Asymmetric Induction in Addition of *N*-Nitrenes to Alkenes: Oxidation of 3-Amino-2-(1,2,2-trimethylpropyl)quinazolin-4(3*H*)-one in the Presence of α-Methylene-γ-butyrolactone: Conformational Analysis of the Aziridines Formed and Comparison with Alkanoylated Cyclopropylamines

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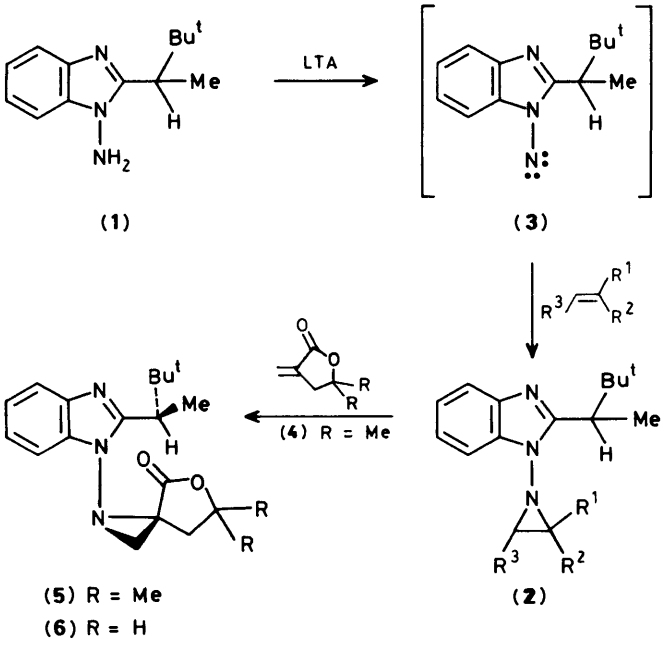
Oxidation of the title *N*-aminoquinazolinone (**11**) in the presence of α-methylene-γ-butyrolactone yields the spiroaziridines (**18a**) and (**18b**) with virtually no asymmetric induction. The same oxidation carried out in the presence of 3.4 mol equiv. of trifluoroacetic acid yielded only a single stereoisomer (**18a**) whose relative configuration was determined by *X*-ray crystallography. This molecular structure also reveals an unexpected orientation around the N–N bond by comparison with other hydrazines. The n.m.r. spectra of compounds (**18a**) and (**18b**) show that both these aziridines exist in solution as single invertomers at nitrogen: (**18b**) shows the presence of both rotamers around the N–N bond but only one rotamer is evident for (**18a**).

In the preceding paper,[1] oxidation of the *N*-aminobenzimidazole (**1**) in the presence of various prochiral alkenes was reported. The two stereoisomers of the aziridine products (**2**), formed *via* addition of the intermediate *N*-nitrene (**3**) to the alkene, were invariably obtained in different proportions and in the case of addition to the α-methylene-γ-butyrolactone (**4**), addition was stereospecific giving only isomer (**5**).



In the course of this work, we examined the stereoselectivity of the *N*-nitrene derived by oxidation of the *N*-aminoquinazolinone (**11**). This *N*-aminoquinazolinone is considerably easier to prepare in quantity than is compound (**1**) by the usual route from 2,3,3-trimethylbutanoic acid (Scheme 1).

The asymmetric induction which obtains in addition of the nitrene (**3**) to prochiral alkenes was ascribed to a transition-state geometry, *e.g.* (**13**), in which the nitrene and lactone are in parallel planes and an attractive secondary interaction exists between the lactone C=O and the benzimidazole C=N.

A predictable drawback to the use of the nitrene (**14**), derived from oxidation of (**11**), in bringing about asymmetric induction in addition to alkenes was that the transition-state geometry (TSG) adopted might be (**16**) rather than (**17**) in the addition to, for example, α-methylene-γ-butyrolactone (Scheme 2).

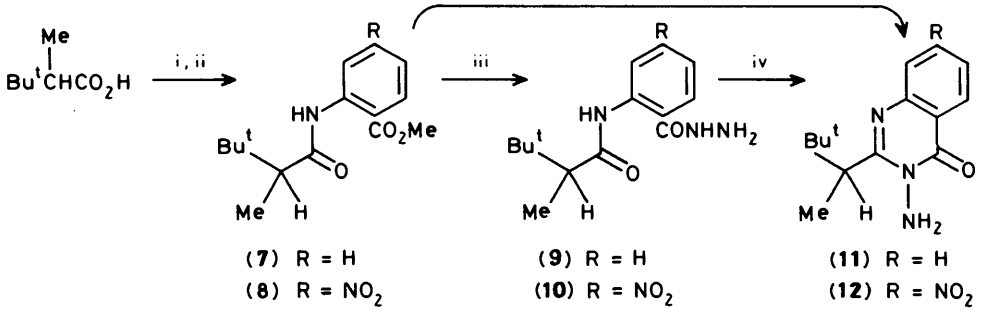
It seemed probable to us that significant asymmetric induction would be unlikely were the reaction to proceed *via* transition state (**16**). In fact, the lack of stereoselectivity which resulted from oxidations of the *N*-aminoquinazolinone (**11**) in dichloromethane in the presence of α-methylene-γ-butyrolactone and other alkenes[2] is consistent with a TSG resembling (**16**) for these nitrene additions. Thus oxidation of (**11**) with lead tetra-acetate (LTA) in the presence of this lactone (2 mol equiv.) gave a 1:1.3 ratio of stereoisomers of aziridines (**18a**):(**18b**) (65%), a selectivity which compares unfavourably with the 5.3:1 ratio obtained in the analogous reaction using the *N*-aminobenzimidazole (**1**). Separation of the two stereoisomers of (**18**) was accomplished by chromatography to give one, (**18a**), as a crystalline solid, m.p. 174—176 °C and the other, (**18b**), as an oil.

