Intramolecular Reactions of *N*-Nitrenes: Oxidation of 3-Amino-2-(2,4-dimethoxyphenylbutyl)quinazolin-4(3*H*)-ones

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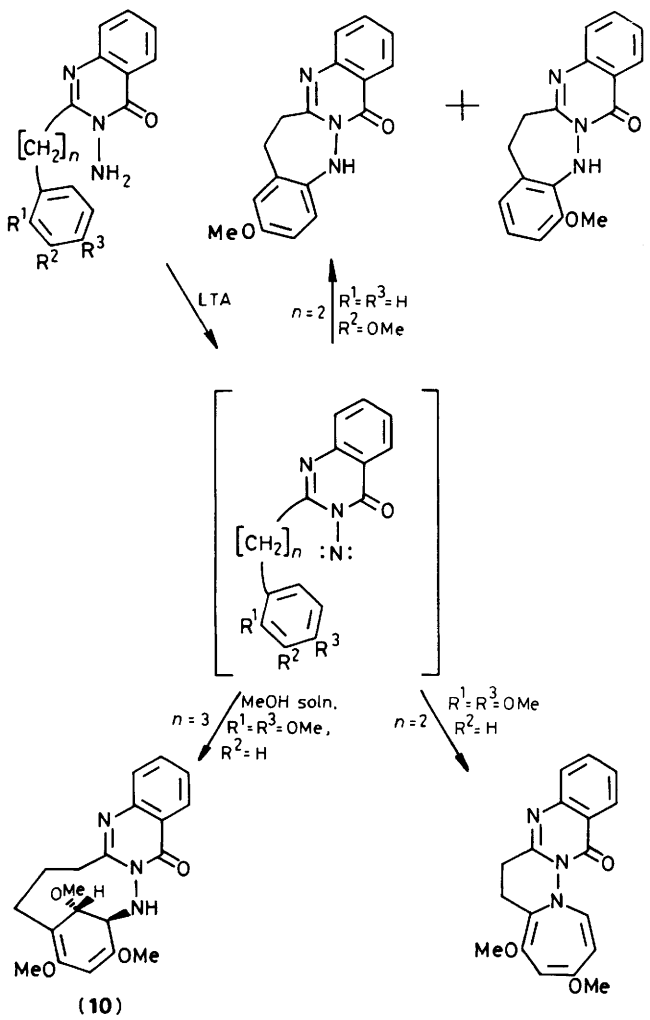
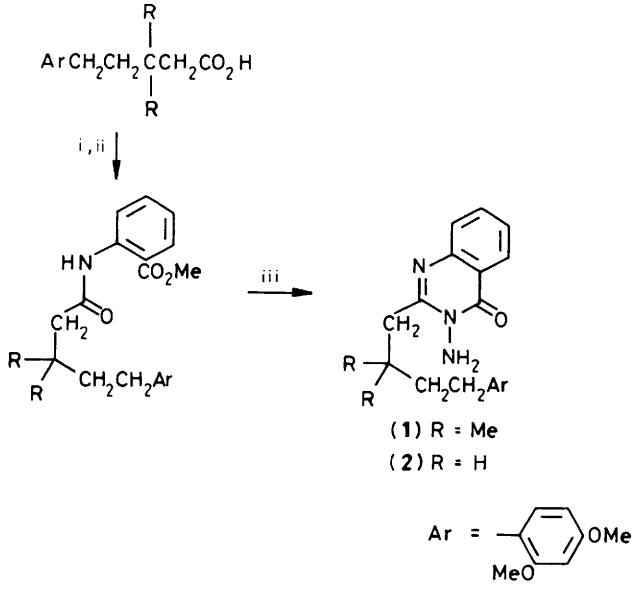
The *N*-nitrenes generated by oxidation of *N*-aminoquinazolones (**1**) and (**2**) are trapped by the remote 2,4-dimethoxyphenyl ring. Oxidation of (**1**) in benzene gives the metacyclophane (**3**) in 60% isolated yield whereas oxidation in methanol gives (**5**), (**6**) and (**8**). The structures of the acetal (**5**) and the imine (**8**) have been confirmed by *X*-ray crystallography. Oxidation of (**2**) in methanol yields (**11**) and (**16**). An explanation is offered for the selectivity for attack on the 2,3- or 5,6-double bonds of the dimethoxyphenyl ring by the *N*-nitrene derived from (**1**).

Oxidation of *N*-aminoquinazolones generates the corresponding *N*-nitrenes which have been trapped intermolecularly by a variety of functional groups including double bonds and aromatic rings.[1] We have shown previously that an appropriately substituted and positioned aryl group in a side-chain at position 2 can trap this *N*-nitrene intramolecularly.[2] Three different types of reaction with methoxylated phenyl rings which the *N*-nitrene undergoes are exemplified in Scheme 1.[3,4]



Scheme 1.

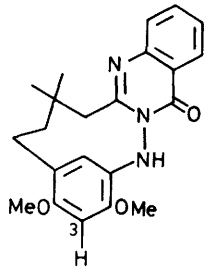
For the case of the 2,4-dimethoxyphenyl ring, the nature of the product appeared to be critically dependent on the length of the chain connecting this ring to the quinazolone. In this paper we describe the products from oxidation of the *N*-aminoquinazolones (**1**) and (**2**) which result from trapping of the derived *N*-nitrene by the more remote 2,4-dimethoxyphenyl ring.[5] Both the crystalline *N*-aminoquinazolones (**1**) and (**2**) were obtained from the corresponding acids by the usual route (Scheme 2).



