Intramolecular Trapping of *N*-Nitrenes: Oxidation Products of 3-Amino-2-(2,4-dimethoxyphenylpropyl)quinazolin-4(3*H*)-one

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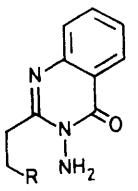
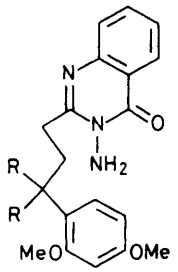
Oxidation of the title *N*-aminoquinazolone (**2**) with lead tetra-acetate in methanol gave the bridged structure (**4**) which, when left in methanol, was converted into (**5**) whose cyclopentane ring-containing structure was confirmed by *X*-ray crystallography.

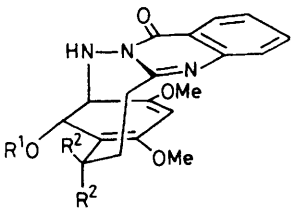
Oxidation of 2-(arylethyl)- or 2-(alkenylethyl)-*N*-amino-quinazolones (**1**) generates *N*-nitrenes which can be trapped intramolecularly by the aryl rings or double bonds.[1,2] In both cases, the effects of substituents in the aryl ring or on the double bond were better explained by a non-concerted addition of the nitrene to the particular π-system involved. In an



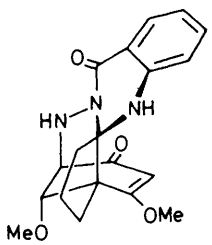
(1) R = Methoxylated benzene ring or a double bond.



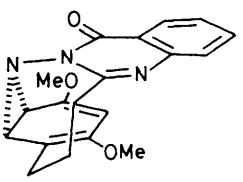
(2) R = H
(7) R = Me



(3) R^1 = COMe, R^2 = H
(4) R^1 = Me, R^2 = H
(8) R^1 = R^2 = Me



(5)



(6)

attempt to identify the factors responsible for this non-concertedness of nitrene addition we have synthesised the 2-(arylpropyl)-*N*-aminoquinazolone (**2**) and oxidised it using conditions which generate the *N*-nitrene as an intermediate.[3]

Thus, oxidation of (**2**), m.p. 120—122 °C, with lead tetra-acetate (LTA) in benzene or chloroform leads to a highly acid-sensitive product (27%, isolated, m.p. 138—140 °C) to which structure (**3**) is assigned ν_{max} (Nujol) 3280, 1737, 1684 (sh), 1678, and 1658 cm^{-1}; ^1H n.m.r., 90 MHz ($CDCl_3$, −23 °C in the presence of K_2CO_3), δ 8.08, 7.8—7.2 (4 × quinazolone H), 6.7 (NH, d, *J* 6 Hz), 5.65 (*H*COAc, d, *J* 2 Hz), 4.83 (C*H*=C, s), 3.65 (OMe + NHC*H*), 2.82 (OMe, s), 2.9—1.9 ($[CH_2]_3$, m), and 2.07 (OCOMe, s). Clearly, acetic acid (a by-product in the LTA oxidation) has been incorporated into this product. Attempted recrystallisation of (**3**) from methanol gave (**4**), m.p. 177—180 °C, in which the acetoxy group had been replaced by a methoxy group. Oxidation of *N*-aminoquinazolone (**2**) in methanol also gave (**4**) directly (29%).

This methoxy-containing product (**4**) was considerably more stable in solution than (**3**) and had the following spectroscopic properties: ν_{max} (Nujol) 3256, 1677, and 1650 cm^{-1}; ^1H n.m.r., 400 MHz ($CDCl_3$) includes δ 6.74 (NH, d, *J* 5.4 Hz), 4.73 (C*H*=C, s, 1H), 4.09 (C*H*OMe, d, *J* 2.4 Hz), 3.43 (NHC*H*, dd, *J* 2.4 and 5.4 Hz), 3.50, 3.35, 2.81 (3 × MeO, 3 × s), 3.41, 2.85, 2.69, 2.53, 2.24, and 1.90 ($[CH_2]_3$, 6 × m).