In an attempt to bring about a change in the preferred TSG for this reaction from (**16**) to (**17**) (Scheme 2), we carried out the oxidation in the presence of acid. Although the precise nature of the secondary interaction referred to earlier is not known, it was expected that protonation of the quinazolinone N-1 might invert the relative affinities of the quinazolinone C-2 and C-4 positions for the lactone carbonyl group and thus lead to a preference for transition state (**17**) over (**16**) in the nitrene addition.

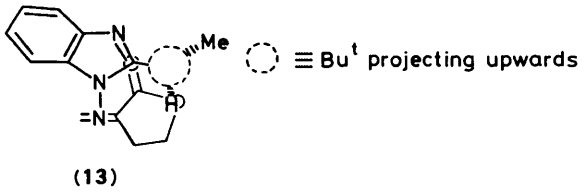
This proved to be the case. Thus an identical oxidation of amine (**11**) with that described above, but with addition of 3.4 mol equiv. of trifluoroacetic acid (TFA) to the dichloromethane solution prior to addition of (**11**) and LTA, gave only the crystalline stereoisomer (**18a**) (72%): none of the signals from the other stereoisomer (**18b**) were visible in the n.m.r. spectrum of the crude reaction product.

The relative configuration of the two chiral centres in product (**18a**) was determined by *X*-ray crystallography (Figure 1). Contrary to our earlier prediction,[3] the induced configuration at the spiro-centre in (**18a**) is opposite to that found in the analogous *N*-aminobenzimidazole-derived major stereoisomer (**6**).

If the transition state (**17**) is retained for this addition, then a configuration for the chiral 2-substituent which will result in



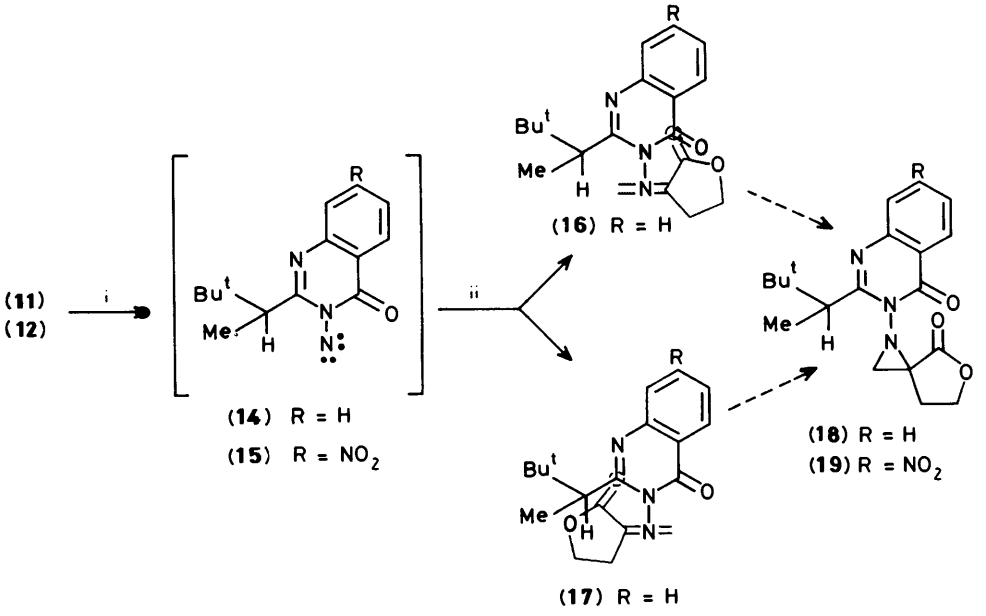
Scheme 1. *Reagents and conditions:* i, $SOCl_2$; ii, $MeO_2CC_6H_3NH_2$-2, R-4; iii, (R = H) NH_2NH_2–EtOH, 119 °C (sealed tube); (R = NO_2) NH_2NH_2–EtOH, 6 h, reflux; iv, (R = H) EtOH–NH_2NH_2, 140—150 °C (sealed tube); (R = NO_2) EtOH, 160—170 °C (sealed tube); v, NH_2NH_2–EtOH, 140—150 °C (sealed tube)



(13)

superior secondary interaction. It is difficult, however, to account for the change in the induced configuration in aziridine (**18a**) by comparison with (**6**) if this were the case.

