Intramolecular Trapping of *N*-Nitrenes: Trapping by a Remote 2,4-Dimethoxyphenyl Ring

Robert S. Atkinson,* John Fawcett, Nagwa A. Gawad, David R. Russell, and Lesley J. S. Sherry

Department of Chemistry, Leicester University, Leicester LE1 7RH, U.K.

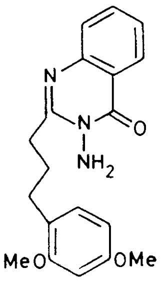
From oxidation of the *N*-aminoquinazolone **(2)** in methanol, three crystalline products **(4)**, **(5)**, and **(6)** have been isolated and the structures of two of them confirmed by *X*-ray crystallography; oxidation of **(2)** in benzene yields the *meta*-bridged *N*-nitrene 'insertion' product **(3)** in 60% yield.

We have shown previously[1] that the *N*-nitrene generated on oxidation of the *N*-aminoquinazolone (**1**) is trapped intramolecularly by the 2,4-dimethoxyphenyl ring.

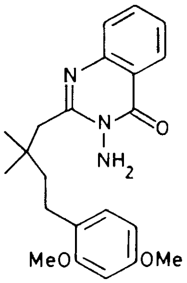
In this communication we report the isolation and structures of four crystalline products from oxidation of the *N*-aminoquinazolone (**2**) which reveal an unexpected selectivity of the *N*-nitrene for particular double bonds in the 2,4-dimethoxyphenyl ring.

Oxidation of (**2**) in benzene solution with lead tetra-acetate gave the *meta*-insertion product (**3**), m.p. 119—121 °C, in 60% isolated yield. The cyclophane-like character of this product is supported by the shielding of one of the methyl groups (δ 0.56) and the non-equivalence of protons within all three methylene groups of the bridging alkyl chain at room temperature together with the absence of discernible *meta*-coupling (at 400 MHz) between the two ring protons of the dimethoxyphenyl ring.

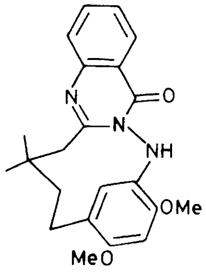
In view of the oxidation products obtained in methanol (see below), it seems likely that this product is formed by nitrene addition to the 5,6-double bond in (**2**) followed by ring-opening and proton loss.



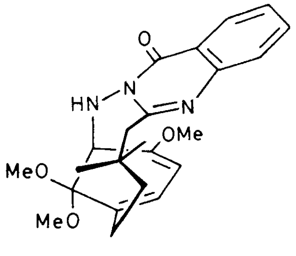
(**1**)



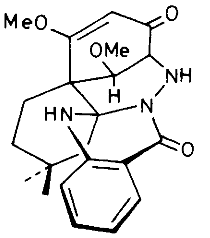
(**2**)



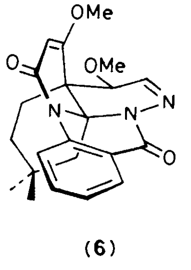
(**3**)



(**4**)



(**5**)



(**6**)

From oxidation of (**2**) in methanol, three products were isolated by crystallisation.[†] The spectroscopic data for the product least soluble in methanol, m.p. 168—171 °C (15%), were consistent with structure (**4**) but the exact location of the

