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

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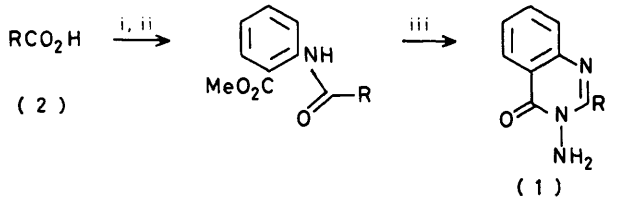
Oxidation of the title compounds yields *N*-nitrenes which react intramolecularly with methoxy-substituted aryl rings. The particular substitution pattern in the aryl rings which is required for effective trapping of the nitrene is in accord with an electrophilic aromatic substitution by the latter *via* a 7-membered transition state rather than a concerted addition.

Two classes of nitrene R–N̈: may at present be identified: those which have a sufficient lifetime to be trapped intermolecularly and those for which only intramolecular trapping is feasible. The former class includes alkoxycarbonyl-, cyano-, and imino-nitrenes [1,2] and a number of heteroatom-substituted nitrenes including nitrogen,[3] sulphur,[4] and oxygen.[5] Prominent in the latter class are a variety of substituted arylnitrenes in which a suitably located aromatic (or heterocyclic) ring may intercept the arylnitrene which otherwise inserts into the parent aryl ring.[6]

A number of *N*-nitrenes are known which have singlet ground states.[3] The ease of isolation of products from reactions of these nitrenes with various substrates is, in part, the result of the absence of C–H insertion reactions which are commonly found with alkoxycarbonyl- and cyano-nitrenes.

A study of *intra*molecular trapping of longer-lived nitrenes is of particular interest. It is reasonable to assume the intermediacy of discrete nitrene intermediates (in view of the many existing intermolecular studies) and to expect a greater selectivity from these less reactive nitrenes in the intramolecular reactions.

We have studied the intramolecular trapping of *N*-nitrenes derived from oxidation of 2-substituted quinazolones (1).[7] These compounds are easily prepared by the route outlined in Scheme 1 and it is evident that the intramolecular trap can be readily incorporated at position 2 as its ω-carboxylic acid (2).

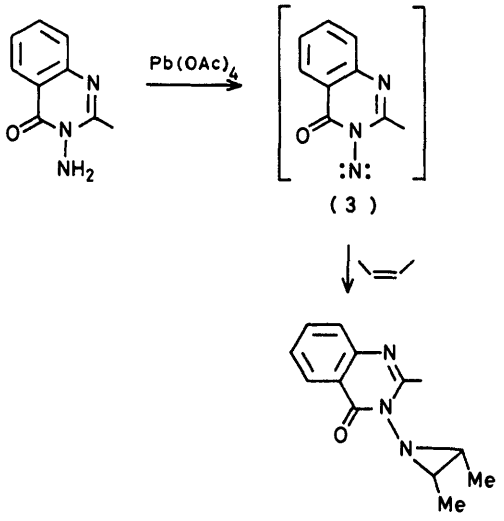


SCHEME 1 *Reagents*: i, $SOCl_2$; ii, methyl anthranilate; iii, NH_2NH_2–EtOH

Like the previously studied phthalimido-[8] and oxobenzoxazolinyl-nitrenes,[9] the 2-methyloxoquinazolinylnitrene (3) reacts stereospecifically with *cis*- and *trans*-but-2-ene even at low alkene concentration [8,10] and presumably also has a singlet ground state (Scheme 2).

It is assumed that all the nitrenes which result from oxidation of the *N*-aminoquinazolones (1) used in this study are reacting *via* their singlet states.

This paper is concerned with the oxidation of compounds in which R is an alkyl side chain bearing a methoxy-substituted benzene ring. The ability of variously substituted aryl rings to achieve intramolecular trapping of the intermediate nitrene is explored.

