stirring; discharge of the blue colour of Sm(II) occurred almost instantaneously. Water (10 cm<sup>3</sup>) was added, followed by triethylamine (0.2 cm<sup>3</sup>) and BOC-ON (107 mg, 0.43 mmol), with stirring throughout. After 2 h the solution was filtered, extracted with ethyl acetate (20 cm<sup>3</sup>), the organic layer sep-

arated, washed with brine (10 cm<sup>3</sup>), dried and evaporated to dryness under reduced pressure. Chromatography (eluent 4:1 light petroleum–ethyl acetate) yielded *DIBOC*-diamine **21** (*R*<sub>f</sub> 0.18, visualised with phosphomolybdic acid) (99 mg, 73%). Crystallisation gave colourless needles, mp 150–152 °C (from light petroleum–ethyl acetate) (Found: C, 64.2; H, 8.25; N, 8.3. C<sub>18</sub>H<sub>28</sub>N<sub>2</sub>O<sub>4</sub> requires C, 64.25; H, 8.4; N, 8.3%);  $a_D$  29.2 (*c* 1.20, CHCl<sub>3</sub>);  $\nu_{\max}/\text{cm}^{-1}$  3450m and 1710s;  $\delta_H$  (–40 °C, 9.4:1 ratio of rotamers) major rotamer 1.41 [9H, s, C(CH<sub>3</sub>)<sub>3</sub>], 1.45 [9H, s, C(CH<sub>3</sub>)<sub>3</sub>], 3.31 (1H, struct. m, CHH), 3.49 (1H, struct. m, CHH), 4.72 (1H, struct. m, CHAr), 4.96 (1H, t, *J* 5.7, CH<sub>2</sub>NH), 5.83 (1H, d, *J* 7.3, CHNH) and 7.27–7.42 [5H, struct. m, 5 × *CH*(Ar)]; minor rotamer observable signals  $\delta_H$  3.12 (1H, struct. m, CHH), 4.59 (1H, struct. m, CHAr), 5.12 (1H, struct. m, CH<sub>2</sub>NH) and 5.68 (1H, d, *J* 7.3, CHNH); *m/z* (%) 359 (MNa<sup>+</sup>, 10), 337 (MH<sup>+</sup>, 33), 281 (21), 225 (100), 181 (87), 164 (60) and 150 (39).

### Q–N bond reduction of *N*-BOC,*N'*-(*Q*)-diamine **17**

Amine **17** (196 mg, 0.42 mmol) was reduced and reacted with BOC-ON as described above using dry, distilled THF (3 cm<sup>3</sup>), *tert*-butyl alcohol (1 cm<sup>3</sup>), samarium diiodide in THF (10 cm<sup>3</sup>, 0.1 mol dm<sup>-3</sup>), water (10 cm<sup>3</sup>), triethylamine (0.2 cm<sup>3</sup>) and BOC-ON (114 mg, 0.46 mmol). Chromatography (eluent 4:1 light petroleum–ethyl acetate) eluted unchanged starting amine (*R*<sub>f</sub> 0.2, 19 mg) followed by *DIBOC*-diamine **19** (*R*<sub>f</sub> 0.18, visualised with phosphomolybdic acid), 96 mg, 75% (based on recovered starting material);  $a_D$  –28.0 (*c* 1.0, CHCl<sub>3</sub>), otherwise identical to the *DIBOC*-diamine as isolated above. Further elution with 2:1 light petroleum–ethyl acetate yielded 3*H*-quinazolinone **20** (78 mg, 89%) identical with that isolated previously.<sup>3</sup>

### Ring-opening of 2-vinylaziridine **6** with dilute sulfuric acid

Aziridine **6** (50 mg, 0.167 mmol) was dissolved in 1,4-dioxane (1 cm<sup>3</sup>) and dilute sulfuric acid (1 cm<sup>3</sup>, 0.2 mol dm<sup>-3</sup>) was added. After 15 min the reaction solution was poured into aqueous saturated sodium hydrogen carbonate (5 cm<sup>3</sup>) and extracted with ethyl acetate (3 × 3 cm<sup>3</sup>). The combined organic extracts were dried and the solvent was removed under reduced pressure to give a clear residue (50 mg.) By NMR spectroscopy this residue comprised a 3:1 mixture of allylic alcohol diastereoisomers **22** and **23** (94%) from comparison of the signals at  $\delta$  5.03 and 4.32 ppm respectively (see below).