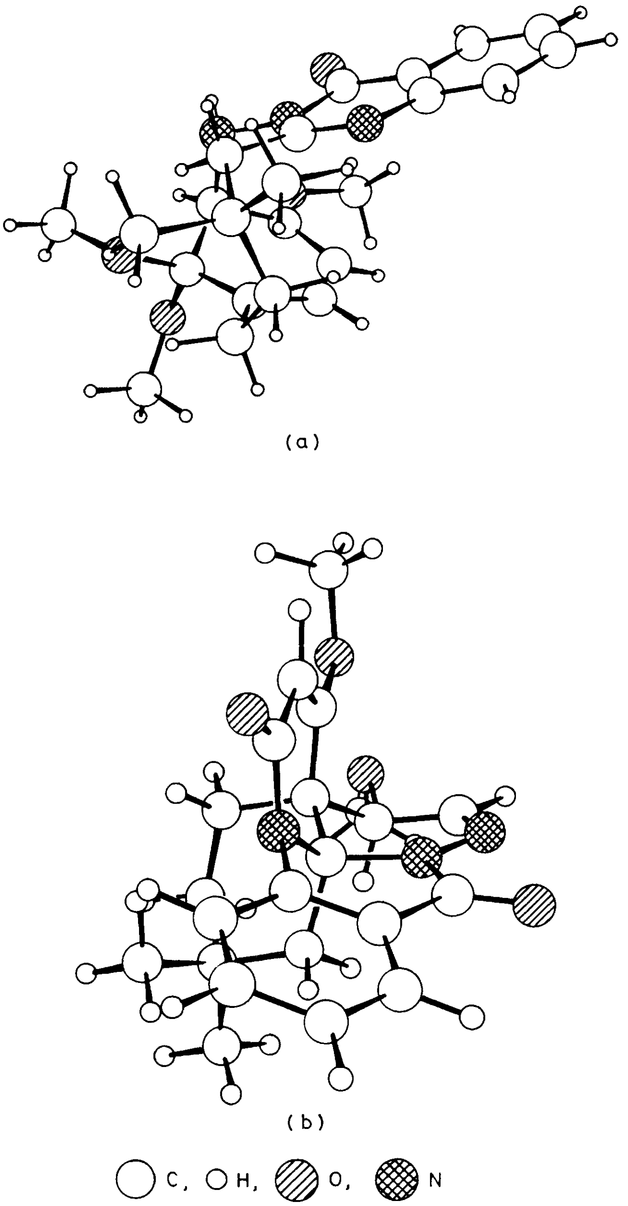
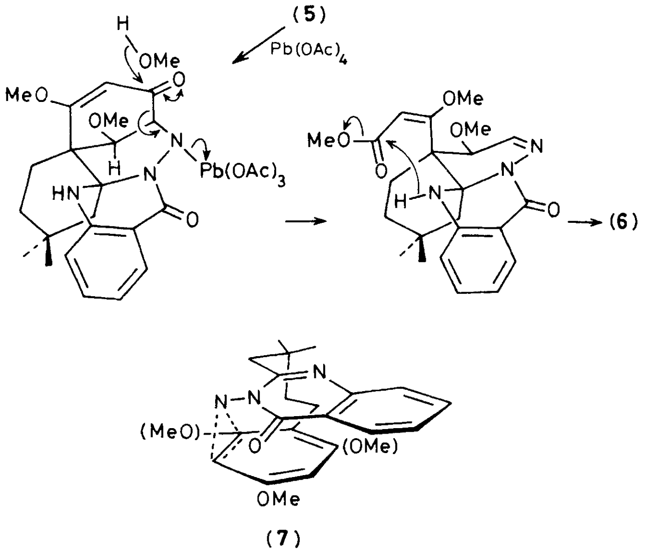


Figure 1. A view of the molecular structure of (a) compound (**4**), and (b) compound (**6**). Atoms are represented by circles of arbitrary radius.

[†] Compound (**3**) was detected as a minor product in the crude reaction mixture.



Scheme 1

additional methoxy group was only proved by an X-ray structure determination [Figure 1(a)].‡ This X-ray structure accounts for the large difference in chemical shift ($\Delta\delta$ 2.23 p.p.m.) between the resonances of the methylene protons adjacent to the quinazolone ring since one of these protons is hydrogen bonded to a lone pair of electrons of a methoxy group. Presumably (**4**) results from ring-opening by methanol of the aziridine formed from addition of the N-nitrene to the 2,3-double bond in (**2**).[2]

Further crystallisation from ethyl acetate–light petroleum gave a product to which we could confidently assign the structure (**5**) from the close similarity of its spectroscopic data to those of an analogous compound we had previously obtained from oxidation of (**1**) [(**5**) with a cyclopentane instead of a dimethylcyclohexane ring].