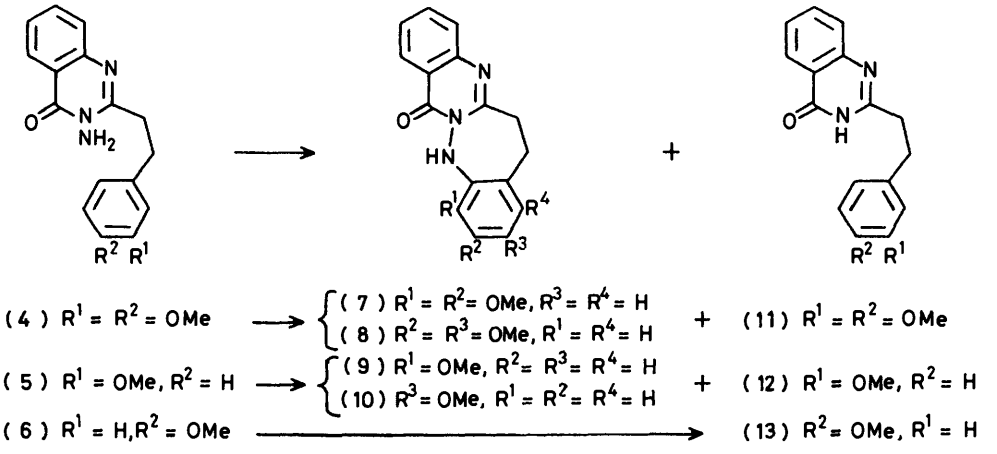


SCHEME 2

A summary of the products from oxidation of 3-amino-2-(2-arylethyl)quinazolones (4)—(6) with lead tetra-acetate in dichloromethane is shown in Scheme 3. The de-amination to give (11)—(13) is the result of a bimolecular reaction between the nitrene and unchanged *N*-aminoquinazolone [11] and the yield of de-amination product is, therefore, a measure of the trapping efficacy of the aryl group used. Samples of the de-amination products (11)—(13) were obtained from the *N*-aminoquinazolones (4)—(6) by the action of nitrous acid and proved to be identical with those isolated above.

When oxidation of the *m*-methoxy-substituted quinazolone (5) was carried out at higher dilution and with simultaneous addition of lead tetra-acetate and (5) in small portions (see Experimental section) the bimolecular de-amination was completely eliminated and an accurate measure of the ratio of the two products (9) and (10) was obtained by n.m.r. spectroscopy.

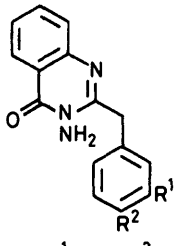
The crystalline oxidation products (7)—(10) are the result of formal insertion into the aromatic C–H bond. The N–H bond in these products occurs at $\nu_{max.}$ 3 250—3 290 cm^{-1} in the i.r. spectrum. Assignment of substitution pattern in the aromatic ring is based on n.m.r. data; the presence of a small coupling between the benzylic methylene protons and a proton in the adjacent *ortho*-position is used as additional evidence for assignment of the latter. The N–H signals due to (7) and (9) are shifted downfield by *ca.* 1.5 p.p.m. by comparison with (8) and (10) presumably as a result of hydrogen bonding with the adjacent methoxy group.



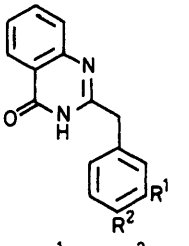
SCHEME 3

It is clear from the products of oxidation of (7)—(10) that successful trapping of the nitrene is critically dependent on the position of the methoxy group(s) in the aryl ring. At least one methoxy group must be *meta* for ' insertion ' products to be obtained.

In similar oxidations of the 3-amino-2-(arylmethyl)-quinazolones (14) and (15), no trapping of the nitrene by the aromatic ring was observed, irrespective of the position of the methoxy-group, and the only homogeneous products isolated were the de-aminated quinazolones (16) and (17), respectively.