Although it seemed clear that protonation of the *N*-nitrene (**14**) directs the secondary interaction wholly towards that shown in (**20**) in reaction with α-methylene-γ-butyrolactone, it was not apparent that addition of the unprotonated *N*-nitrene



Scheme 2. *Reagents:* i, LTA; ii, α-methylene-γ-butyrolactone

attack on the alkene from the required face is that shown in structure (**20**).*

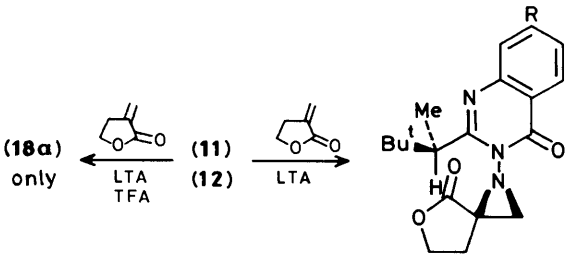
The reversal of the site occupancy of hydrogen and methyl in structure (**20**), by comparison with the analogous substituted benzimidazole case (**13**), may be the result of protonation of the quinazolinone N-1 with some associated solvation taking place preferentially from the underside of the quinazolinone ring (*i.e.* opposite to the t-butyl group). The change to TSG (**17**) in the presence of acid could have been interpreted as the result of protonation on the quinazolinone carbonyl oxygen, giving an aromatic quinazolinium species (**21**) in which C-2 has the

takes place entirely *via* the C=O (lactone)–C=O (quinazolinone)-dominated transition state (**16**). The poor stereoselectivity in the absence of TFA could have resulted from reaction *via* (**16**) and (**17**) in competition.

To test this point, the 3-amino-7-nitroquinazolinone (**12**) was prepared by a modification of the usual route (Scheme 1). Thus heating of the corresponding nitro-substituted anthranilate (**8**) with an excess of hydrazine at 140—150 °C brought about reduction of the ring nitro group to an amino group as well as *N*-aminoquinazolinone formation. However, isolation of the intermediate hydrazide (**10**) and heating of the latter in the absence of hydrazine at 160—170 °C avoided this problem.

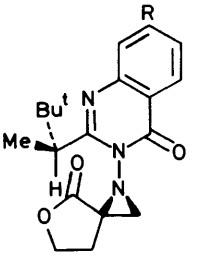
Oxidation of compound (**12**) to (**15**) in the presence of α-methylene-γ-butyrolactone in the absence of TFA under conditions identical with those used for oxidation of (**11**) gave a

* Since (**11**) is racemic, (**20**) and (**21**) represent in each case only one of the two enantiomeric TSGs.

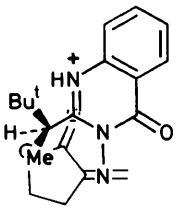


(18a) R = H
(19a) R = NO_2

+



(18b) R = H
(19b) R = NO_2



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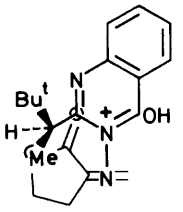

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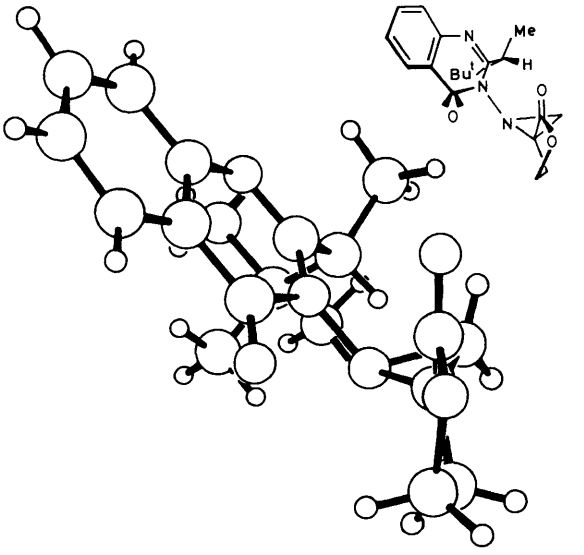


Figure 1. *X*-Ray molecular structure of compound (**18a**)

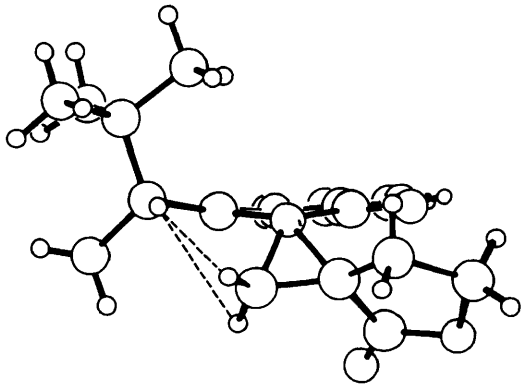


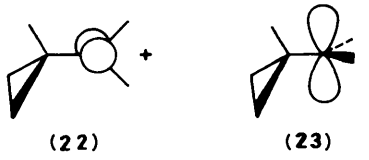
Figure 2. *X*-Ray molecular structure of compound (**18a**). View along the N–N bond

mixture of analogous aziridine stereoisomers (**19a**) and (**19b**). The ratios (**18a**):(**18b**) and (**19a**):(**19b**) were measured from n.m.r. spectra of the oxidation products of (**11**) and (**12**), respectively (at 90 MHz), and were found to be identical.