### Ring-opening of 2-vinylaziridine **6** with dilute hydrochloric acid

Aziridine **6** (147 mg, 0.492 mmol) was dissolved in 1,4-dioxane (4 cm<sup>3</sup>) and dilute hydrochloric acid (3 cm<sup>3</sup>, 0.2 mol dm<sup>-3</sup>) added. After stirring for 15 min the reaction was poured into aqueous saturated sodium hydrogen carbonate (5 cm<sup>3</sup>) and extracted with ethyl acetate (3 × 5 cm<sup>3</sup>). The organic extracts were combined, dried and the solvent was removed under reduced pressure to give a clear oil. Chromatography (eluent 2:1 light petroleum–ethyl acetate) yielded the allylic chloride **24** (*R*<sub>f</sub> 0.33), (32 mg, 20%) (Found: MH<sup>+</sup> 336.1479. C<sub>17</sub>H<sub>23</sub>ClN<sub>3</sub>O<sub>2</sub> requires MH<sup>+</sup> 336.1479);  $a_D$  165.0 (*c* 1.0, ethanol);  $\nu_{\max}/\text{cm}^{-1}$  3480w, 3380w, 1675s and 1590s;  $\delta_H$  1.03 [9H, s, C(CH<sub>3</sub>)<sub>3</sub>], 3.11 (1H, struct. m, CHH), 3.62 (2H, struct. m, CHH, OH), 4.58 (1H, struct. m, CHCl), 5.04 (1H, br s, CHOH), 5.32 (1H, d, *J* 10.1, H<sub>T</sub>H<sub>C</sub>C), 5.46 (1H, d, *J* 17.0, H<sub>T</sub>H<sub>C</sub>C), 5.64 (1H, dd, *J* 4.1 and 9.8, NH), 6.03 (1H, ddd, *J* 7.9, 10.1 and 17.0, =CH), 7.49 [1H, struct. m, 6-H(Q)], 7.69 [1H, d, *J* 7.2, 8-H(Q)], 7.77 [1H, struct. m, 7-H(Q)] and 8.25 [1H, dd, *J* 1.0 and 8.2, 5-H(Q)];  $\delta_C$  25.8 [C(CH<sub>3</sub>)<sub>3</sub>], 37.7 [C(CH<sub>3</sub>)<sub>3</sub>], 55.9 (CH<sub>2</sub>), 59.0 (CH), 74.2 (CH), 118.9 (CH<sub>2</sub>=), 120.5 [CCO(Q)], 126.5, 126.9, 127.3, 134.6, 135.3 [4 × CH(Q), CH=], 145.8 [CN=C(Q)], 158.1 [C=N(Q)] and 161.0 [CO(Q)]; *m/z* (%) 336 (MH<sup>+</sup>, 100), 278 (20) and 215 (20). Further elution with the

same solvent gave the allylic alcohol diastereoisomers **22** and **23** ( $R_f$  0.13) as a 3:1 mixture (69 mg, 46%) identical with those isolated above.

#### Ring-opening of aziridine **6** with a solution of hydrogen chloride gas in ether

A suspension of aziridine **6** (93 mg, 0.31 mmol) was stirred rapidly in sodium-dried ether (5 cm<sup>3</sup>) whilst hydrogen chloride gas was slowly bubbled into the mixture. The suspended solid dissolved before a white solid rapidly precipitated. The reaction solution was neutralised by careful addition of excess saturated sodium hydrogen carbonate; the organic layer was separated, dried, and the solvent removed to give allylic chloride **24** (101 mg, 97%), identical with that isolated above.

#### Re-conversion of chloride **24** to aziridine **6**

To a solution of chloride **24** (175 mg, 0.52 mmol) in THF (2 cm<sup>3</sup>) was added sodium hydride (23 mg of a 60% dispersion in oil, 0.57 mmol) and the reaction stirred for 45 min. After addition of water (5 cm<sup>3</sup>) the solution was extracted with ethyl acetate (3 × 5 cm<sup>3</sup>), the organic extracts were dried and solvent was removed under reduced pressure to give aziridine **6** (123 mg, 79%).

#### Ring-opening of 2-vinylaziridine **6** with hot glacial acetic acid

Aziridine **6** (100 mg, 0.33 mmol) was dissolved in glacial acetic acid (2 cm<sup>3</sup>) and heated at 70 °C for 17 h. After evaporating the bulk of the acetic acid under reduced pressure, the residue was dissolved in ethyl acetate (5 cm<sup>3</sup>) and remaining acetic acid neutralised with excess aqueous saturated sodium hydrogen carbonate. The organic layer was separated, washed with saturated brine (1 cm<sup>3</sup>), dried and solvent removed under reduced pressure. Chromatography (2:1 light petroleum–ethyl acetate) yielded diacetate **25** ( $R_f$  0.35) (90 mg, 67%) which crystallised as a colourless solid, mp 118–121 °C (from light petroleum–ethyl acetate) (Found: C, 62.8; H, 6.8; N, 10.45. C<sub>21</sub>H<sub>27</sub>N<sub>3</sub>O<sub>5</sub> requires C, 62.8; H, 6.8; N, 10.5%);  $a_D$  154.0 (*c* 1.03, ethanol);  $\nu_{\max}/\text{cm}^{-1}$  3050m, 1740s, 1680s and 1595s;  $\delta_{\text{H}}$  1.00 [9H, s, C(CH<sub>3</sub>)<sub>3</sub>], 2.09 (3H, s, COCH<sub>3</sub>), 2.11 (3H, s, COCH<sub>3</sub>), 3.46 (2H, struct. m, CH<sub>2</sub>), 5.23 (1H, dd, *J* 1.0 and 10.4, H<sub>C</sub>H<sub>T</sub>C=), 5.32 (1H, dd, *J* 1.0 and 17.3, H<sub>C</sub>H<sub>T</sub>C=), 5.50 (2H, struct. m, NH, CHOAc), 5.85 (1H, Bu<sup>t</sup>CHOAc), 5.90 (1H, ddd, *J* 5.7, 10.4 and 17.3, CH=), 7.39 [1H, ddd, *J* 3.1, 5.7 and 8.0, 6-H(Q)], 7.65 [2H, struct. m, 7-H, 8-H(Q)] and 8.16 [1H, d, *J* 8.0, 5-H(Q)];  $\delta_{\text{C}}$  20.9, 21.2 (2 × COCH<sub>3</sub>), 26.1 [C(CH<sub>3</sub>)<sub>3</sub>], 35.9 [C(CH<sub>3</sub>)<sub>3</sub>], 51.9 (CH<sub>2</sub>), 72.2, 76.5 (2 × CHOCO), 117.8 (CH<sub>2</sub>=), 120.9 [CCO(Q)], 126.4, 126.8, 127.9, 134.0, 134.3 (4 × CH(Q), CH=), 146.6 [CN=C(Q)], 154.2 [C=N(Q)], 161.3 [CO(Q)], 170.0 and 171.3 (2 × CO<sub>2</sub>CH<sub>3</sub>); *m/z* (%) 402 (MH<sup>+</sup> 100), 342 (47), 302 (43), 215 (92) and 175 (27). A crystal was grown from light petroleum–ethyl acetate for X-ray structure determination.<sup>11b</sup>

