Oxidation of *N*-Aminoquinazolones in the Presence of Alkenes: Evidence against Involvement of *N*-Nitrenes

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Solutions of 2-ethyl-3-acetoxyamino-4(3*H*)-quinazolone (**6**) have been obtained by oxidation of the corresponding 3-aminoquinazolone (**4**) with lead tetra-acetate at −20 °C; (**6**) brings about aziridination of alkenes by a mechanism that does not involve *N*-nitrene or *N*-nitrenium ion intermediates.

There exists a family of *N*-aminoheterocyclic compounds (**1**) whose oxidation with lead tetra-acetate (LTA) in the presence of alkenes gives aziridines.[1] The intermediates in these aziridinations have hitherto been assumed to be the corresponding *N*-nitrenes (**2**).

Following on from some observations made on intramolecular aziridination using the quinazolone (**3**),[2] we examined the oxidation of the 2-ethyl-3-aminoquinazolone (**4**) with LTA.

Oxidation of (**4**) in dichloromethane solution at −20 °C in the absence of any alkene gave a product which was stable below 0 °C in solution but has not been isolated. The n.m.r. spectrum of this product at −20 °C in solution after separation of the insoluble lead di-acetate showed a distinctive ABX_3 pattern for the two apparently diastereotopic protons of the ethyl methylene group, a low field singlet proton (δ 10.93), and the expected triplet for the methyl group. The characteristic pattern for the quinazolone ring protons at 300 MHz confirmed that this heterocycle was intact. Other than residual acetic acid (a by-product in the oxidation) the only other species present in the above solution was a small amount (*ca.* 5%) of the de-aminated quinazolone (**5**).

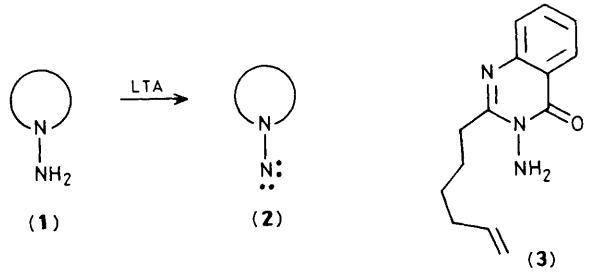
Removal of acetic acid from the above solution by careful washing with aqueous sodium hydrogen carbonate at low temperature revealed that the major product from the oxidation also contained a methyl group which was obscured by the acetic acid signal. Assignment of the *N*-acetoxyaminoquinazolone structure (**6**) to this major product is supported by a low temperature (−20 °C) i.r. spectrum on the oxidation product (in $CDCl_3$) which contained a prominent band at 1768 cm^{-1} that disappeared when the temperature was raised to ambient, and by a ^{13}C n.m.r. spectrum containing two additional carbon resonances (δ 169.46 and 18.98) besides those expected from the quinazolone.

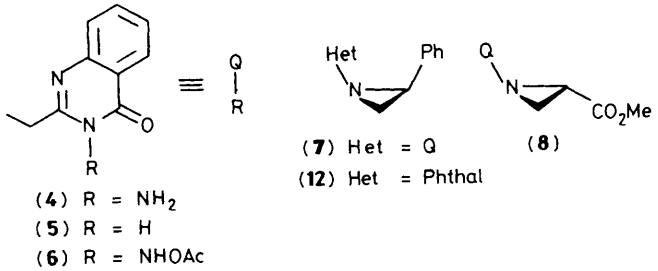
The non-equivalence of the protons in the methylene group of (**6**) may be the result of hindered rotation around the N–N bond (a chiral axis) or retarded inversion at a pyramidal nitrogen N-*N*HOAc, or conceivably a combination of both these factors.

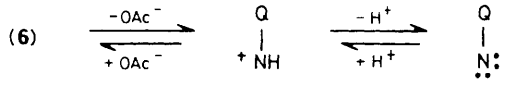
Decomposition of (**6**) was followed at 10 °C by n.m.r. spectroscopy (300 MHz) and was found to exhibit first order kinetics over four half-lives ($k = 3.68 \times 10^{-4}\ s^{-1}$). Addition of styrene to solutions of (**6**) at −40 °C produced the aziridine (**7**) as its *syn*-invertomer[3] which was isolated in good yield (76% using 1.5 mol equiv. styrene) as its thermodynamically more stable *trans*-invertomer. The rate of disappearance of (**6**), therefore, was increased by the presence of styrene and this increase was dependent on the concentration of styrene. Thus at −10 °C the initial rate of disappearance of (**6**) in the presence of 4 mol equiv. of styrene ($k = 2.9 \times 10^{-3}\ s^{-1}$; treated as first order) is *ca.* twice as fast as in the presence of 1.5 mol equiv. Even methyl acrylate brings about an increase in the rate of disappearance of (**6**) by a factor which depends on its concentration. Thus the presence of 4 mol equiv. of methyl acrylate at 10 °C results in an initial rate constant $k = 2.43 \times 10^{-3}\ s^{-1}$ (treated as first order) for disappearance of (**6**). Aziridine (**8**) is the major product (80%) from this reaction when 1.5 mol equiv. of methyl acrylate is used.