This negative result, however, does not prove that addition of *N*-nitrene (**14**) to α-methylene-γ-butyrolactone takes place only by transition state (**16**). If addition were taking place by both transition states (**16**) and (**17**), we cannot be sure that the introduction of the 7-nitro substituent would significantly affect the relative contributions of these two pathways.

Whilst the n.m.r. spectrum of the major stereoisomer (**18a**) is unexceptional, that of (**18b**) at room temperature and 300 MHz shows broadened envelopes rather than peaks and was characteristic of a molecule undergoing a conformational change close to the coalescence temperature. At −40 °C, signals from both these conformations were present as sharp peaks and the ratio of the two was *ca.* 1:1. The characteristic n.m.r. spectral changes of lactone (**18b**) on lowering the temperature were also exhibited by the 7-nitroquinazolinone analogue (**19b**).

Examination of the *X*-ray molecular structure of compound (**18a**) shows a remarkably small dihedral angle between the electron pair in the p-orbital on the quinazolinone N-3 and the lone pair of electrons on the aziridine ring nitrogen. Figure 2 shows this more clearly with the plane of the quinazolinone ring horizontal and the N–N bond projecting towards the viewer. The barrier to rotation in such a substituted hydrazine is, to our knowledge, unknown and it cannot be assumed that this barrier will necessarily correspond to the conformation in which these two pairs of electrons are eclipsed as would be the case in normal hydrazines.[4] The high s-character of the aziridine lone pair will probably mean that the eclipsing interaction is reduced in any case but more significant may be the unfavourable interaction of the quinazolinone N-3 lone pair with the ring bonds of the aziridine. Whereas the preferred conformation of the cyclopropylmethyl cation has the bisected conformation (**22**) which allows maximum stabilisation of the cation by



(22) (23)

delocalisation of the ring bonds,[5] it is reasonable to suppose that a filled p-orbital (cyclopropylmethyl anion*) may result in the perpendicular conformation (**23**) becoming more stable.[6]

With appropriate substitution of carbons by nitrogens, (**23**) is the conformation present in product (**18a**) (Figure 2).

* These species readily ring-open to but-3-enyl anions.

The two conformations present in the aziridine (**18b**) are assigned as rotamers around the N–N bond with both having preferred orientations which are closer to the perpendicular (**23**) than to the bisected (**22**). That compound (**18a**) prefers to exist as a single rotamer and isomer (**18b**) as a *ca.* 1:1 ratio of rotamers is presumed to be the result of non-bonded interactions between the C-2 chiral substituent and either the aziridine ring methylene protons or the lactone ring. From examination of structure (**18a**) (Figure 2) it is expected that, since the methine hydrogen and the aziridine ring protons lie just outside their combined van de Waals' radii* (dotted lines in Figure 2), interchange of the hydrogen and methyl group on the chiral substituent at C-2, which corresponds to a conversion of (**18a**) ⟶ (**18b**), will result in greater non-bonding interactions with the aziridine ring methylene protons. On the other hand, models suggest that, in the other rotamers, (**18a**) may encounter greater non-bonded interactions than would (**18b**) with the lactone ring.

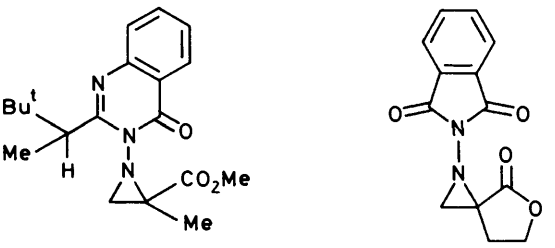
It seems probable that the augmented non-bonded interactions present in both rotamers of compound (**18b**) by comparison with isomer (**18a**) will require a larger dihedral angle between the lone pairs of electrons of the adjacent nitrogens in the former. Some support for this supposition comes from the corresponding dihedral angle in the *X*-ray molecular structure of (**5**), which is the benzimidazole analogue of one rotamer of (**18b**). This dihedral angle† has a value of 20° in (**5**), compared with a value of 1° in (**18a**).

There are a number of reasons why the conformational equilibrium present in isomer (**18b**) must be ascribed to that between *rotamers* rather than *invertomers*. The barrier which separates the two conformers, which can be calculated from the data at the coalescence temperature to be *ca.* 14 kcal mol^{-1}, is grossly different from that normally found for inversion in these N–N-bond-containing aziridines.[7] For example, the aziridine (**24**), formed by oxidation of the *N*-aminoquinazolinone (**11**) in the presence of methyl methacrylate, showed the presence of two invertomers (ratio 1.3:1) and, from the coalescence of the aziridine ring methyl signals in the n.m.r. spectrum at 150 °C, an inversion barrier of 21 kcal mol^{-1} is calculated. The absence of an observable barrier (at room temperature) to rotation in the (major) invertomer of (**24**) with the quinazolinone ring and ester *cis*[8] is not surprising since the ester is free to rotate around the aziridine–CO_2Me bond which facilitates N–N bond rotation by comparison with (**18a**) or (**18b**).