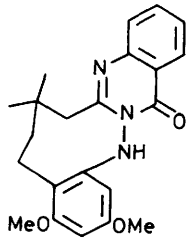
Scheme 2. *Reagents*: i, Na^+ salt, $(COCl)_2$; ii, methyl anthranilate; iii, NH_2NH_2–EtOH.

Oxidation was carried out by slow addition of equimolar quantities of solid *N*-aminoquinazolone and lead tetra-acetate (LTA) to dry benzene or methanol. From oxidation of (**1**) in benzene we isolated a single crystalline product in 60% yield whose solutions decomposed readily on brief warming to give a deep red colouration. Assignment of the metacyclophane structure (**3**) to this product rather than the *ortho*-'insertion' product (**4**) was supported by the n.m.r. spectrum: there was no evidence for *meta*-coupling between the two remaining methoxylated phenyl ring protons. Moreover, the n.m.r. spectrum also suggested that the alkyl chain in (**3**) had little conformational mobility since the two methyl groups and the protons within each of the three methylene groups were non-equivalent at room temperature. This conformational mobility

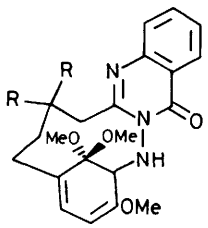
in (**3**) is evidently less than in a metacyclophane containing a saturated alkyl chain of seven carbon atoms.[6]



(**3**)



(**4**)



(**5**) R = Me
(**13**) R = H

Examination of the crude reaction mixture containing (**3**) showed that azepine ring-containing products (from addition of the nitrene to the 1,2- or 1,6-double bonds; see Scheme 1) were absent.

Oxidation of (**1**) in methanol yielded different results. Three crystalline products were isolated by crystallisation: (**3**) was obtained as a minor product (5%) after chromatography on alumina.

The major isolated product (15%) was least soluble in methanol. Its spectroscopic properties showed the incorporation of 1 molecular-equivalent of methanol from the solvent and were in agreement with the structure (**5**) but we were able to eliminate possible double-bond isomers (with appropriate placement of the additional methoxy group) only by an *X*-ray crystal structure determination (Figure 1). This *X*-ray structure shows clearly the answer to what was a puzzling feature of the n.m.r. spectrum, namely that the two protons in the methylene group adjacent to the quinazolone ring are separated by 2.23 p.p.m. (assignment of these protons is unambiguous since they are the only aliphatic protons which are doublets). One of these protons is positioned close to electron pairs (see Figure 2) on one of the methoxy groups and the N-H and presumably there is a hydrogen-bonding effect which results in its downfield shift.[7]

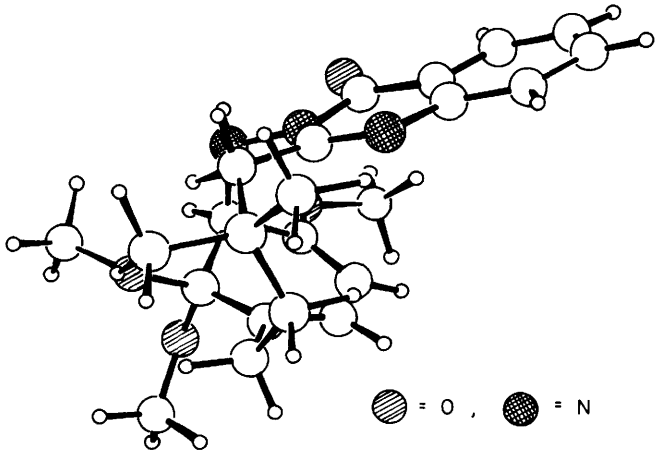


Figure 1. A view of the molecular structure of (**5**) from *X*-ray diffraction data.

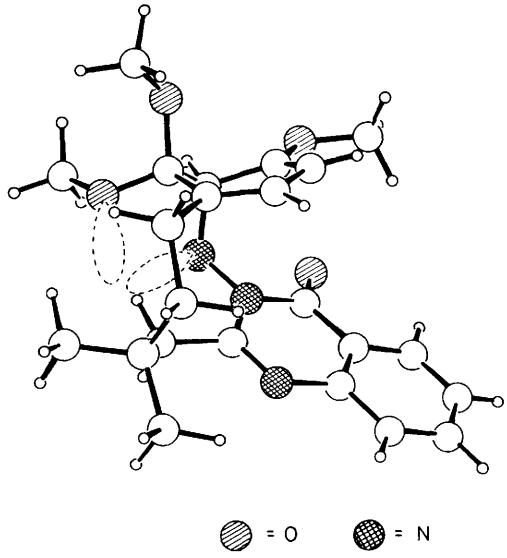
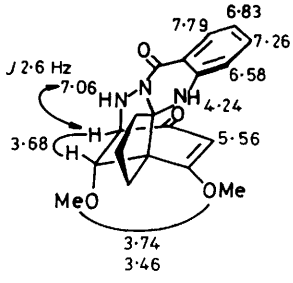
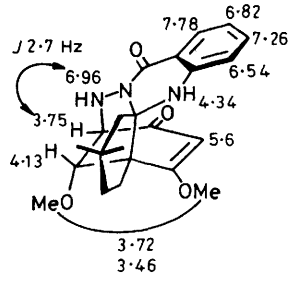


Figure 2. Alternative view of the structure of (**5**) from *X*-ray diffraction data showing the proximity of a proton of the methylene group adjacent to the quinazolone ring to lone pairs on oxygen and nitrogen.