It appears that the *N*-acetoxyaminoquinazolone (**6**) is playing the role previously assigned to the corresponding *N*-nitrene. The possibility that a nitrenium ion[4] or even the *N*-nitrene could still be the reactive intermediate in these aziridinations through the existence of the equilibria shown in Scheme 1 was excluded by the lack of exchange in (**6**) (in a CH_2Cl_2 solution free from acetic acid), in the presence of excess of tetra-deuteriated acetic acid, either of its acetoxy group or of its NH proton.

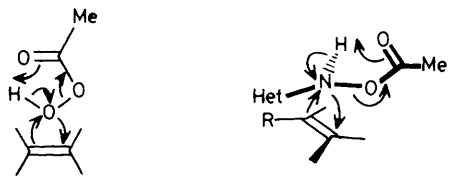
From the evidence available it appears that these aziridinations may proceed in a manner analogous to the Bartlett mechanism for peracid oxidation of alkenes to give epoxides (Scheme 2).[5]



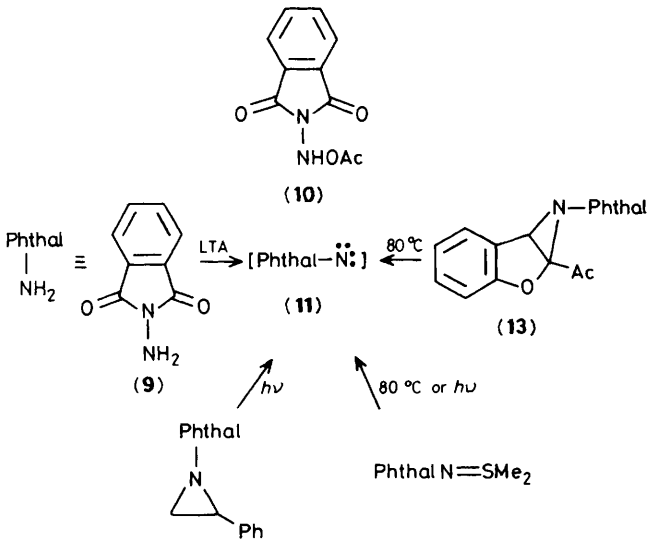




Scheme 1



Scheme 2



Scheme 3

The parallel behaviour observed in aziridinations using (**6**) and *via* oxidative (LTA) addition of *N*-aminophthalimide (**9**) to alkenes leads us to suspect that in this latter case also, the *N*-acetoxyaminophthalimide (**10**) rather than the phthalimido nitrene (**11**) (Scheme 3) is the intermediate involved. Thus, in both cases, *syn*-stereospecificity obtains in addition to styrene at < -20 °C to give (**7**) and (**12**), respectively, and in competitive additions to α-methylene-γ-butyrolactone and methyl methacrylate, a selectivity of 2.1 : 1 *vs.* 2.3 : 1, respectively, is found. Moreover, to our knowledge, no oxidant other than LTA or phenyl iodosodiacetate has been successfully used to bring about aziridination of alkenes using (**9**).[6]

Previously, the best evidence for the intermediacy of *N*-nitrenes in oxidations of members of the family of *N*-amino heterocycles referred to above has been the generation of apparently the same intermediate *i.e.* the phthalimidonitrene (**11**) by three additional independent routes (Scheme 3).[7–9] However, the intermediate in the oxidation with LTA of the *N*-aminophthalimide (**9**) at 80 °C is clearly different from that in the thermal decomposition of (**13**) at this temperature as shown by the selectivity of addition in the two cases to a 1 : 1 mixture of styrene and methyl acrylate in benzene solution. Preferential addition to styrene (ratio 1.5 : 1) occurs in the LTA oxidation of (**9**) under these conditions whereas preferential (3 : 1) addition to methyl acrylate occurs using thermal decomposition of (**13**).

The use of solutions of (**6**) for aziridinations is of significance since, as we have shown, the method can be applied to alkenes which would otherwise be attacked by LTA.

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References

1 R. S. Atkinson, 'Azides and Nitrenes,' ed. E. F. V. Scriven, Academic Press, Orlando, Florida, 1984, ch. 5.
2 R. S. Atkinson and M. J. Grimshire, unpublished work.
3 R. S. Atkinson and J. R. Malpass, *J. Chem. Soc., Perkin Trans. 1*, 1977, 2242.
4 J. I. G. Cadogan and I. Gosney, *J. Chem. Soc., Perkin Trans. 1*, 1974, 466.
5 P. D. Bartlett, *Rec. Chem. Prog.*, 1950, **11**, 47.
6 See T. G. Back, *J. Chem. Soc., Chem. Commun.*, 1981, 530.
7 D. W. Jones, *J. Chem. Soc., Chem. Commun.*, 1972, 884.
8 M. Edwards, T. L. Gilchrist, C. J. Harris, and C. W. Rees, *J. Chem. Res. (S)*, 1979, 114.
9 T. L. Gilchrist, C. W. Rees, and E. Stanton, *J. Chem. Soc. (C)*, 1971, 988; see also D. J. Anderson, D. C. Horwell, G. Stanton, T. L. Gilchrist, and C. W. Rees, *J. Chem. Soc., Perkin Trans.* 1, 1972, 1317.