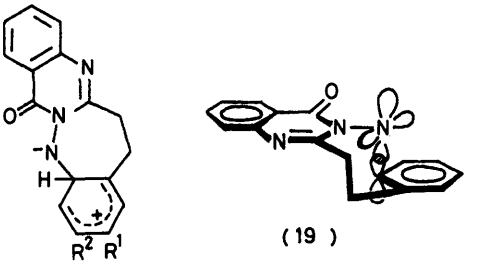


(14) R^1 = H, R^2 = OMe
(15) R^1 = OMe, R^2 = H



(16) R^1 = H, R^2 = OMe
(17) R^1 = OMe, R^2 = H

To rationalise these results, we make three assumptions: (i) that the singlet nitrene nitrogen is sp-hybridised and contains its two pairs of electrons in an sp-hybrid orbital and a p-orbital in the plane of the heterocyclic ring [this results in a vacant p-orbital parallel to the filled p-orbital on the adjacent (amide) nitrogen and minimises repulsion between electron pairs]; (ii) that attack by the electron-rich aromatic ring on the nitrene takes place by electron donation into the vacant p-orbital resulting in a species (18) with high dipolar character; (iii) that the geometry of the system under study requires a minimum of 7 atoms in the cyclic transition state (19) for operation of (ii). Examination of molecular models supports this latter assumption and, in particular, shows that a 6-membered transition state does not bring the aromatic ring into the required alignment with the empty p-orbital on the nitrene nitrogen.* The reason for the effective stabilisation by a *meta*-methoxy-group now becomes apparent since it is only with this group that the charge resulting from attack at either of the two *ortho*-positions can be stabilised. Viewed in this mechanistic light, attack of the nitrene on the aromatic ring is an electrophilic aromatic substitution, albeit an unusual one.



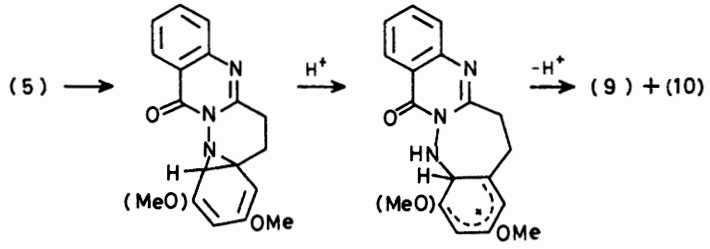
(18) (19) (20)

Electrophilic substitution *via* a 6-membered ring spiro-intermediate (20) followed by protonation and preferential migration of the NH bond would account for the products (7)—(10) but does not explain the pattern of trapping with methoxy-substitution in the benzene ring. More significantly, concerted nitrene addition to one of the benzene ring bonds to form an

* This requirement for a 7-membered transition state also holds for the intramolecular addition to alkenes: R. S. Atkinson, J. R. Malpass, K. Skinner, and K. L. Woodthorpe, *J. Chem. Soc., Chem. Commun.*, 1981, 549.

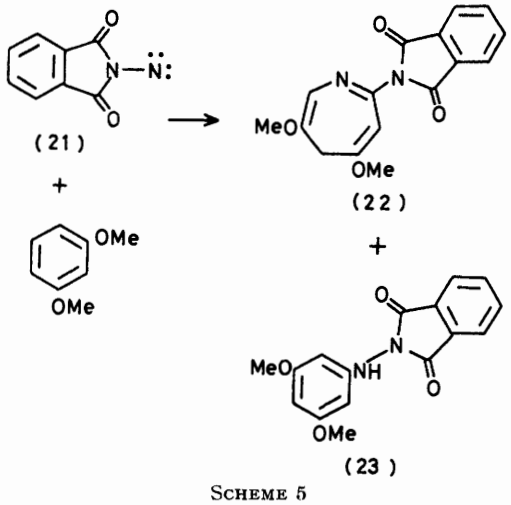
azanorcaradiene followed by acid-catalysed ring opening (Scheme 4) (acetic acid is a by-product in the lead tetra-acetate oxidation) seems to be eliminated by these results. Attack of ethoxycarbonylnitrene on toluene takes place with little discrimination between the three different double bonds [12] nor would the observed difference in products from oxidation of (5) and (6) be expected.

Similar considerations eliminate a direct insertion of the nitrene into aromatic C–H bonds as the mechanism of substitution; in any case *N*-nitrenes do not insert into C–H bonds directly.



SCHEME 4

Intermolecular trapping of phthalimidonitrene (21) by aromatic rings has been studied by Jones.[13] A minimum of two methoxy-groups on a benzene ring is required for successful trapping and the products are azepines [*e.g.* (22)] or insertion products [*e.g.* (23)] analogous to those isolated in the present study. It is significant that insertion products are obtained when phthalimidonitrene is generated in the presence of acetic acid (from oxidation of *N*-aminophthalimide with lead tetra-acetate) whereas azepine formation is preferred when phthalimidonitrene is generated by an alternative route in the absence of acid.

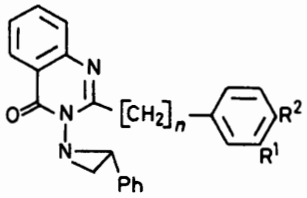


SCHEME 5

When the *N*-aminoquinazolones (5), (6), and (14) were oxidised with lead tetra-acetate in the presence of styrene, the aziridines (24), (25), and (26) respectively, were obtained.