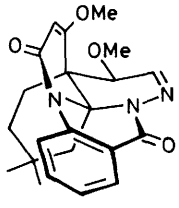
The structure of the second product (11%) isolated by crystallisation from ether could be confidently assigned as (**6**) from the close similarity of its spectroscopic properties (and particularly its n.m.r. spectrum) to that of (**7**) whose structure has been confirmed by *X*-ray crystallography.



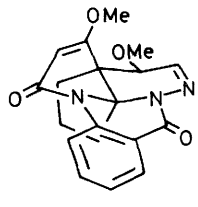
(**7**)



(**6**)



(**8**)



(**9**)

For comparison, the chemical shifts of selected protons in (**6**) and (**7**) are shown and it is clear that the only significant difference is between the values for the *H*COMe protons which might reasonably be expected to be the result of the proximity of this proton in (**6**) to a methyl group in the 6-membered ring.

The structure of the third crystalline product (5%) from oxidation of (**1**) with LTA in methanol was shown to be (**8**), also by an *X*-ray crystallographic determination (Figure 3). It seems probable that (**8**) is formed by further oxidation of (**6**) and oxidation of (**6**) with LTA in methanol in a separate experiment gave (**8**) in 60% isolated yield presumably by the route indicated in Scheme 3.

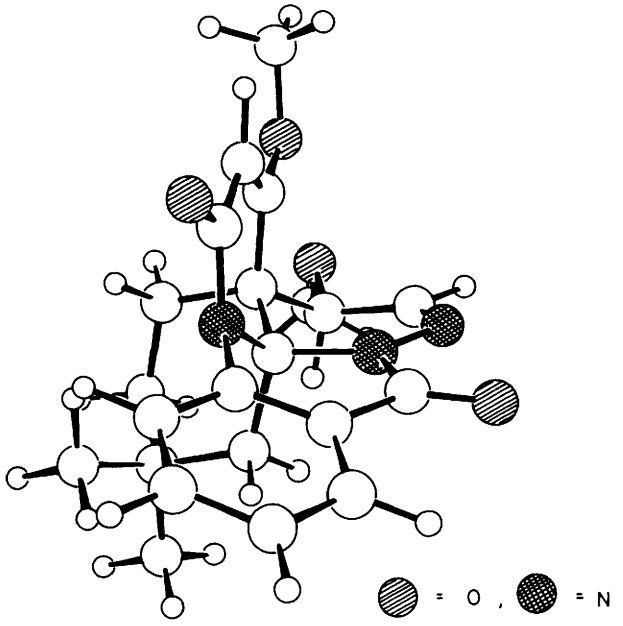
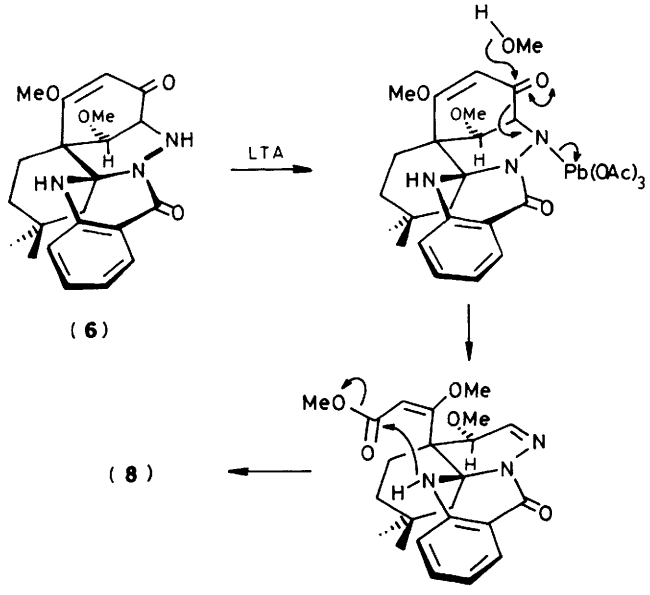


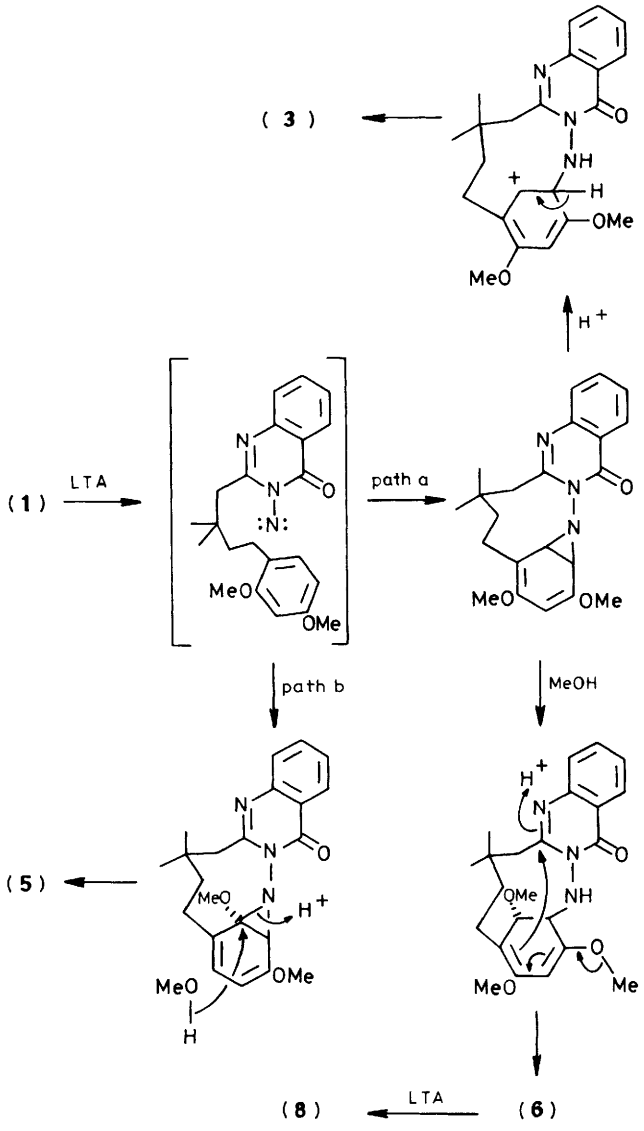
Figure 3. A view of the molecular structure of (**8**) from *X*-ray diffraction data.