Further elution with the same solvent gave acetoxyl allylic alcohol **26** ( $R_f$  0.22) (9 mg, 7%) (Found: MH<sup>+</sup> 360.1923. C<sub>19</sub>H<sub>26</sub>N<sub>3</sub>O<sub>4</sub> requires MH<sup>+</sup> 360.1923);  $\nu_{\max}/\text{cm}^{-1}$  3450w, 3295w, 1740s, 1680s and 1590s;  $\delta_{\text{H}}$  1.10 [9H, s, C(CH<sub>3</sub>)<sub>3</sub>], 2.18 (3H, s, COCH<sub>3</sub>), 3.22 (1H, ddd, *J* 3.8, 8.5 and 11.7, CHH), 3.45 (1H, ddd, *J* 3.5, 10.0 and 11.7, CHH), 4.43 (1H, struct. m, CHOH), 5.19 (1H, ddd, *J* 1.3, 1.6 and 10.7, H<sub>C</sub>H<sub>T</sub>C=), 5.41 (1H, ddd, *J* 1.3, 1.6 and 17.3, H<sub>C</sub>H<sub>T</sub>C=), 5.70 (1H, dd, *J* 3.8 and 10.0, NH), 5.93 (1H, ddd, *J* 5.0, 10.7 and 17.3, CH=), 6.11 (1H, s, Bu<sup>t</sup>CHOCOCH<sub>3</sub>), 7.48 [1H, struct. m, 6-H(Q)], 7.74 [2H, struct. m, 7-H, 8-H(Q)] and 8.24 [1H, d, *J* 7.9, 5-H(Q)]; *m/z* (%) 360 (MH<sup>+</sup>, 100), 302 (39), 215 (73) and 175 (28).

The same reaction was carried out but with addition of water (120 mg, 20 eq.) and heating for only 5 h at 70 °C. After the same work up, chromatography of the crude product (3:2 light petroleum–ethyl acetate) yielded allylic acetate **27** ( $R_f$  0.38) (43

mg, 36%) (Found: MH<sup>+</sup> 360.1924. C<sub>19</sub>H<sub>26</sub>N<sub>3</sub>O<sub>4</sub> requires MH<sup>+</sup> 360.1923);  $\nu_{\max}/\text{cm}^{-1}$  3480w, 3290w, 1745s, 1650s and 1590s;  $\delta_{\text{H}}$  0.94 [9H, s, C(CH<sub>3</sub>)<sub>3</sub>], 2.10 (3H, s, COCH<sub>3</sub>), 2.90 (1H, struct. m, CHH), 3.40 (1H, unresolved ddd, *J* 4 and 8 visible, CHH), 3.57 (1H, br d, *J* 7.5, OH), 4.89 (1H, d, *J* 7.5, CHOH), 5.24 (1H, dd, *J* 10.7 and 1.0, H<sub>C</sub>H<sub>T</sub>C=), 5.32 (1H, dd, *J* 17.0 and 1.0, H<sub>C</sub>H<sub>T</sub>C=), 5.45 (1H, struct. m, CHOAc), 5.51 (1H, dd, *J* 4.0 and 10.4, NH), 5.82 (1H, ddd, *J* 5.9, 10.7 and 17.0, CH=), 7.43 [1H, ddd, *J* 1.0, 6.9 and 8.2, 6-H(Q)], 7.62 [1H, dd, *J* 1.0 and 8.2, 8-H(Q)], 7.71 [1H, ddd, *J* 1.6, 6.9 and 8.2, 7-H(Q)] and 8.18 [1H, dd, *J* 1.6 and 8.2, 5-H(Q)];  $\delta_{\text{C}}$  21.0 (COCH<sub>3</sub>), 25.8 [C(CH<sub>3</sub>)<sub>3</sub>], 37.6 [C(CH<sub>3</sub>)<sub>3</sub>], 53.3 (CH<sub>2</sub>), 71.9, 74.3 (CHOH, CHOAc), 118.3 (CH<sub>2</sub>=), 120.5 [CCO(Q)], 126.5, 126.8, 127.2, 133.4, 134.5 [4 × CH(Q), CH=], 145.9 (CN=C), 158.2 [C=N(Q)], 161.1 [CO(Q)] and 169.9 (COCH<sub>3</sub>); *m/z* (%) 360 (MH<sup>+</sup> 100), 215 (53) and 175 (37).