This indicates that the species involved in the intermolecular addition reactions (the nitrene) is that involved in the intramolecular reactions and that the intramolecular reactions do not involve the interception of an intermediate on the oxidation pathway between amine and nitrene (*e.g.* a lead-containing species). The preferential trapping of the nitrene by an excess of styrene accords with the earlier observation that styrene is an excellent trap for nitrenes.[14]

The present work shows that, with certain geometric restraints, intramolecular nitrene attack on substituted aromatic rings is a non-concerted addition. Whether this non-concertedness of addition is directly the result of such geometric restraints remains to be determined. It is clear that the freedom of a nitrene to attack an aryl ring at any position *inter*molecularly will make any conclusion as to concertedness of such additions difficult to draw.



(24) R^1 = OMe, R^2 = H, *n* = 2
(25) R^1 = H, R^2 = OMe, *n* = 2
(26) R^2 = OMe, R^1 = H, *n* = 1

EXPERIMENTAL

For details of instrumentation and general experimental details see ref. 14. Most n.m.r. spectra were determined using a Varian EM 390 spectrometer.

General Procedure for Synthesis of 3-Amino-2-(2-arylethyl)-quinazolin-4(3H)-ones: Methyl N-(3-Arylpropanoyl)-anthranilates.—The appropriate 3-arylpropanoic acid was converted into its acid chloride with thionyl chloride and the acid chloride (20 mmol) added dropwise to a stirred solution of methyl anthranilate (45 mmol) in dry diethyl ether (200 ml). The mixture was set aside overnight, and the crystalline hydrochloride was then separated off and washed with ether. The combined ether filtrates were washed three times with hydrochloric acid (2M) and then with water, dried, and evaporated. Crystallisation of the residual solids from ethanol gave the following: methyl *N*-[3-(3,4-dimethoxyphenyl)propanoyl]anthranilate (61%), m.p. 54—57 °C; δ($CDCl_3$) 11.00 br (s, exch. D_2O, NH), 8.75 (dd, *J* 8 and 1 Hz, H *ortho* to NH), 8.00 (dd, *J* 7 and 2 Hz, H *ortho* to CO_2Me), 7.49 (ddd, *J* 8, 8, and 2 Hz, H *meta* to NH), 7.04 (ddd, *J* 8,

7, and 1 Hz, H *meta* to CO_2Me), 6.93 (m, phenyl 2-, 5-, and 6-H), 3.86, 3.72 (2 × s, 2 × OMe + CO_2Me), and 2.95 (m, 2 × CH_2); $\nu_{max.}$ 3 255s, 1 680s, and 1 600s cm^{-1}; methyl *N*-[3-(3-methoxyphenyl])propanoyl]anthranilate (40%), m.p. 68—70 °C; δ($CDCl_3$) 11.00 br (s, exch. D_2O, NH), 8.74 (dd, *J* 8 and 1 Hz, H *ortho* to NH), 7.80 (dd, *J* 7 and 2 Hz, H *ortho* to CO_2Me), 7.35 (ddd, *J* 8, 8, and 2 Hz, H *meta* to NH), 7.1—6.6 (m, H *meta* to CO_2Me; phenyl 2-, 4-, 5-, and 6-H), 3.82, 3.75 (2 × s, OMe, CO_2Me), and 3.0 (m, 2 × CH_2); $\nu_{max.}$ 3 290s, 1 683s, and 1 595s cm^{-1}; *methyl* N-[3-(4-*methoxyphenyl*)*propanoyl*]*anthranilate* (63%), m.p. 79—80 °C (Found: C, 68.7; H, 6.1; N, 4.4. $C_{18}H_{19}NO_4$ requires C, 69.0; H, 6.1; N, 4.5%); δ($CDCl_3$) 11.00 br (s, exch. D_2O, NH), 8.69 (dd, *J* 8 and 1 Hz, H *ortho* to NH), 7.95 (dd, *J* 7 and 2 Hz, H *ortho* to CO_2Me), 7.46 (ddd, *J* 8, 8, and 2 Hz, H *meta* to NH), 7.02 (ddd, *J* 8, 7, and 1 Hz, H *meta* to CO_2Me), 6.80 (AA'BB', phenyl 2-, 3-, 5-, and 6-H), 3.81, 3.68 (2 × s, OMe, CO_2Me), and 2.6—3.0 (m, 2 × CH_2); $\nu_{max.}$ 3 265s, 1 685s, and 1 600s cm^{-1}.