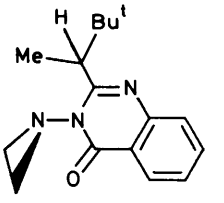
Although the minor invertomer in the case of compounds (**18a**) and (**18b**) is not visible in either of their n.m.r. spectra, this equilibrium is not wholly on one side in the corresponding phthalimidonitrene adduct with α-methylene-γ-butyrolactone (**25**). This compound shows clearly the presence of both invertomers‡ in a ratio of *ca.* 5:1. From the coalescence of the aziridine ring-proton signals in the n.m.r. spectrum at ~150 °C, an approximate barrier to inversion of 21 kcal mol^{-1} is calculated from which it appears that the aziridine–lactone spiro ring fusion does not significantly lower the aziridine nitrogen inversion barrier in (**25**) and presumably, therefore, would not be expected to lower this barrier in (**18b**) either.

To summarise; the preferred orientation around the N–N bond from the crystal structure of compound (**18a**) has the lone pairs of electrons on the adjacent nitrogens eclipsed. Some distortion from this orientation is probably present in (**18b**) to accommodate non-bonded interactions but the preferred conformation is still identifiably perpendicular (**23**) rather than bisected (**22**). The existence of two rotamers in stereoisomer (**18b**) is the result of their non-bonded interactions being of a similar magnitude whereas for (**18a**) these non-bonded interactions in one rotamer are significantly smaller than in the other and only one rotamer is detectable by n.m.r. in solution.

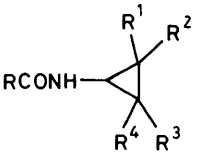
It would be very difficult to account for the different rotamer distributions in (**18a**) and (**18b**) if the preferred orientation in solution for these stereoisomers was a bisected one, *e.g.* (**26**).



(**24**) (**25**)



(**26**)



(**27**)

It was of interest to examine cyclopropyl analogues of aziridines (**18**) since these would also be expected to have a preference for the perpendicular conformation particularly since the lone-pair–lone-pair interaction of the aziridine has been replaced by a less repulsive bonded-pair–lone-pair one.

From the Cambridge Data File of Crystallographic Structures, data for six alkanoylated cyclopropylamines (**27**) were retrieved and, in each case, the angle θ between the normal to the RC(:O)N plane and the plane bisecting the N—$\widehat{CHCH_2—CH_2}$ angle (orthogonal to the plane of the cyclopropane ring) was requested and the results are tabulated in Figure 3.

The values of θ in Figure 3 are all significantly closer to 0° than to 90°, which illustrates the preference of these cyclopropylamine derivatives for the perpendicular rather than the bisected conformation but clearly some deviation from 0° can be accommodated.

In contrast to the alkanoylated cyclopropylamines (**27**) in Figure 3, ring nitro-substituted cyclopropanes have been recognised[13] as having an angle θ close to 90° corresponding to the bisected conformation. This has been attributed to a favourable overlap of one of the degenerate pair of HOMOs of the cyclopropane ring with the LUMO of the nitro substituent.[14]

* In Figure 2, it can be seen that this is assisted by C-2 of the quinazolinone ring lying above the plane containing the other atoms of this ring.

† The dihedral angles calculated are those between the plane orthogonal to the aziridine ring plane which bisects the C–N–C angle in this ring and the normal to the N–N–CO (quinazolinone) or N–N–C=N (benzimidazole) plane.

‡ The symmetry of the phthalimido group means that these two species must be invertomers.

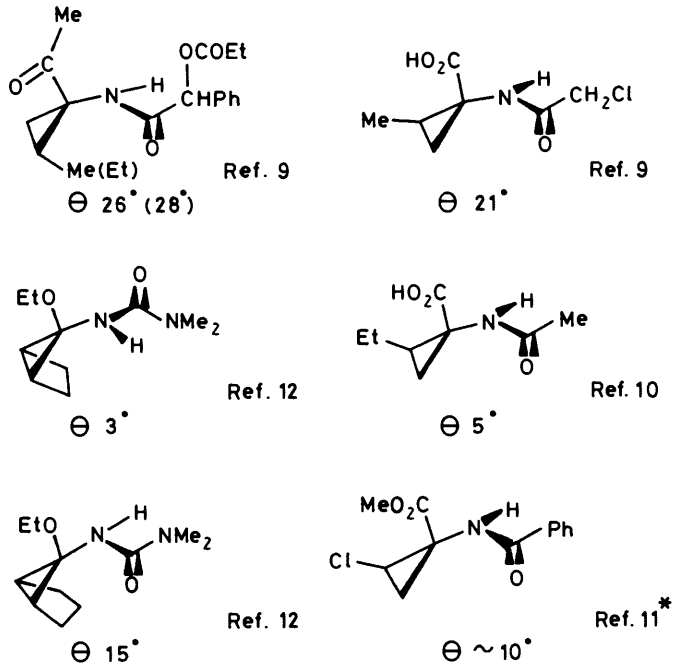
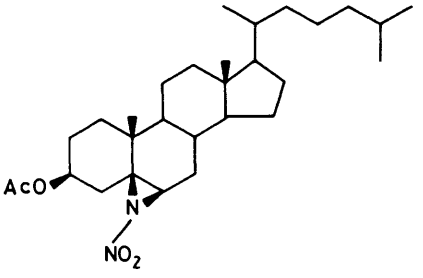