In view of the similarity between (**6**) and (**7**) it was not surprising to find that oxidation of the latter with LTA in methanol proceeded to give an analogous product (**9**). Examination of the n.m.r. spectrum of (**9**), however, reveals that the quinazolone ring proton *ortho* to N is strongly deshielded by comparison with its position in (**8**). Examination of models reveals that this shift is best accommodated by a change in the configuration of the (pyramidal) nitrogen in (**9**) relative to (**8**) since this brings the quinazolone ring proton into the deshielding region of the adjacent carbonyl group.



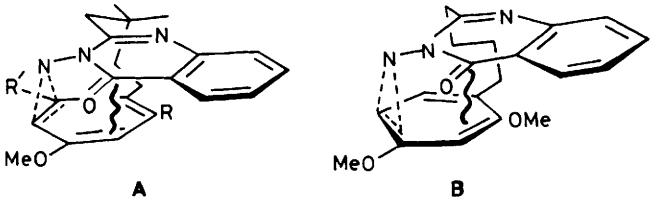
Scheme 3.

Mechanisms of Formation of Compounds (**3**), (**5**), and (**6**). Formation of the oxidation products (**3**), (**5**), and (**6**) can be rationalised by attack of the *N*-nitrene on the dimethoxyphenyl ring double bonds indicated followed by ring opening of the resultant aziridines (Scheme 4).



Scheme 4.

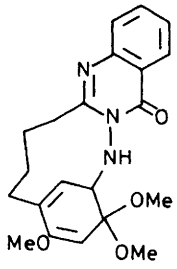
This selectivity of the *N*-nitrene for the more distant 2,3- and 5,6-double bonds of the aromatic ring is striking. As in the formation of (**10**) (Scheme 1), we believe this selectivity for the double bonds indicated in Scheme 4 is the result of a preferred transition state for *N*-nitrene addition which has quinazolone and dimethoxyphenyl rings overlapping in parallel planes with an attractive interaction between the methoxylated double bond and carbonyl carbon as shown (Figure 4A).[8]



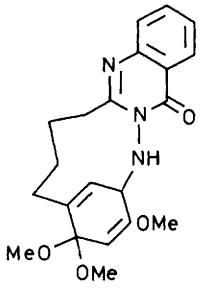
R = H or OMe
R′ = OMe or H

Figure 4. Proposed transition state geometries for *N*-nitrene addition to the 2,3-(or 5,6) double bonds of the dimethoxyphenyl ring of (**1**) (A) or the 4,5-double bond of (**2**) (B). The heavy curly line represents an attractive secondary interaction.

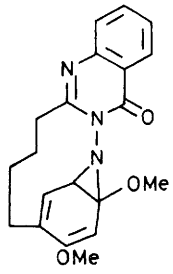
Oxidation of the *N*-aminoquinazolone (**2**) in methanol did not give entirely similar results to those described above. Two products were obtained by fractional crystallisation from methanol. The major product m.p. 204—207 °C (27%) was clearly not analogous to any of the products isolated from the similar oxidation of (**1**). Although a molecular equivalent of methanol had again been incorporated into the product and a CH–CH–NH system was apparently still present [as in (**10**); (Scheme 1)], (δ 5.64 (d, *J* 2.8 Hz NH), 5.46 (d, *J* 5.8 Hz), and 4.01 (ddd, *J* 5.8, 2.8 and 1.4 Hz, NHC*H*), the chemical shift and coupling constant of the signal at δ 5.46 was in better agreement with its assignment as an olefinic proton. Assignment of the conjugated diene structure (**11**) to this product rather than the non-conjugated diene (**12**) comes from the u.v. spectrum which shows that the intensity of the absorption band at 277 nm is more consistent with the superimposition of quinazolone and diene chromophores at this wavelength.



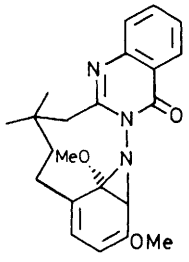
(**11**)



(**12**)



(**14**)

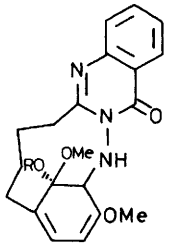


(**15**)

The crystalline minor product (7%), m.p. 213—217 °C could be assigned structure (**13**) from the similarity of its spectroscopic data to that of (**5**). In particular, the signals in the n.m.r. spectrum from protons in the methylene group adjacent to the quinazolone ring showed a similar massive difference in chemical shift (Δδ 2.03 p.p.m.) and those from the NH–CH and methoxylated ring protons were very similar in chemical shift and coupling constant.