Further elution gave the allylic alcohol **23** ( $R_f$  0.22), 40 mg, 38% (Found: MH<sup>+</sup> 318.1818. C<sub>17</sub>H<sub>24</sub>N<sub>3</sub>O<sub>3</sub> requires MH<sup>+</sup> 318.1818);  $\delta_{\text{H}}$  0.96 [9H, s, C(CH<sub>3</sub>)<sub>3</sub>], 2.95 (1H, struct. m, CHH), 3.08 (1H, ddd, *J* 3.8, 8.8 and 12.0, CHH), 4.32 (1H, struct. m, CHOHCH<sub>2</sub>), 5.00 (1H, br s, Bu<sup>t</sup>CHOH), 5.13 (1H, d, *J* 10.7, H<sub>C</sub>H<sub>T</sub>C=), 5.32 (1H, d, *J* 17.3, H<sub>C</sub>H<sub>T</sub>C=), 5.73 (1H, dd, *J* 3.8, 10.4, NH), 5.80 (1H, ddd, *J* 5.0, 10.7 and 17.3, CH=), 7.42 [1H, unresolved ddd, *J* ~8 visible, 6-H(Q)], 7.63 [1H, d, *J* 7.9, 8-H(Q)], 7.71 [1H, unresolved ddd, *J* ~8 visible, 7-H(Q)] and 8.18 [1H, d, *J* 8.2, 5-H(Q)];  $\delta_{\text{C}}$  25.9 [C(CH<sub>3</sub>)<sub>3</sub>], 37.6 [C(CH<sub>3</sub>)<sub>3</sub>], 55.9 (CH<sub>2</sub>), 70.2 (CH), 74.4 (CH), 116.0 (CH<sub>2</sub>=), 120.3 [CCO(Q)], 126.5, 126.7, 127.2, 134.4 [4 × CH(Q)], 137.8 (CH=), 146.0 [CN=C(Q)], 158.1 [C=N(Q)] and 171.1 [CO(Q)]; *m/z* (%) 318 (MH<sup>+</sup>, 100), 260 (20), 215 (42) and 147 (31).

#### Ring-opening of 2-vinylaziridine **6** in acetic acid in the presence of hydrogen sulfide

Aziridine **6** (100 mg, 0.33 mmol) was dissolved in acetic acid (2 cm<sup>3</sup>) saturated with hydrogen sulfide and the resulting solution heated at 70 °C for 17 h. After cooling the bulk of the acetic acid was removed by evaporation under reduced pressure and residual acid neutralised by addition of excess aqueous saturated sodium hydrogen carbonate. The solution was extracted with ethyl acetate (3 × 5 cm<sup>3</sup>) and the combined organic extracts were washed with brine (5 cm<sup>3</sup>), dried and evaporated under reduced pressure. The resulting colourless oil was dissolved in pyridine (2 cm<sup>3</sup>), acetic anhydride (0.1 cm<sup>3</sup>, 1.06 mmol) added and the solution left to stand overnight at room temperature. After addition of saturated aqueous sodium hydrogen carbonate (5 cm<sup>3</sup>) the solution was extracted with ethyl acetate (3 × 5 cm<sup>3</sup>), the combined organic fractions washed with brine (5 cm<sup>3</sup>), dried and the solvent removed under reduced pressure. Chromatography (eluent 4:1 light petroleum–ethyl acetate) yielded quinazoline-4-thione diacetate **32** ( $R_f$  0.31) (33 mg, 24%) (Found: MH<sup>+</sup> 418.1801. C<sub>21</sub>H<sub>28</sub>N<sub>3</sub>O<sub>4</sub>S requires MH<sup>+</sup> 418.1801);  $\nu_{\max}/\text{cm}^{-1}$  1740s and 1590s;  $\delta_{\text{H}}$  1.01 [9H, s, C(CH<sub>3</sub>)<sub>3</sub>], 2.09 (3H, s, COCH<sub>3</sub>), 2.10 (3H, s, COCH<sub>3</sub>), 3.40 (1H, ddd, *J* 4.1, 11.6 and 11.6, CHH), 3.66 (1H, ddd, *J* 4.4, 7.2, 11.6, CHH), 5.23 (1H, d, *J* 10.7, H<sub>C</sub>H<sub>T</sub>C=), 5.34 (1H, d, *J* 17.3, H<sub>C</sub>H<sub>T</sub>C=), 5.54 (1H, struct. m, CHOCOCH<sub>3</sub>), 5.83 (1H, ddd, *J* 5.7, 10.7, 17.3, CHC=), 6.05 [1H, s, CHC(CH<sub>3</sub>)], 6.88 (1H, dd, *J* 4.4, 11.6, NH), 7.44 [1H, br dd, *J* 8.2 visible, 6-H(Q)], 7.67 [2H, struct. m, 7-H, 8-H(Q)] and 8.60 [1H, d, *J* 8.5, 5-H(Q)];  $\delta_{\text{C}}$  20.9, 21.1 (2 × CH<sub>3</sub>), 26.1 [C(CH<sub>3</sub>)<sub>3</sub>], 36.5 [C(CH<sub>3</sub>)<sub>3</sub>], 49.8 (CH<sub>2</sub>), 72.5, 77.3 (2 × CHO), 117.9 (CH<sub>2</sub>=), 128.3, 128.5 [2 × CH(Q)], 128.7 [CCS(Q)], 130.9, 133.6, 134.4 [2 × CH(Q), CH=], 141.7 [CN=C(Q)], 153.3 [C=N(Q)], 170.2, 171.3 (2 × CO) and 186.3 [CS(Q)]; *m/z* (%) 418 (MH<sup>+</sup>, 83), 358 (77), 305 (24), 291 (48), 231 (100), 215 (32) and 191 (36). Further elution with the same solvent mixture yielded quinazoline-4-one diacetate **25** ( $R_f$  0.18) 67 mg, 50% identical to an authentic sample prepared previously.