Methyl N-(2-*Arylethanoyl*)*anthranilates*.—The appropriate 2-arylethanoic acid was converted into its acid chloride and treated with methyl anthranilate as described above for 3-arylpropanoic acids. Crystallisation of the solids obtained from ethanol gave the following: methyl *N*-(3-methoxyphenyl)ethanoylanthranilate (61%), m.p. 41—44 °C; δ($CDCl_3$) 10.92 br (s, exch. D_2O, NH), 8.62 (dd, *J* 8 and 1 Hz, H *ortho* to NH), 7.92 (dd, *J* 7 and 2 Hz, H *ortho* to CO_2-Me), 7.45 (ddd, *J* 8, 8, and 2 Hz, H *meta* to NH), 7.1—6.5 (m, H *meta* to CO_2Me, phenyl 2-, 4-, 5-, and 6-H), 3.78, 3.72 (2 × s, OMe, CO_2Me), and 3.68 (s, CH_2); $\nu_{max.}$ 3 235s, 1 680s, and 1 600s cm^{-1}; methyl *N*-(4-methoxyphenyl-ethanoylanthranilate (76%), m.p. 54—56 °C; δ($CDCl_3$) 10.95 br (s, NH), 8.65 (dd, *J* 8 and 1 Hz, H *ortho* to NH), 7.92 (dd, *J* 7.5 and 2 Hz, H *ortho* to CO_2Me), 7.6—6.7 (m, H *meta* to NH, H *meta* to CO_2Me, phenyl 2-, 3-, 5-, and 6-H), 3.87, 3.83 (2 × s, OMe, CO_2Me), and 3.69 (s, CH_2); $\nu_{max.}$ 3 275s and 1 675s, br cm^{-1}.

3-*Amino*-2-(2-*arylethyl*)*quinazolin*-4(3H)-*ones*.—The appropriate amide prepared as above (0.01 mol) and hydrazine hydrate (95%, 0.05 mol) were dissolved in methanol and heated under reflux overnight. Cooling in ice gave the following as colourless solids (from ethanol) 3-*amino*-2-[2-(3,4-*dimethoxyphenyl*)*ethyl*]*quinazolin*-4(3H)-*one* (4) (84%), m.p. 141—142 °C (Found: C, 64.4; H, 6.0; N, 12.8. $C_{18}H_{19}N_3O_3$ requires C, 64.45; H, 5.9; N, 12.9%); δ($CDCl_3$) 8.20 (d, *J* 8 Hz, quinaz. 5-H), 7.7—7.2 (m, quinaz. 6-, 7-, and 8-H), 6.78 (m, phenyl 2-, 5-, and 6-H), 4.76 br (s, exch. D_2O, NH_2), 3.82 (s, 2 × OMe), and 3.22 (m, 2 × CH_2); $\nu_{max.}$ 3 325s, 1 680s, 1 590s, 1 240s, 1 145m, 780s, and 690s cm^{-1}; *m/z* 325, 310, 305, 165, 151 (base), and 120.

3-*Amino*-2-[2-(3-*methoxyphenyl*)*ethyl*]*quinazolin*-4(3H)-*one* (5) (81%), m.p. 129—130 °C (Found: C, 69.1; H, 5.8; N, 14.25. $C_{17}H_{17}N_3O_2$ requires C, 69.1; H, 5.8; N, 14.2%); δ($CDCl_3$) 8.20 (d, *J* 8 Hz, quinaz. 5-H), 7.7—7.1 (m, quinaz. 6-, 7-, and 8-H), 6.8—6.6 (m, phenyl 2-, 4-, 5-, and 6-H), 4.69 br (s, exch. D_2O, NH_2), 3.72 (s, OMe), and 3.20 (m, 2 × CH_2); $\nu_{max.}$ 3 315s, 1 675s, 1 600s, 1 265s, 1 165m, 1 060m, 780s, and 690s cm^{-1}; *m/z* 295 (base), 279, 277, 264, 189, 161, 145, 137, 122, 92, and 78.