As in the formation of (**3**), (**5**), and (**6**) (Scheme 4), it seems probable that the precursors to (**11**) and (**13**) are the corresponding aziridines (**14**) and (**15**) respectively, since α-alkoxyaziridines are known to undergo alcoholysis to α-aminoacetals.[9] Formation of (**15**) proceeds by a transition state analogous to that in Figure 4 but for formation of (**14**) attack at the most distant double bond as in Figure 4B is required. It may be no coincidence that formation of both (**14**) and (**15**) result from involvement of the two methoxylated double bonds either in aziridine formation or in the secondary interaction referred to earlier.

At an early stage in this work we oxidised the *N*-aminoquinazolone (**2**) in benzene–allyl alcohol in the expectation that the derived acetal (**16**) might be induced to undergo an intramolecular Diels–Alder reaction. A crystalline product from this reaction isolated in low yield was identified as (**16**) but it failed to undergo the required intramolecular cycloaddition on heating.



(**16**) R = $CH_2CH{=}CH_2$

Intramolecular nitrene additions to aromatic rings are well-known[10] 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. *N*-Nitrenes derived from (**1**) and (**2**) survive to react by the favourable transition states shown in Figures 4A and B because they are apparently stable to alternative unimolecular reactions including C–H or C–N insertion or nitrogen extrusion.

Experimental

For general experimental details see ref. 3. U.v. spectra were recorded on a Schimadzu PR1 spectrophotometer.

3-*Amino*-2-[4-(2,4-*dimethoxyphenyl*)*butyl*]*quinazol*-4(3H)-*one* (**2**).—Methyl *N*-[5-(2,4-dimethoxyphenyl)pentanoyl]-anthranilate was prepared from the sodium salt of 5-(2,4-dimethoxyphenyl)pentanoic acid, oxalyl chloride and methyl anthranilate by the method given in ref. 3 as a colourless solid, m.p. 86—88 °C (75%); 10.92 (s, br, NH), 8.6 (dd, *J* 8 and 1 Hz, H *ortho* to NH), 7.92 (dd, *J* 7 and 2 Hz, H *ortho* to CO_2Me), 7.47 (ddd, *J* 8, 8 and 2 Hz, H *meta* to NH), 7.1—6.9 (m, H *meta* to CO_2Me, Ar 6-H), 6.4—6.25 (m, Ar 3- and 5-H), 3.85, 3.71 (2 × s, 2 × OMe + CO_2Me), 2.6—1.48 (m, 4 × CH_2); $\nu_{max.}$ 3 300br, 1 700s, and 1 600s cm^{-1}. This amide was heated with hydrazine and ethanol as described in ref. 3. The N-*aminoquinazolone* (**2**) was obtained as a colourless solid (80%), m.p. 114—116 °C (from ethanol) (Found: C, 67.9; H, 6.6; N, 11.95 $C_{20}H_{23}N_3O_3$ requires C, 68.0; H, 6.55; N, 12.0%); δ 8.19 (d, *J* 8 Hz, quinaz. 5-H), 7.7—7.2 (m, quinaz. 6-, 7-, and 8-H), 6.95 (d, *J* 8 Hz, Ar 6-H), 6.4—6.25 (m, Ar 3- and 5-H), 4.76 (s, NH_2), 3.75 (s, 2 × OMe), 3.95, 2.52 (2 × t, both *J* 6 Hz, 2 × CH_2), and 1.72 (m, 2 × CH_2); $\nu_{max.}$ 3 315w, 1 669s, and 1 600s cm^{-1}.

3-*Amino*-2-[4-(2,4-*dimethoxyphenyl*)-2,2-*dimethylbutyl*]*quinazol*-4(3H)-*one* (**1**).—Methyl *N*-[5-(2,4-dimethoxyphenyl)-3,3-dimethylpentanoyl]anthranilate was prepared from the sodium salt of 5-(2,4-dimethoxyphenyl)-3,3-dimethylpentanoic acid (prepared as described below) and oxalyl chloride by the method given in ref. 3 as a colourless solid (75%), m.p. 66—68 °C (from ethanol) (Found: C, 69.2; H, 7.3; N, 3.5. $C_{23}H_{29}NO_5$ requires C, 69.15; H, 7.3; N, 3.5%); δ 10.9 (s, br, NH), 8.7 (d, *J* 8 Hz, H *ortho* to NH), 7.93 (dd, *J* 8 and 2 Hz, H *ortho* to CO_2Me), 7.52 (ddd, *J* 8, 8 and 2 Hz, H *meta* to CO_2Me), 7.1—6.58 (m, H *meta* to NH, Ar 6-H), 6.52 (m, Ar 3- and 5-H), 3.82 (s, OMe), 3.70 (s, OMe), 2.52 (m, CH_2), 2.32 (s, CH_2), 1.52 (m, CH_2), and 1.12 (s, 2 × Me); $\nu_{max.}$ 3 320br, 1 680s, and 1 590s cm^{-1}.