### Conversion of quinazoline-4-thione diacetate **32** to quinazolin-4-one diol **23**

Quinazoline-4-thione **32** (12 mg, 0.029 mmol) was dissolved in a mixture of ethanol (0.5 cm<sup>3</sup>) and sodium hydroxide solution (0.5 cm<sup>3</sup>, 1.0 mol dm<sup>-3</sup>) and hydrogen peroxide (20 volume, 3 drops) added. After 30 min the solution was extracted with ethyl acetate (10 cm<sup>3</sup>), the organic layer separated and washed successively with water (2 × 5 cm<sup>3</sup>) and brine (5 cm<sup>3</sup>), then dried and evaporated to give quinazolin-4-one diol **23** (5 mg, 55%), identical by comparison of its NMR spectrum with that of an authentic sample prepared previously.

### Ring-opening of 2-vinylaziridine **6** with samarium nitrate hexahydrate

Aziridine **6** (300 mg, 1.00 mmol) was heated at 60 °C for 50 min in acetonitrile (4 cm<sup>3</sup>) containing samarium nitrate hexahydrate (446 mg, 1.00 mmol). Water (5 cm<sup>3</sup>) was then added and the solution extracted with ethyl acetate (10 cm<sup>3</sup>). The organic layer was separated, washed with brine, dried and concentrated. Chromatography (eluent 5:2 light petroleum–ethyl acetate) yielded *nitrate ester* **33** as an oil (*R*<sub>f</sub> 0.30) (26 mg, 7%) (Found: *MH*<sup>+</sup> 363.1668. C<sub>17</sub>H<sub>23</sub>N<sub>4</sub>O<sub>5</sub> requires *MH*<sup>+</sup> 363.1669); δ<sub>H</sub> 0.93 [9H, s, C(CH<sub>3</sub>)<sub>3</sub>], 3.03 (1H, struct. m, CHH), 3.47 (2H, struct. m, CHOH, CHH), 5.38 (1H, d, *J* 10.7, H<sub>C</sub>H<sub>T</sub>C=), 5.46 (1H, d, *J* 17.3, H<sub>C</sub>H<sub>T</sub>C=), 5.55 (1H, struct. m, CHONO<sub>2</sub>), 5.80 (1H, ddd, *J* 6.6, 10.7, 17.3, CH=), 7.43 [1H, ddd, *J* 1.0, 6.9, 8.1, 6-H(Q)], 7.63 [1H, br d, *J* ~8, 8-H(Q)], 7.71 [1H, ddd, *J* 1.0, 6.9, 8.5, 7-H(Q)] and 8.18 [1H, dd, *J* 1.0, 8.1, 5-H(Q)]; *m/z* (%) 363 (MH<sup>+</sup>, 100), 260 (33), 233 (52), 215 (47) and 176 (96).

Further elution with the same solvent yielded a mixture of allylic alcohols **22** and **23** (*R*<sub>f</sub> 0.1) (242 mg, 76%) in a 1:13 ratio by comparison of the NMR signals at δ 5.03 and 4.32 ppm respectively with those of authentic samples.

### Hydrolysis of diacetate **25**

Diacetate **25** (50 mg, 0.125 mmol) was dissolved in 1,4-dioxane (1 cm<sup>3</sup>), sodium hydroxide solution (2 cm<sup>3</sup>, 2.0 mol dm<sup>-3</sup>) was added and the resulting solution left to stand overnight. The solution was then diluted with ethyl acetate (3 cm<sup>3</sup>), washed with water (2 cm<sup>3</sup>) then brine (2 cm<sup>3</sup>), dried and evaporated under reduced pressure to give *diol* **22** (34 mg, 86%) (Found: *MH*<sup>+</sup> 318.1818. C<sub>17</sub>H<sub>24</sub>N<sub>3</sub>O<sub>3</sub> requires *MH*<sup>+</sup> 318.1818); *v*<sub>max</sub>/cm<sup>-1</sup> 3450m, 3290m, 1675s and 1590s; δ<sub>H</sub> 1.03 [9H, s, C(CH<sub>3</sub>)<sub>3</sub>], 2.97 (1H, struct. m, CHH), 3.23 (1H, ddd, *J* 3.5, 7.2 and 10.8, CHH), 3.69 (2H, br s, 2 × OH), 4.25 (1H, struct. m, CHCH=), 5.03 (1H, br s, CHOH), 5.20 (1H, dd, *J* 1.3 and 11.7, CH<sub>C</sub>H<sub>T</sub>=), 5.34 (1H, dd, *J* 1.3 and 17.3, CH<sub>C</sub>H<sub>T</sub>=), 5.88 (2H, struct. m, CH=, NH), 7.49 [1H, ddd, *J* 1.3, 6.9, ~8, 6-H(Q)], 7.70 [1H, br d, *J* ~8, 8-H(Q)], 7.78 [1H, ddd, *J* 1.0, 6.9, 8.2, 7-H(Q)] and 8.25 [1H, dd, *J* 1.0 and 8.2, 5-H(Q)]; δ<sub>C</sub> 25.9 [C(CH<sub>3</sub>)<sub>3</sub>], 37.8 [C(CH<sub>3</sub>)<sub>3</sub>], 56.1 (CH<sub>2</sub>), 69.7, 74.6, (2 × CHOH), 116.4 (CH<sub>2</sub>=), 120.3 [CCO(Q)], 126.7, 126.9, 127.3, 134.7, 137.2 [4 × CH(Q), CH=], 146.1 [CN=C(Q)], 158.3 [C=N(Q)] and 162.1 [CO(Q)]; *m/z* (%) 318 (MH<sup>+</sup>, 100), 260 (20), 215 (42) and 147 (30).