The structure of the third product (**6**), m.p. 245—249 °C (11%) (obtained by crystallisation from Et_2O), was only apparent after X-ray crystallography [Figure 1(b)].‡ It presumably arises by further oxidation of (**5**) since it was subsequently obtained in 60% yield by independent oxidation of the latter with lead tetra-acetate; the route shown in Scheme 1 is a possibility.

Evidently (**5**) and (**6**), as with (**3**), originate from addition of the N-nitrene to the 5,6-bond of the dimethoxylated phenyl ring. It is noteworthy that no products were isolated or identified in the crude reaction mixture from addition of the nitrene to the 1,2- or 1,6-double bonds although we have identified products resulting from such additions from oxidation of N-aminoquinazolones bearing a 2,4-dimethoxyphenylethyl substituent at position 2.[3]

Intramolecular nitrene additions to aromatic rings are well known but for successful reaction there appear to be severe limitations on the number of atoms separating the nitrene and aromatic ring; nitrene addition to a remote aryl ring as in the present case is unprecedented. The N-nitrene from (**2**) survives to react *via* the favourable transition state(s) (**7**)[4] because it is apparently stable to alternative unimolecular reactions including C–H or C–N insertion or nitrogen extrusion.

Received, 9th April 1984; Com. 505

References

1 R. S. Atkinson, N. A. Gawad, D. R. Russell, and L. J. S. Sherry, *J. Chem. Soc., Chem. Commun.*, 1983, 568.
2 N. D. Kimpe, R. Verhé, L. D. Buyck, P. Sulmon, and N. Schamp, *Tetrahedron Lett.*, 1983, 2885.
3 R. S. Atkinson and N. A. Gawad, *J. Chem. Soc., Chem. Commun.*, 1984, 557.
4 R. S. Atkinson and J. R. Malpass, *J. Chem. Soc., Perkin Trans. 1*, 1977, 2242.

---

‡ *Crystal data:* (**4**), $C_{23}H_{29}O_4N_3$, $M = 411.50$, triclinic, space group $P\bar{1}$ (No. 2), $a = 11.730(2)$, $b = 11.019(3)$, $c = 10.472(5)$ Å, $\alpha = 95.6(1)$, $\beta = 120.5(1)$, $\gamma = 95.6(1)°$, $U = 1143.64$ Å^3, $Z = 2$, $\lambda(\text{Mo-}K_\alpha) = 0.7107$ Å. The intensities of 3622 unique reflections with $2\theta < 50°$ were measured using a Stoe STADI-2 Weissenberg diffractometer: of these 2363 reflections had $|F_O| > 3\sigma(|F_O|)$. The structure was solved by direct methods and refined to $R = 0.0505$, $R_w = 0.0552$. Hydrogen atoms were included in calculated positions for structure factor calculations.

Crystal data: (**6**), $C_{22}H_{25}O_4N_3$, $M = 395.22$, triclinic, space group $P\bar{1}$ (No. 2), $a = 13.191(4)$, $b = 9.935(3)$, $c = 8.665(9)$ Å, $\alpha = 113.9(2)$, $\beta = 79.5(1)$, $\gamma = 106.7(2)°$, $U = 991.87$ Å^3, $Z = 2$. The intensities of 3359 unique reflections with $2\theta < 50°$ were measured using a Stoe STADI-2 Weissenberg diffractometer: of these 1987 reflections had $|F_O| > 3\sigma(|F_O|)$. The structure was solved by direct methods and refined to $R = 0.1009$, $R_w = 0.1028$. Hydrogen atoms were included in calculated positions for structure factor calculations.

The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.