5-(2,4-Dimethoxyphenyl)-3,3-dimethylpentanoic acid was prepared by reaction of 3,3-dimethylglutaric anhydride, aluminium chloride, and dimethylresorcinol to give 4-(2,4-dimethoxybenzoyl)-3,3-dimethylbutyric acid (75%), m.p. 63—

65 °C; δ 8.5 (s, br, CO_2H), 7.7 (d, *J* 8.5 Hz, Ar 6-H), 6.55 (dd, *J* 8.5 Hz, Ar 5-H), 6.55 (d, *J* 2 Hz, Ar 3-H), 3.85 (s, 2 × OMe), 3.15 (s, $COCH_2$), 2.55 (s, CH_2CO_2H), 1.15 (s, 2 × Me); $\nu_{max.}$ 1 700s, 1 650s, and 1 600s cm^{-1}, followed by Clemmensen reduction [11] and was obtained as a colourless solid (63%), m.p. 78—80 °C, δ 10.32 (s, br, CO_2H), 6.95 (d, *J* 8.5 Hz, Ar 6-H), 6.35 (m, Ar 3- and 5-H), 3.72 (s, 2 × OMe), 2.5 (m, 2 × CH_2), 1.5 (m, CH_2), and 1.5 (s, 2 × Me). The amide prepared above was heated with hydrazine and ethanol in a sealed tube as described in ref. 3 and the N-*aminoquinazolone* (**1**) was obtained as a colourless solid (75%), m.p. 100—102 °C (from ethanol) (Found: C, 69.35; H, 7.15; N, 11.05. $C_{22}H_{27}N_3O_3$ requires C, 69.25; H, 7.15; N, 11.0%); δ 8.19 (d, *J* 8 Hz, quinaz. 5-H), 7.75—7.2 (m, quinaz. 6-, 7-, and 8-H), 7.1 (d, *J* 8.5 Hz, Ar 6-H), 6.6 (m, Ar 3- and 5-H), 4.81 (s, NH_2), 3.71 (s, 2 × OMe), 3.1 (s, CH_2Ar), 2.6 (m, CH_2C=N), 1.65 (s, $CH_2CH_2CMe_2$), and 1.15 (s, 2 × Me); $\nu_{max.}$ 3 318m, 3 208m, 1 660s, and 1 585s cm^{-1}.

Oxidation of 3-*Amino*-2-[4-(2,4-*dimethoxyphenyl*)*butyl*]*quinazolin*-4(3H)-*one* (**2**).—The solid quinazolone (**2**) (200 mg) was oxidised with LTA (276 mg) in methanol (100 ml) as described in ref. 3. After removal of the organic solvent under reduced pressure, the residue was treated with methanol and the solid separated (27%). Crystallisation from chloroform–methanol gave the acetal (**11**) as a colourless solid, m.p. 204—207 °C (Found: C, 65.35; H, 6.5; N, 10.65. $C_{21}H_{25}N_3O_4$ requires C, 65.75; H, 6.55; N, 10.95%); δ 8.22 (dd, *J* 8 and 1.3 Hz, quinaz. H *ortho* to C=O), 7.73 (ddd, *J* 8.5, 7 and 1.3 Hz, quinaz. H *meta* to N), 7.63 (d, *J* 8.5 Hz, quinaz. H *ortho* to N), 7.43 (ddd, *J* 7, 8, and 1.4 Hz, quinaz. H *meta* to C=O), 5.64 (d, *J* 2.8, NH), 5.46 (d, *J* 5.8 Hz, =C*H*–CHNH), 4.82 (d, *J ca.* 1.3 Hz, =C*H*COMe), 4.01 (ddd, *J* 5.8, 2.8, and 1.3 Hz, C*H*NH), 3.70, 3.63, 3.26 (3 × s, 3 × OMe), 3.32 (m, HC*H*), 2.77 (m, *H*CH), 2.62 (m, HC*H*), 2.35 (m, *H*CH), 1.84 (m, HC*H*), and 1.65 (m, 3 × CH); ^{13}C 162.1 (s), 161.6 (s), 155.5 (s), 147.3 (s), 138.7 (s), 134.3 (d), 126.9 (d), 126.3 (d), 126.0 (d), 122.0 (d), 120.2 (s), 101.0 (s), 95.6 (d), 54.8 (q), 53.7 (d), 49.2 (q), 48.6 (q), 31.4 (t), 31.4 (t), 31.0 (t), 27.1 (t), and 26.7 (t); $\nu_{max.}$ 3 298m, 1 680sh, and 1 673s cm^{-1}; $\lambda_{max.}$($CHCl_3$) 277 (ε 11 500 dm^3 mol^{-1} cm^{-1}), 307sh (ε 5 700), and 321sh nm (ε 3 800): for comparison, 3-amino-2-methylquinazolin-4(3*H*)-one has $\lambda_{max.}$($CHCl_3$) 270 (ε 6 500 dm^3 mol^{-1} cm^{-1}), 305 (ε 3 800), and 317 nm (ε (3 000). Cooling of the methanol filtrate in ice after removal of (**11**) above gave the *acetal* (**13**) as a colourless solid (7%), m.p. 213—217 °C (from chloroform–methanol) (Found: C, 65.6; H, 6.55; H, 10.85. $C_{21}H_{25}N_3O_4$ requires C, 65.75; H, 6.55; N, 10.95%); 8.09 (dd, *J* 8 and 1.4 Hz, quinaz. H *ortho* to C=O), 7.66 (ddd, *J* 8, 7 and 1.5 Hz, quinaz. H *meta* to N), 7.56 (d, *J* 8 Hz, quinaz. H *ortho* to N), 7.34 (ddd, *J* 8, 7 and 1.1 Hz, quinaz. H *meta* to C=O), 6.38 (d, *J* 5.3 Hz, NH), 5.38 (dd, *J* 6.2 and 2.3 Hz, C*H*–CH=COMe), 4.63 (d, *J* 6.2 Hz, CH–C*H*=COMe), 4.40 (dd, *J* 17, 13.5 and 4 Hz, CH*H*C=N), 3.54 (d, *J* 5.3 Hz, C*H*NH), 3.48, 3.47, 3.03 (3 × s, 3 × OMe), 2.47 (ddd, *J* 17, 4.5, and 3 Hz, *H*CH–C=N), 2.35 (m, 2 × CH), 2.06 (m, HC*H*), 1.84 (m, HC*H*), and 1.63 (m, 2 × CH); $\nu_{max.}$ 3 290w and 1 675 s cm^{-1}.