### Ring-opening of aziridine **5** by ethanol–water

Aziridine **5** (50 mg, 0.14 mmol) was heated in a mixture of ethanol (2 cm<sup>3</sup>) and water (2 drops) under reflux for 34 h. The reaction mixture was cooled, diluted with ethanol (5 cm<sup>3</sup>), dried and evaporated under reduced pressure. Chromatography (eluent 2:1 light petroleum–ethyl acetate) gave the *ether* **37** (*R*<sub>f</sub> 0.35), (14 mg, 25%) (Found: *MH*<sup>+</sup> 396.2287. C<sub>23</sub>H<sub>30</sub>N<sub>3</sub>O<sub>3</sub> requires *MH*<sup>+</sup> 396.2287); *v*<sub>max</sub>/cm<sup>-1</sup> 3375w, 3290w, 1680s and 1595s; δ<sub>H</sub> (400 MHz) 0.90 [9H, s, C(CH<sub>3</sub>)<sub>3</sub>], 1.21 (3H, t, *J* 7.0, CH<sub>3</sub>), 3.09 (1H, br s, CHH), 3.49 (3H, struct. m, CH<sub>2</sub>CH<sub>3</sub>, OH), 3.72 (1H, br s, CHH), 4.54 (1H, dd, *J* 3.7 and 6.2, CHPh), 4.72 (1H, d, *J* 10.0, CHOH), 5.68 (1H, dd, *J* 4.8 and 8.5, NH), 7.35 [5H, struct. m, 5 × CH(Ar)], 7.46 [1H, br dd, *J* ~8 and ~8,

6-H(Q)], 7.66 [1H, d, *J* 7.5, 8-H(Q)], 7.74 [1H, ddd, *J* 1.3, 7.5 and 8.4, 7-H(Q)] and 8.24 [1H, dd, *J* 1.3 and 8.1, 5-H(Q)]; δ<sub>C</sub> 15.3 (CH<sub>3</sub>), 25.9 [C(CH<sub>3</sub>)<sub>3</sub>], 37.5 [C(CH<sub>3</sub>)<sub>3</sub>], 53.4, 56.3 (2 × CH<sub>2</sub>), 74.4 (CHOH), 79.7 (CHPh), 120.7 [CCO(Q)], 126.6, 126.7, 127.3, 127.9, 128.5, 134.4 [6 × CH(Ph), CH(Q)], 139.9 [C(Ph)], 146.1 (CN=C), 158.4 [C=N(Q)] and 161.4 [CO(Q)]; *m/z* (%) 396 (100 MH<sup>+</sup>), 260 (39) and 215 (50).

Further elution with the same solvent gave alcohol **36** (*R*<sub>f</sub> 0.1) (25 mg, 48%) identical with that isolated below.

### Ring-opening of aziridine **5** with samarium nitrate hexahydrate

Aziridine **5** (100 mg, 0.28 mmol) was heated at 60 °C for 50 min in acetonitrile (1 cm<sup>3</sup>) containing samarium nitrate hexahydrate (127 mg, 0.28 mmol). Water (5 cm<sup>3</sup>) was added and the solution extracted with ethyl acetate (5 cm<sup>3</sup>), the organic layer separated, washed with brine, dried and evaporated under reduced pressure. Chromatography (eluent 4:1 light petroleum–ethyl acetate) yielded *nitrate ester* **38** (9 mg, 8%) (Found: *MH*<sup>+</sup> 413.1826. C<sub>21</sub>H<sub>25</sub>N<sub>4</sub>O<sub>5</sub> requires *MH*<sup>+</sup> 413.1825); δ<sub>H</sub> 0.90 [9H, s, C(CH<sub>3</sub>)<sub>3</sub>], 3.25 (1H, s m, CHH), 3.45 (1H, d, *J* 10.4, OH), 3.59 (1H, s m, CHH), 4.82 (1H, d, *J* 10.4, CHOH), 5.57 (1H, dd, *J* 5.3 and 8.2, CHPh), 5.99 (1H, dd, *J* 3.8 and 8.5, NH), 7.61 [5H, br s, 5 × CH(Ph)], 7.43 [1H, struct. m, 6-H(Q)], 7.70 [2H, m, 7-H, 8-H(Q)] and 8.17 [1H, dd, *J* 1.2, 7.8, 5-H(Q)]; *m/z* (%) 413 (MH<sup>+</sup>, 100), 260 (35), 233 (33), 215 (48), 176 (100) and 147 (71).