Figure 3. Alkanoylated cyclopropylamines and their preference for the perpendicular conformation (**23**) (θ ideally 0°) (for definition of θ see text).* The required bond angles were not available from the Data File: this value is an estimate from the diagram shown in the paper

The only aziridine containing an (aziridine ring) N–N bond retrieved from the Cambridge Data File was the *N*-nitroaziridine (**28**)[15] which appears to adopt a conformation closer to the perpendicular conformation (θ = 22°) than to the bisected.



(**28**)

Experimental

For general experimental details see ref. 1 and 16—18. N.m.r. spectra were run in $CDCl_3$ at 90 MHz unless otherwise indicated. Light petroleum refers to the fraction boiling the range 60—80 °C.

3-*Amino*-2-(1,2,2-*trimethylpropyl*)*quinazolin*-4(3H)-*one* (**11**).—Methyl *N*-(2,3,3-trimethylbutanoyl)anthranilate (7) was obtained from 2,2,3-trimethylbutanoic acid[1] by conversion into the acid chloride and then reaction of this with methyl anthranilate in ether as previously described.[17] After evaporation of the ether solution, the product was obtained as a light yellow oil (63%); δ 11.00 (br s, exch. D_2O, NH), 8.73 (dd, *J* 8 and 1 Hz, 3-H), 7.98 (dd, *J* 7 and 2 Hz, 6-H), 7.46 (ddd, *J* 8, 8, and 2 Hz, 4-H), 7.02 (ddd, *J*, 8, 7, and 1 Hz, 5-H), 3.87 (s, CO_2Me), 2.23 (q, *J* 7 Hz, C*H*Me), 1.24 (d, *J* 7 Hz, CH*Me*), and 1.03 (s, Bu^t); $\nu_{max.}$ 3 320s and 1 685s cm^{-1}.

Heating of the anthranilate (7) overnight with an excess of hydrazine hydrate in ethanol in a degassed sealed tube as described previously[17] but with an oven temperature of 140—150 °C gave the *aminoquinazolinone* (**11**) on cooling as crystals (74%), m.p. 118—120 °C (from ethanol) Found: C, 68.6; H, 7.8; N, 17.2. C, 68.6; H, 7.8; N, 17.2%); δ_H 8.17 (dd, *J* 8 and 1 Hz, 5-H), 7.74—7.17 (m, 6-, 7-, and 8-H), 4.78 (br s, exch. D_2O, NH_2), 3.85 (q, *J* 7 Hz, C*H*Me), 1.30 (d, *J* 7 Hz, CH*Me*), and 1.02 (s, Bu^t); δ_C [$(CD_3)_2SO$; 100 MHz] 165.4 (s), 164.9 (s), 150.2 (s), 138.0 (d), 131.2 (d), 130.0 (d), 129.9 (d), 123.8 (s), 45.9 (d), 38.2 (s), 31.4 (q), and 18.7 (q); $\nu_{max.}$ 3 315s, 3 210m, and 1 640br s cm^{-1}; *m/z* (%) 245 (9), 230 (18), 190 (15), 189 (100), 188 (9), 175 (29), 173 (24), 120 (35), and 119 (36).

In an experiment in which the oven temperature was maintained at 119 °C overnight, the yield of the quinazolinone (**11**) was 24%. After removal of the bulk of the ethanol filtrate under reduced pressure, the residue was dissolved in ether, and the solution washed once with water, dried, and evaporated to give the *hydrazide* (**9**) (55%) as crystals, m.p. 125—126 °C (from dichloromethane–light petroleum) (Found: C, 63.9; H, 7.95; N, 15.95. $C_{14}H_{21}N_3O_2$ requires C, 63.85; H, 8.05; N, 15.95%); δ 10.63 (br s, exch. D_2O NH), 8.54 (dd, *J* 8 and 1 Hz, 3-H), 7.56—6.78 (m, 4-, 5-, and 6-H), 4.67 (br s, exch. D_2O, $NHNH_2$), 2.17 (q, *J* 7 Hz, C*H*Me), 1.20 (d, *J* 7 Hz, CH*Me*), and 1.00 (s, Bu^t); $\nu_{max.}$ 3 305s, 1 665s, and 1 603s cm^{-1}; *m/z* (%) 263 (6), 233 (100), 189 (15), 176 (71), 175 (43), 158 (20), 146 (18), 120 (73), 92 (21), and 85 (67).