Oxidation of (**2**) *in the Presence of Allyl Alcohol.*—Oxidation of (**2**) was carried out in benzene solution containing 15% by volume of allyl alcohol using the procedure described in ref. 3. Addition of methanol to the oil remaining after removal of organic solvents gave the *acetal* (**16**) (7%) as a colourless solid (from methanol), m.p. 180—183 °C (Found: C, 67.25; H, 6.7; N, 10.25. $C_{23}H_{27}N_3O_4$ requires C, 67.45; H, 6.65; N, 10.25%); δ 8.03 (d *J* 8 Hz, quinaz. H *ortho* to C=O), 7.7—7.1 (m, 3 × quinaz. H), 6.38 (d, *J* 6 Hz, NH), 6.0—5.5 (m, CH_2=C*H*), 5.3—4.9 (m, CH_2=CH, C*H*–CH=COMe), 4.56 (d, *J* 6 Hz, CH–C*H*=COMe), 4.45—4.1 (m, CH*H*C=N), 3.9—3.3 (m, 2 × OMe, NHC*H*, CH_2CH=CH_2), and 2.8—1.4 (m, 7 × aliphat. CH); $\nu_{max.}$ 3.282s and 1 680 s cm^{-1}.

Oxidation of 3-*Amino*-2-[4-(2,4-*dimethoxyphenyl*)-2,2-*dimethylbutyl*]*quinazolin*-4(3H)-*one* (**1**).—(a) *In benzene.* An intimate mixture of solid (**1**) (300 mg) and solid LTA (384 mg) was added to benzene (150 ml) as described in ref. 3. Addition of methanol to the residue obtained after removal of benzene gave the *product* (**3**) as a colourless solid (from methanol with the minimum of heating), m.p. 119—121 °C (Found: C, 68.9; H, 6.7; N, 10.8. $C_{22}H_{25}N_3O_3$ requires C, 69.65; H, 6.65; N, 11.1%); δ 8.85 (s, NH), 8.31 (dd, *J* 8.1 and 1.2 Hz, quinaz. H *ortho* to C=O), 7.75 (ddd, *J* 8, 7, and 1.4 Hz, quinaz. H *meta* to N), 7.70 (d, *J* 8 Hz, quinaz. H *ortho* to N), 7.48 (ddd, *J* 8, 7, and 1.4 Hz, quinaz. H *meta* to C=O), 6.50 (s, Ar 6-H), 6.46 (s, Ar 3-H), 3.92, 3.83 (2 × s, 2 × OMe), 2.77 (ddd, *J* 16.5, 13.2, and 4.9 Hz, C*H*Ar), 2.56 (dd, *J* 16.5 and *ca.* 5 Hz, CHAr), 2.36 (d, *J* 15.6 Hz, C*H*C=N), 2.19 (ddd, *J* 15.8, 13.2 and 5.3 Hz, C*H*CMe_2), 2.03 (d, *J* 15.6 Hz, C*H*C=N), 1.55 (s, Me), 1.50 (ddd, *J* 15.8, 4.9, and 2.2 Hz, C*H*CMe_2), and 0.56 (s, Me); $\nu_{max.}$ 3 280m, 1 660s, and 1 590s cm^{-1}. Concentration of the methanol filtrate by evaporation under reduced pressure gave (**5**) (5%) (see below).

(b) *In methanol.* An intimate mixture of solid (**1**) (400 mg) and solid LTA (512 mg) was added to dry methanol (200 ml) as described in ref. 3. The oil remaining after work-up gave the *acetal* (**5**) as a colourless solid (15%) (from methanol), m.p. 168—171 °C (Found: C, 67.2; H, 7.05; N, 10.2. $C_{23}H_{29}N_3O_4$ requires C, 67.2; H, 7.1; N, 10.2%); δ 8.06 (d *J* 8 Hz, quinaz. H *ortho* to C=O), 7.64 (dd, *J* 8 and 8 Hz, quinaz. H *meta* to N), 7.54 (d, *J* 8 Hz, quinaz. H *ortho* to N), 7.33 (dd, *J* 8 and 8 Hz, quinaz. H *meta* to C=O), 6.39 (d, *J* 5 Hz, NH), 5.37 (dd, *J* 6.1 and 1.7 Hz, C*H*CH=COMe), 4.58 (d, *J* 6.1 Hz, CHC*H*=COMe), 4.36 (d, *J* 17.4 Hz, C*H*C=N), 3.49, 3.47 (2 × s, 2 × OMe) *ca.* 3.49 (obscured, C*H*NH), 3.04 (s, OMe), 2.6 (dd, *J* 14 and 14 Hz (+ further splitting), C*H*Ar), 2.13 (d, *J* 17.4 Hz, C*H*C=N), 1.99 (m, HC*H*C*H*HCMe_2), 1.53 (s, Me), 1.42 (dd, *J* 14 and *ca.* 5 Hz, C*H*CMe_2), and 1.12 (s, Me); $\nu_{max.}$ 3 390m, 1 679s, and 1 595s cm^{-1}.