Further elution with 2:1 light petroleum–ethyl acetate gave *alcohol* **36** (*R*<sub>f</sub> 0.1) (72 mg, 68%) as colourless crystals mp 125–128 °C (from 2:1 light petroleum–ethyl acetate) (Found: C, 68.75; H, 6.8; N, 11.4. C<sub>21</sub>H<sub>25</sub>N<sub>3</sub>O<sub>3</sub> requires C, 68.65; H, 6.85; N, 11.45%; *v*<sub>max</sub>/cm<sup>-1</sup> 3600w, 3420w, 3300w, 1675s and 1590s; δ<sub>H</sub> 0.90 [9H, s, C(CH<sub>3</sub>)<sub>3</sub>], 2.86 (1H, d, *J* 4.7, CHOHPh), 3.01 (1H, struct. m, CHH), 3.30 (1H, struct. m, CHH), 3.54 (1H, d, *J* 10.4, CHOH), 4.83 (1H, struct. m, CHPh), 4.91 (1H, d, *J* 10.4, CHOH), 5.73 (1H, dd, *J* 3.7 and 9.4, NH), 7.09–7.30 [5H, struct. m, 5 × CH(Ph)], 7.36 [1H, ddd, *J* 1.2, 6.9 and 8.2, 6-H(Q)], 7.56 [1H, br d, *J* ~7, 8-H(Q)], 7.65 [1H, ddd, *J* 1.0, 6.9 and 8.2, 7-H(Q)] and 8.12 [1H, dd, *J* 1.0 and 8.2, 5-H(Q)]; *m/z* (%) 368 (MH<sup>+</sup>, 100), 260 (24), 215 (22) and 175 (20).

### Ring-opening of aziridine **5** in ethanol containing hydrogen sulfide

A Young's tube was charged with aziridine **5** (100 mg, 0.29 mmol) dissolved in ethanol (4 cm<sup>3</sup>). The solution was saturated with hydrogen sulfide and then heated under reflux for 94 h before being evaporated under reduced pressure. Chromatography (eluent 3.5:1 light petroleum–ethyl acetate) yielded *ether* **37** (*R*<sub>f</sub> 0.38) (39 mg, 34%), identical to a sample prepared previously by comparison of their NMR spectra. Further elution with the same solvent yielded *quinazolin-4-thione diol* **39** (*R*<sub>f</sub> 0.25) as a yellow oil, (51 mg, 46%) (Found: *MH*<sup>+</sup> 384.1746. C<sub>21</sub>H<sub>26</sub>N<sub>3</sub>O<sub>2</sub>S requires *MH*<sup>+</sup> 384.1746); *v*<sub>max</sub>/cm<sup>-1</sup> 3450s, 1735w, 1680s and 1590s; δ<sub>H</sub> 0.98 [9H, s, C(CH<sub>3</sub>)<sub>3</sub>], 2.61 (1H, br s, CHPhOH), 3.01 (1H, ddd, *J* 3.5, 3.8 and 11.0, CHH), 3.55 (1H, d, *J* 10.0, CHOH), 3.60 (1H, ddd, *J* 3.5, 8.5 and 11.0, CHH), 4.97 (1H, dd, *J* 3.5, 8.5, CHPh), 5.14 (1H, d, *J* 10.0, CHOH), 7.18–7.43 [6H, struct. m, 5 × H(Ph), NH], 7.53 [1H, ddd, *J* 1.0, 6.9 and 8.2, 6-H(Q)], 7.70 [1H, d, *J* 8.2, 8-H(Q)], 7.79 [1H, ddd, *J* 1.0, 6.9 and 8.2, 7-H(Q)] and 8.69 [1H, dd, *J* 1.0 and 8.2, 5-H(Q)]; δ<sub>C</sub> 25.8 [C(CH<sub>3</sub>)<sub>3</sub>], 38.2 [C(CH<sub>3</sub>)<sub>3</sub>], 56.0 (CH<sub>2</sub>), 72.1, 75.2 (2 × CHOH), 125.9 [CCO(Q)], 127.9, 128.3, 128.4, 128.7, 128.9, 131.0, 134.8 (7 × CH), 141.1, 141.4 [CN=C(Q), C(Ph)], 157.0 [C=N(Q)] and 185.9 [CS(Q)] (1 C missing); *m/z* (%) 384 (MH<sup>+</sup>, 49), 267 (32), 231 (20) and 191 (22).

### Conversion of quinazolin-4-thione diol **39** to quinazolin-4-one diol **36**

The quinazolin-4-thione diol **39** (25 mg, 0.065 mmol) was dissolved in a mixture of ethanol (0.5 cm<sup>3</sup>) and sodium hydroxide

(0.5 cm<sup>3</sup>, 1.0 mol dm<sup>-3</sup>) and hydrogen peroxide (3 drops, 20 volume) added. After 30 min the solution was diluted with ethyl acetate (10 cm<sup>3</sup>), washed with water (2 × 5 cm<sup>3</sup>), brine (5 cm<sup>3</sup>), dried and evaporated to give quinazolin-4-one diol **36** (12 mg, 50%), identical with an NMR spectrum of an authentic sample prepared previously.