Further heating of the above hydrazide (**9**) in a degassed sealed tube in ethanol at 140—150 °C overnight resulted in conversion to the aminoquinazolinone (**11**).

3-*Amino*-7-*nitro*-2-(1,2,2-*trimethylpropyl*)*quinazolin*-4(3H)-*one* (**12**).—Methyl 4-nitro-*N*-(2,3,3-trimethylbutanoyl)-anthranilate (**8**) was obtained from 2,3,3-trimethylbutanoic acid (4.0 g) by conversion into the acid chloride and then dropwise addition of this chloride to a stirred solution of methyl 4-nitroanthranilate (6.63 g) and dry pyridine (2.73 ml) in dichloromethane (150 ml). After setting aside overnight, the insoluble material was separated, and the solution was washed successively with dil. hydrochloric acid and then with water before being dried and evaporated. The crude product obtained contained *ca.* 50% of the required amide, which was separated from the more insoluble unchanged methyl 4-nitroanthranilate by trituration with ether. Evaporation of the ether and crystallisation from chloroform–light petroleum gave the 4-nitroanthranilate (**8**) (48%) as orange crystals, m.p. 82—85 °C; δ 11.04 (br s, exch. D_2O, NH), 9.64 (d, *J* 2 Hz, 3-H), 8.27—7.27 (m, 5- and 6-H), 3.98 (s, CO_2Me), 2.26 (q, *J* 7 Hz, C*H*Me), 1.25 (d, *J* 7 Hz, CH*Me*), and 1.03 (s, Bu^t).

This amide (**8**) (2.9 g) was heated under reflux with hydrazine hydrate (2.37 g) in ethanol (50 ml) under nitrogen. After the mixture had cooled, the ethanol was removed under reduced pressure, the residue was dissolved in dichloromethane (100 ml), and the organic layer was washed once with water, dried, and evaporated. Crystallisation of the residue from dichloromethane–light petroleum gave the hydrazide (**10**) (27%) as pale orange crystals, m.p. 170—175 °C; δ 10.82 (br s, exch. D_2O, NH), 9.43 (d, *J* 2 Hz, 3-H), 7.87—7.20 (m, 5- and 6-H), 4.44 (br s, exch. D_2O, $NHNH_2$), 2.21 (q, *J* 7 Hz, C*H*Me), 1.24 (d, *J* 7 Hz, CH*Me*), and 1.01 (s, Bu^t); $\nu_{max.}$ 3 340s, 3 130s, 1 685s, and 1 660s cm^{-1}.

The foregoing hydrazide (2 g) was heated in oxygen-free ethanol (30 ml) in a Carius tube at 160—170 °C overnight. Evaporation of the ethanol and crystallisation of the N-*aminoquinazolinone* (**12**) gave pale yellow needles (51%), m.p. 187—189 °C (from ethanol) (Found: C, 58.1; H, 6.45; N, 19.05. $C_{14}H_{18}N_4O_3$ requires C, 57.9; H, 6.25; N, 19.3%); δ_H 8.54—8.0 (m, 5-, 6-, and 8-H), 4.80 (br s, exch. D_2O, NH_2), 3.85 (q, *J* 7 Hz,

C*H*Me), 1.30 (d, *J* 7 Hz, CH*Me*), and 1.00 (s, Bu^t); δ_C [$(CD_3)_2SO$; 100 MHz] 168.2 (s), 164.0 (s), 155.0 (s), 150.4 (s), 132.5 (d), 127.8 (s), 126.1 (d), 123.7 (d), 46.2 (d), 38.5 (s), 31.5 (q), and 18.6 (q); $\nu_{max.}$ 3 330s, 3 270s, and 1 675s cm^{-1}; *m/z* (%) 275 (6), 234 (100), 218 (24), 164 (33), and 75 (10).