3-*Amino*-2-[2-(4-*methoxyphenyl*)*ethyl*]*quinazolin*-4(3H)-*one* (6) (90%), m.p. 139—140 °C (Found: C, 69.0; H, 5.8; N, 14.2%); δ($CDCl_3$) 8.20 (d, *J* 8 Hz, quinaz. 5-H), 7.7—7.2 (m, quinaz. 6-, 7-, and 8-H), 7.0 (AA'BB', phenyl 2-, 3-, 5-, and 6-H), 4.70br (s, exch. D_2O, NH_2), 3.73 (s, OMe), and 3.3—3.0 (m, 2 × CH_2); $\nu_{max.}$ 3 315s, 1 665s, 1 600s, 1 190m, 1 045w, 775s, and 695s cm^{-1}; *m/z* 295, 280, 263, 160, 144, 136, 121 (base), 91, and 77.

3-*Amino*-2-(2-*arylmethyl*)*quinazolin*-4(3H)-*ones*.—The corresponding amide prepared as above was heated with hydrazine hydrate (95%) in methanol as described above to give the following as colourless solids (from ethanol) 3-*amino*-2-(4-*methoxyphenyl*)*methylquinazolin*-4(3H)-*one* (14) (57%), m.p. 154—155 °C (Found: C, 68.2; H, 5.4; N, 14.95. $C_{16}H_{15}N_3O_2$ requires C, 68.3; H, 5.4; N, 14.9%); δ($CDCl_3$) 8.18 (d, *J* 8 Hz, quinaz. 5-H), 7.8—6.6 (m, 7 × ArH), 4.82 br (s, NH_2), 4.31 (s, CH_2), and 3.77 (s, OMe); $\nu_{max.}$ 3 315s, 1 685s, 1 631m, 1 613m, 1 594s, 1 018s, 779s, and 768 cm^{-1}. 3-*Amino*-2-(3-*methoxyphenyl*)*methylquinazolin*-4(3H)-*one* (15) (60%), m.p. 134—135 °C (Found: C, 68.2; H, 5.4; N, 15.1%), δ($CDCl_3$) 8.18 (d, *J* 8 Hz, quinaz. 5-H), 7.7—6.7 (m, 7 × ArH), 4.86 br (s, exch. D_2O, NH_2), 4.32 (s, CH_2), and 3.74 (s, OMe); $\nu_{max.}$ 3 285s, 1 670s, 1 600s, 1 275s, 1 060s, 795s, and 700m cm^{-1}; *m/z* 281, 266, 265 (base), 251, 236, 222, 146, 119, 90, and 77.

Oxidation of 3-*Aminoquinazolin*-4(3H)-*ones with Lead Tetra-acetate*: *General Procedure*.—The quinazolone (1 mol equiv.) was dissolved in dichloromethane (2 ml/100 mg quinazolone) and magnetically stirred at room temperature. Powdered lead tetra-acetate (1 mol equiv.) was added in small portions during 5 min, and the mixture stirred for a further 10 min. Lead diacetate was separated off and washed with dichloromethane and the filtrate evaporated under reduced pressure.