#### Ring-opening of aziridine **4** with a solution of hydrogen chloride in diethyl ether

A suspension of aziridine (67 mg, 0.185 mmol) in sodium dried ether (3 cm<sup>3</sup>) was stirred rapidly whilst hydrogen chloride gas was bubbled in for ~30 s. The initially cloudy solution cleared during the reaction before a white solid precipitated out. Residual acid in the solution was neutralised by careful addition of excess saturated aqueous sodium hydrogen carbonate, then more ether (3 cm<sup>3</sup>) added before the organic layer was separated, dried and evaporated to give a clear oil (80 mg, 90%). Examination of the crude product by NMR spectroscopy showed it to be a 1:1.2 mixture of chloride diastereoisomers **40** and **41**, by comparison of the signals at  $\delta$  5.57 and 5.99 ppm, respectively.  $\delta_{\text{H}}$  (major diastereoisomer **41**) 1.06 [9H, s, C(CH<sub>3</sub>)<sub>3</sub>], 3.09 (1H, dd, *J* 6.6 and 15.4, CHH), 3.35 (1H, dd, *J* 9.1 and 15.4, CHH), 3.62 (1H, br d, *J* 10.0, OH), 3.82 (1H, struct. m, CHNH), 5.15 (1H, br d, *J* 10.0, CHOH), 5.47 (1H, d, *J* 5.0, CHCl), 5.99 (1H, d, *J* 7.9, NH), 7.06–7.85 [7H, struct. m, 4 × CH(Ph), 6-H, 7-H, 8-H(Q)] and 8.26 [1H, dd, 1.2 and 8.5, 5-H(Q)]; for NMR data of minor diastereoisomer **40** see below.

#### Ring-opening of the *cis*-*N*-invertomer of aziridine **3** with hydrogen chloride

A lead diacetate-free solution of quinazolinone **3** in dichloromethane (4 cm<sup>3</sup>) was prepared as described previously<sup>2</sup> from **1** (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), indene (0.13 cm<sup>3</sup>, 1.11 mmol) and dry dichloromethane (1 cm<sup>3</sup>) held at -20 °C. The temperature of the reaction mixture was held at -20 °C for 2 min and then allowed to reach 0 °C over 10 min, with stirring throughout. Hydrogen chloride gas was then bubbled into the reaction solution for 10 s and the temperature of the solution then allowed to reach ambient. Excess acid was then neutralised by careful addition of excess aqueous saturated sodium hydrogen carbonate solution, the resulting white gelatinous precipitate was separated and the organic layer of the filtrate separated, washed with saturated brine (2 × 5 cm<sup>3</sup>), dried, and the solvent evaporated under reduced pressure to give a white crystalline solid. Examination of the crude product by NMR spectroscopy showed it to consist of a single diastereoisomer of the chloride **40** identical to the minor diastereoisomer from the previous experiment. Crystallisation gave chloride **40** (100 mg, 62%) as colourless crystals mp 163–165 °C (from ethanol) (Found: MH<sup>+</sup> 398.1635. C<sub>22</sub>H<sub>25</sub>ClN<sub>3</sub>O<sub>2</sub> requires MH<sup>+</sup> 398.1635);  $\alpha_{\text{D}}$  236.0 (*c* 0.5, ethanol);  $\nu_{\text{max}}$ /cm<sup>-1</sup> 3490w, 3290w, 1660s and 1595s;  $\delta_{\text{H}}$  0.89 [9H, s, C(CH<sub>3</sub>)<sub>3</sub>], 2.95 (1H, dd, *J* 5.7 and 16.0, CHH), 3.46 (1H, dd, *J* 6.9 and 16.0, CHH), 3.56 (1H, d, *J* 10.0, OH), 4.29 (1H, struct. m, CHNH), 4.96 (1H, d, *J* 10.0, CHOH), 5.25 (1H, d, *J* 5.0, CHCl), 5.57 (1H, d, *J* 3.8, NH), 7.20–7.56 [5H, struct. m, 4 × CH(Ar), 6-H(Q)], 7.77 [2H, struct. m, 7-H, 8-H(Q)] and 8.28 [1H, dd, *J* 1.2 and 7.9, 5-H(Q)]; *m/z* (%) 398 (MH<sup>+</sup>, 100), 215 (21) and 175 (32).

#### Ring-opening of indene-derived aziridine **4** with hydrogen chloride in dichloromethane

The aziridine **4** (100 mg, 0.277 mmol) was dissolved in dichloromethane (5 cm<sup>3</sup>) and cooled to 0 °C in an ice–water bath. Hydrogen chloride was bubbled in slowly for 20 s, the excess acid then neutralised by careful addition of excess saturated aqueous sodium hydrogen carbonate and the organic layer separated, washed with saturated brine, dried and concentrated to give a clear oil (105 mg). Examination by NMR spectroscopy showed the product to consist of a 1:4 ratio of chloride diastereoisomers **40** and **41** (95%) by comparison of the signals at  $\delta$  5.57 and 5.99 ppm respectively (see above).

#### Reconversion of chloride **40** to aziridine **4**

To a solution of the chloride **40** (69 mg, 0.174 mmol) in THF (2 cm<sup>3</sup>) was added sodium hydride (10 mg of a 60% dispersion in oil, 0.25 mmol) and the solution stirred for 45 min. After the addition of water (5 cm<sup>3</sup>) the solution was extracted with ethyl acetate (3 × 5 cm<sup>3</sup>), the organic extracts were separated, dried and solvent was removed under reduced pressure to give aziridine **4**, (65 mg, 91%).

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