Oxidation of the N-*Aminoquinazolinone* (**11**) *in the Presence of* α-*Methylene*-γ-*butyrolactone*.—(a) *In the absence of* TFA. The powdered *N*-aminoquinazolinone (**11**) (0.1 g) and lead tetra-acetate (LTA) (0.19 g) were added alternately and continuously in very small amounts during 15 min to a vigorously stirred solution of α-methylene-γ-butyrolactone (0.16 g) in dry dichloromethane (1 ml) at room temperature. After the mixture had been stirred for a further 30 min, the insoluble lead di-acetate was separated and washed with dichloromethane and the total filtrate was washed successively with aqueous sodium hydrogen carbonate and water, then dried and evaporated. Examination of the residue by n.m.r. spectroscopy at 90 MHz showed the presence of aziridines (**18a**) and (**18b**) in the ratio 1:1.3. Chromatography over alumina and elution with ethyl acetate–light petroleum (1:1) gave isomer (**18b**) as an oil (21 mg), whose n.m.r. spectrum (300 MHz; −40 °C) showed the presence of 2 rotamers in a 1:1 ratio; 8.25—7.38 (m, 5-, 6-, 7-, and 8-H, both rotamers), 5.05 (ddd, *J* 8, 8, and 8 Hz, CH_2CHHO_2C, both rotamers), 4.66 (m, CH_2CHHO_2C, both rotamers), 3.49 (d, *J* 1 Hz, 2 × aziridine H in one rotamer), 3.31 (q, *J* 7 Hz, C*H*Me in one rotamer), 3.23 (d, *J* 1 Hz, aziridine ring H *cis* to quinazoline in one rotamer), 3.04 (d, *J* 1 Hz, aziridine ring H *trans* to quinazoline in one rotamer), 3.00—2.63 (m, $CH_2CH_2O_2C$, both rotamers, C*H*Me in one rotamer), 1.37 and 1.28 (2 × d, *J* 7 Hz, CH*Me*), and 1.25 and 1.00 (2 × s, Bu^t). Further elution with ethyl acetate–light petroleum (1:1) gave *isomer* (**18a**) as crystals (5 mg), m.p. 174—176 °C (from ethanol) (Found: C, 67.0; H, 6.85; N, 12.35. $C_{19}H_{23}N_3O_3$ requires C, 66.85; H, 6.8; N, 12.3%); δ (300 MHz), 8.15 (ddd, *J* 8, 1.5, and 0.6 Hz, 5-H), 7.68 (ddd, *J* 8.3, 6.6, and 1.5 Hz, 7-H), 7.64 (ddd, *J* 8.3, 1.6, and 0.6 Hz, 8-H), 7.39 (ddd, *J* 8, 6.6, and 1.6 Hz, 6-H), 5.00 (ddd, *J* 8.4, 8.4, and 8.4 Hz, CH_2CHHO_2C), 4.56 (ddd, *J* 8.9, 8.9, and 3.6 Hz, CH_2CHHO_2C), 3.30 (q, *J* 7 Hz, C*H*Me), 3.11 (d, *J* 1 Hz, aziridine ring H *cis* to quinazoline), 2.92 (m, $CHHCH_2O_2C$), 2.88 (d, *J* 1 Hz, aziridine ring H *trans* to quinazoline), 2.65 (ddd, *J* 15.1, 8.9, and 8.1 Hz, $CHHCH_2O_2C$), 1.45 (d, *J* 7 Hz, CH*Me*), and 0.98 (s, Bu^t); $\nu_{max.}$ 1 755s and 1 655s cm^{-1}; *m/z* (%) 341 (3), 286 (41), 215 (15), 189 (29), 174 (100), 173 (61), 159 (38), 131 (28), 117 (38), and 98 (41).

(b) *In the presence of* TFA. The procedure described above was employed but TFA (158 mg, 3.4 mol equiv.) was added to the dichloromethane prior to addition of the amine (**11**) and LTA. After the same work-up, crystallisation of the crude product was ethanol gave compound (**18a**) (100 mg, 72%), identical with that isolated above.

Oxidation of the N-*Aminoquinazolinone* (**12**) *in the Presence of* α-*Methylene*-γ-*butyrolactone*.—Oxidation of (**12**) (100 mg) was carried out as described for (**11**) above (in the absence of TFA). Chromatography of the crude product over silica and elution with ethyl acetate–light petroleum (1:1) gave aziridines (**19a**) and (**19b**) as a light yellow solid (49 mg, 37%). Crystallisation of this solid from dichloromethane–ethyl acetate did not separate the two stereoisomers. From the n.m.r. spectrum of the mixture obtained after chromatography at 90 MHz, the ratio (**19a**):(**19b**) was 1:1.3 (this ratio was little changed from that in the mixture before chromatography). For (**19a**), δ (300 MHz) 8.55—8.10 (m, 5-, 6-, and 8-H), 4.98 (ddd, *J* 8.5, 8.5, and 8.2 Hz, CH_2CHHO_2C), 4.60 (m, CH_2CHHO_2C), 3.32 (q, *J* 6.9 Hz, C*H*Me), 3.17 (d, *J* 1.3 Hz, aziridine ring H *cis* to quinazoline), 2.97 (m, $CHHCHO_2C$) 2.89 (d, *J* 1.2 Hz, aziridine ring H *trans* to quinazoline), 2.67 (m, $CHHCH_2O_2C$), 1.48 (d, *J* 7 Hz, CH*Me*), and 1.00 (s, Bu^t). For (**19b**), at 300 MHz all signals were broadened [rotamers: see (**18b**)]; at 90 MHz, δ 8.55—8.10 (m, 5-, 6-, and 8-H), 4.98 (br s, CH_2CHHO_2C), 4.60 (br s, CH_2CHHO_2C), 3.30 (br s, C*H*Me), 2.90 (br s, aziridine ring H *cis* to quinazoline), 2.90 (br s, aziridine ring H *trans* to quinazoline, and $CHHCH_2O_2C$), 2.68 (br s, $CHHCH_2O_2C$), 1.32 (d, *J* 6.8 Hz, CH*Me*), and 1.15 (br s, Bu^t).

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