Evaporation of the filtrate and crystallisation from ether gave the *imine* (**8**) (11%), m.p. 245—249 °C (Found: C, 66.4; H, 6.2; N, 10.4. $C_{22}H_{25}N_3O_4$ requires C, 66.8; H, 6.3; N, 10.6%); ^1H δ 8.13 (dd, *J* 7.7 and 1.6 Hz, quinaz. H *ortho* to C=O), 7.62 (ddd, *J* 7.7 and 7.7 Hz, quinaz. H *meta* to N), 7.50 (dd, *J* 7.7 and 1.1 Hz, quinaz. H *ortho* to N), 7.41 (ddd, *J* 7.7, 7.7 and 1.1 Hz, quinaz. H *meta* to C=O), 7.37 (d *J* 1.4 Hz, *H*C=N), 5.31 (s, C*H*=COMe), 4.34 (d, *J ca.* 1 Hz, C*H*OMe), 3.73, 3.62 (2 × s, 2 × OMe), 2.51 (ddd, *J* 14, 3.4 and 3.4 Hz, HC*H*CH_2), 2.11 (dd, *J* 15.6 and 1.4 Hz, CMe_2HC*H*CN), 2.06 (ddd, *J* 18, 14, and 5.3 Hz, HC*H*CH_2), 1.76 (d, *J* 15.6 Hz, CMe_2*H*CHCN), and 1.4 (m, 2 × CH); irradiation at δ 7.37 caused the signal at 5.31 to sharpen; δ_C 173.0, 165.1, 158.8, 147.7, 139.5, 132.3, 128.6, 128.5, 126.9, 125.3, 94.9, 79.1, 73.2, 60.0, 56.5, 44.8, 43.8, 33.0, 32.7, 31.0, 27.2, and 25.3; $\nu_{max.}$ 1 675s and 1 639s cm^{-1}; *m/z* 395 (M^+), 379, 365, 364, 352, 350, 336, 310 (base), 285, 280, and 269.

Evaporation of the ether filtrate above and crystallisation from ethyl acetate–light petroleum gave the *ketone* (**6**) (5%), m.p. 248—250 °C (Found: C, 66.1; H, 6.75; N, 10.4. $C_{22}H_{27}N_3O_4$ requires C, 66.5; H, 6.85; N, 10.5%); δ 7.78 (dd, *J* 8 and 1.5 Hz, quinaz. H *ortho* to C=O), 7.26 (ddd, *J* 8,7, and 1.5 Hz, quinaz. H *meta* to NH), 6.96 (d, *J* 2.7 Hz, NN*H*), 6.82 (ddd, *J* 8, 7, and 0.8 Hz, quinaz. H *meta* to C=O), 6.54 (d, *J* 8 Hz, quinaz. H *ortho* to NH), 5.6 (s, C*H*=COMe), 4.34 (s, NH), 4.13 (d, *J* 3.5 Hz, *H*COMe), 3.75 (m, *H*CNH), 3.72 (s, OMe), and 3.46 (s, OMe), $\nu_{max.}$ 3 378m, 3 260m, 1 640s, and 1 590s cm^{-1}.

Further oxidation of the above ketone (**6**) (15 mg) with LTA (16 mg) in dry methanol (15 ml) using the same procedure as above gave, after the same work-up, a crystalline product (60%) identical with the imine (**8**).

Oxidation of (**10**) *with LTA in Methanol.*—A solid mixture of (**10**) (235 mg) and LTA (252 mg) was added to stirred dry

methanol (60 ml) as described in ref. 3. After the same work-up procedure, the crude product was crystallised from methanol to give a colourless solid (50%), m.p. 255—260 °C (Found: C, 64.0; H, 5.55; N, 11.6. $C_{19}H_{19}N_3O_4$ requires C, 64.6; H, 5.4; N, 11.9%); δ 8.20 (dd, *J* 8 and 1.6 Hz, quinaz. H *ortho* to C=O), 8.00 (dd, *J* 8.4 and 0.9 Hz, quinaz. H *ortho* to N), 7.82 (d, *J* 3.4 Hz, *H*C=N), 7.53 (ddd, *J* 8.4, 7.3 and 1.6 Hz, quinaz. H *meta* to N), 7.32 (ddd, *J* 8, 7.3 and 0.9 Hz, quinaz. H *meta* to C=O), 5.47 (s, C*H*=COMe), 3.79 (d, *J* 3.4 Hz, C*H*OMe), 3.78 (s, OMe), 3.35 (s, OMe), 2.41 (ddd, *J* 13.9, 7.6, and 7.6 Hz, C*H*H), 2.21 (m, 2 × CH), 1.82 (ddd, 13.7, 7.8, and 5.6 Hz, C*H*H), and 1.59 (m, 2 × CH); $\nu_{max.}$ 1 690s and 1 660s cm^{-1}; *m/z* 353 (M^+), 337, 323, 385, 370, and 355.

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