Oxidation of compound (4). The residual oil obtained from oxidation of (4) (1.2 g) using the procedure above was chromatographed on Kieselgel. Elution with light petroleum–ethyl acetate (3 : 1) gave the 13,14-*dihydro*-3,4-*dimethoxyquinazolino*[3,2-b][1,2]*benzodiazepin*-7(5H)-*one* (7), (170 mg, 14%), as colourless crystals (from ethanol), m.p. 162—164 °C (Found: C, 66.7; H, 5.3; N, 13.0. $C_{18}H_{17}N_3O_3$ requires C, 66.9; H, 5.3; N, 13.0%); δ($CDCl_3$) 9.12 br [s, exch. D_2O (slowly), NH], 8.20 (d, *J* 8 Hz, quinaz. H *ortho* to C=O), 7.7—7.2 (m, 3 × quinaz. H), 6.73, 6.57 (2 halves of AB, *J* 8.4 Hz, 2 ArH), 3.82, 4.02 (2 × s, 2 × OMe), and 3.6—3.2 (m, 2 × CH_2); irradiation of the AB system at δ 6.57 sharpened the multiplet at δ 3.3 and *vice versa*; $\nu_{max.}$ 3 270s, 1 680s, 1 600s, 1 290m, 1 180m, 1 045m, 765s, and 685w cm^{-1}; *m/z* 323 (base), 308, 280, 246, 197, 160, 120, 119, 90, and 77. Further elution with light petroleum–ethyl acetate (1 : 1) gave the 13,14-*dihydro*-2,3-*dimethoxyquinazolino*[3,2-b][1,2]*benzodiazepin*-7(5H)-*one* (8) (250 mg, 21%) as colourless crystals (from ethanol), m.p. 167—170 °C (Found: C, 66.5; H, 5.3; N, 12.9%); δ($CDCl_3$) 8.18 (d, *J* 8 Hz, quinaz. H *ortho* to C=O), 7.8—7.3 [m, NH (exch. D_2O), 3 × quinaz. H], 6.66 (s, ArH *ortho* to NH), 6.55 br (s, ArH *meta* to NH), 3.83, 3.75 (2 × s, 2 × OMe), and 3.6—3.1(m, 2 × CH_2): irradiation of the multiplet at δ 3.3 sharpened the singlet at δ 6.55; $\nu_{max.}$ 3 265s, 1 655s, 1 600s, 1 265m, 1 025m, 970w, 795s, and 685s cm^{-1}; *m/z* 323 (base), 295, 280, 246, 197, 160, 120, 119, 90, and 77. Further elution with light petroleum–ethyl acetate (1 : 1) gave 2-[2-(3,4-*dimethoxyphenyl*)*ethyl*]*quinazolin*-4(3H)-*one* (11) (250 mg, 21%) as crystals (from ethanol), m.p. 210.5—211 °C (Found: C, 69.3; H, 5.85; N, 9.0. $C_{18}H_{18}N_2O_3$ requires C, 69.65; H, 5.85; N, 9.0%); δ($CDCl_3$) 8.22 (d, *J* 8 Hz, quinaz. 5-H), 7.8—7.3 [m, NH (exch. D_2O), quinaz. 6-, 7-, and 8-H], 6.76 br (s, phenyl 2-, 5-, and 6-H), 3.80 (s, 2 × OMe), and 3.12 (m, 2 × CH_2); $\nu_{max.}$ 3 140w, 1 675s, 1 610s, 1 260m, 1 150m, 1 020m, and 775s cm^{-1}; *m/z* 310, 296, 279, 164, 160, 153 (base), 120,

119, 90, and 77. An authentic sample of the de-aminated quinazolone (11) was obtained as follows: the 3-amino-quinazolone (4) (0.2 g) was suspended in hydrochloric acid (4M; 5.5 ml) and a solution of sodium nitrite (0.33 g) in water (1.75 ml) added dropwise with stirring at room temperature. The solution was set aside overnight, neutralised with aqueous sodium hydroxide (1M), and then extracted with ethyl acetate (3 × 5 ml). The combined extracts were dried, the solvent was removed under reduced pressure, and the residual solid crystallised twice from ethanol and once from ethyl acetate to give a sample with m.p. 210—211 °C identical with that eluted above.

Oxidation of compound (5). Chromatography of the residue obtained from oxidation of (5) (0.4 g) according to the procedure above, using alumina and elution with light petroleum–ethyl acetate (2 : 1) gave the *quinazolino-benzodiazepinone* (9), (0.13 g, 32%) as colourless crystals (from ethanol), m.p. 155—157 °C (Found: C, 69.5; H, 5.2; N, 14.4. $C_{17}H_{15}N_3O_2$ requires C, 69.6; H, 5.15, N, 14.3%); δ($CDCl_3$) 9.00 br (s, exch. D_2O, NH), 8.20 (d, *J* 8 Hz, quinaz. H *ortho* to C=O), 7.7—7.2 (m, 3 × quinaz. *H*), 6.92 (dd, *J* 8 and 7 Hz, H *para* to NH), 6.70, 6.64 (dd, *J* 8, 2 and dd, *J* 7, 2 Hz respectively, 2 × H *meta* to NH), 3.97 (s, OMe), and 3.7—3.3 (m, 2 × CH_2); irradiation of the multiplet at δ 3.4 sharpened the double doublet at δ 6.64; $\nu_{max.}$ 3 260br,s, 1 680s, 1 605s, 1 265m, 1 025m, and 770m cm^{-1}; *m/z* 293 (base), 278, 265, 251, 223, 207, 160, 144, 131, 120, and 77. Further elution with ethyl acetate gave the *quinazolinobenzodiazepinone* (10) (0.11 g, 27%) as colourless crystals (from ethanol), m.p. 187—190 °C (Found: C, 69.4; H, 5.2; N, 14.4%); δ($CDCl_3$) 8.18 (d, *J* 8 Hz, quinaz. H *ortho* to C=O), 7.7—7.3 [m, NH (exch. D_2O), 3 × quinaz. H], 7.10 (m, ArH *ortho* to NH), 6.55, 6.62 (s, br and dd *J* 8 and 2 Hz respectively, 2 × ArH *meta* to NH), 3.68 (s, OMe), and 3.6—3.3 (m, 2 × CH_2); irradiation of the multiplet at δ 3.4 sharpens the singlet at δ 6.55; $\nu_{max.}$ 3 285s, 1 665s, 1 605s, 1 295m, 1 180m, and 770m cm^{-1}; *m/z* 293 (base), 278, 266, 251, 223, 207, 183, 160, 132, 120, and 77.