A solution of (**4**) in methanol is slowly converted on standing into a product, m.p. 210—215 °C (decomp.); ν_{max} (Nujol) 3338, 3245, and 1645 cm^{-1}; ^1H n.m.r., 400 MHz ($CDCl_3$) 7.79, 7.26, 6.83, 6.58 (4 × quinazolone H), 7.06 (NH, d, *J* 6.6 Hz), 5.56 (C*H*=C, s), 4.24 (NH, s), 3.74 (OMe, s,), 3.68 (NHC*H* + MeOC*H*, m), 3.46 (OMe, s), 2.57 (1H), 2.45 (1H), 2.21 (2H), and 1.96 (2H) ($[CH_2]_3$, 6 × m). From these data, it is apparent that a methyl group has been lost and the quinazolone ring has been modified with the formation of a second N–H bond. The structure (**5**) which accommodates the data is confirmed by an *X*-ray crystallographic analysis† in which the formation of a new C–C bond, and consequently a cyclopentane ring, is evident (Figure 1).

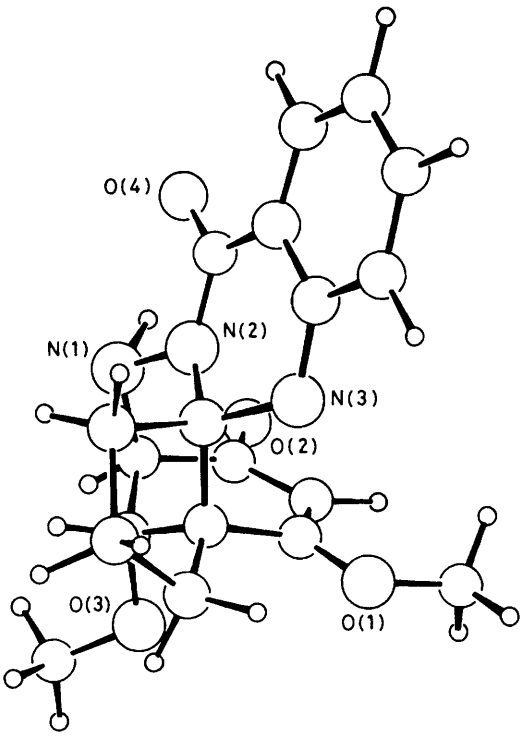


Figure 1. A view of the molecular structure of (**5**). Unlabelled atoms are carbon (larger circles) or hydrogen (small circles). All hydrogen atoms are shown apart from the one attached to N(3) which could not unambiguously be located.

Formation of (**3**) and (**4**) is most easily explained by the unexpected addition of the nitrene to the double bond indicated, *via* (**6**), followed by acetic acid or methanol ring-opening of the resulting aziridine. Acid-catalysed ring-opening of the aziridine would be expected to be regio- and stereo-specific as obtains in (**4**). It is likely that (**3**) and (**4**) have the same relative configuration at their two chiral centres, *i.e.*, that conversion of (**3**) → (**4**) takes place with retention of configuration and participation by the neighbouring NH.

A model of the transition state (**6**) indicated that the possibility exists for an attractive interaction between the quinazolone and the double bond of the aromatic ring of a type which we have previously shown to be important in intermolecular additions of other *N*-nitrenes.[4]

To encourage nitrene attack as indicated in (**6**) and to reduce the likelihood of competitive electrophilic attack at the activ-

† *Crystal data:* (**5**), $C_{19}H_{21}N_3O_4$, *M* = 355.4, monoclinic, *a* = 11.214(4), *b* = 12.364(6), *c* = 13.02(1) Å, β = 104.4(1)°, *U* = 1747 Å^3, space group $P2_1/n$, *Z* = 4. 1036 Independent reflections were measured on a Stoe 2-circle diffractometer using Mo-K_α radiation (λ = 0.7107 Å) for $2\theta < 45°$; of these 679 had $|F_o| > 5\sigma(|F_o|)$. The structure was solved by direct methods and refined isotropically to *R* = 0.094, R_w = 0.080. The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Rd., Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

ated *para*-position of the dimethoxy aromatic ring, we synthesised and oxidised the dimethyl analogue of (**2**), namely (**7**). In this case, a product (**8**), m.p. 198—201 °C, was isolated in 55% yield by oxidation using LTA in methanol whose spectroscopic properties indicated it to be analogous to (**4**).

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References

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2 R. S. Atkinson, J. R. Malpass, K. L. Skinner, and K. L. Woodthorpe, *J. Chem. Soc., Chem. Commun.*, 1981, 549.
3 For intermolecular nitrene addition to dimethoxylated aromatic rings see D. W. Jones, *J. Chem. Soc., Chem. Commun.*, 1973, 67.
4 R. S. Atkinson and J. R. Malpass, *J. Chem. Soc., Perkin Trans.* 1, 1977, 2242.