Further elution with ethyl acetate gave 2-[2-(3-*methoxyphenyl*)*ethyl*]*quinazolin*-4(3H)-*one* (12) (0.11 g, 27%) as colourless crystals (from ethanol), m.p. 180—181 °C (Found: C, 72.6; H, 5.8; N, 10.0. $C_{17}H_{16}N_2O_2$ requires C, 72.8; H, 5.75; N, 10.0%); δ($CDCl_3$) 8.28 (d, *J* 8 Hz, quinaz. 5-H), 7.8—7.1 [m, NH (exch. D_2O), 3 × quinaz. H], 6.80 (m, 4 × ArH), 3.74 (s, OMe), and 3.06 (m, 2 × CH_2); $\nu_{max.}$ 3 140w, 1 680s, 1 605s, 1 280m, 1 160s, 1 060s, 780s, and 690s cm^{-1}; *m/z* 280 (base), 265, 247, 173, 160, 121, 119, 91, and 77. An authentic sample of this quinazolone was obtained by de-amination of (5) as described for (4) above.

Oxidation of 3-*Amino*-2-[2-(3-*methoxyphenyl*)*ethyl*]*quinazolin*-4(3H)-*one* (5) *with Lead Tetra-acetate at Higher Dilution*.—The quinazolone (5) (200 mg) and dry lead tetra-acetate (300 mg) were powdered together in a small sample tube (*CAUTION*: this procedure has not been carried out on greater than 500 mg total solid) and then added in small portions during 6 min to chloroform (50 ml; distilled immediately prior to use from P_2O_5) with vigorous magnetic stirring. After stirring for a further 10 min, the precipitated lead di-acetate was separated off and the chloroform evaporated off under reduced pressure. Examination of the residue by n.m.r. spectroscopy showed the ratio of (10) : (9) to be 3 : 1 respectively; no other products [including the de-aminated quinazolone (12)] were present. Crystallisation of the residual solid from ethanol gave (10) (83 mg, 46%). Evaporation of the bulk of the ethanol and crystallisation again gave (9) (58 mg, 29%).

Oxidation of (6).—Using the general procedure described earlier, (6) (0.5 g) gave a tarry product from which sublimation (170 °C; 0.1 mmHg) yielded a colourless crystalline product identified as 2-[2-(4-*methoxyphenyl*)*ethyl*]*quinazolin*-4(3H)-*one* (13) (0.19 g, 38%), m.p. 210—212 °C (Found: C, 72.6; H, 5.7; N, 10.1. $C_{17}H_{16}N_2O_2$ requires C, 72.8; H, 5.75; N, 10.0%); δ($CDCl_3$) 8.28 (d, *J* 8 Hz, quinaz. 5-H), 7.7—7.2 (m, quinaz. 6-, 7-, and 8-H), 7.2—6.7 (AA'BB', phenyl 2-, 3-, 5-, and 6-H), 3.74 (s, OMe), and 3.08 (m, 2 × CH_2); $\nu_{max.}$ 3 160w, 1 680s, 1 610s, 1 260m, 1 180m, 880m, and 770s cm^{-1}; *m/z* 280, 263, 230, 173, 134, 121 (base), 120, 90, and 77.

Oxidation of Compound (15).—Removal of solvent after oxidation of (15) (0.5 g) according to the procedure described earlier gave a black tar from which sublimation (160 °C; 0.2 mmHg) yielded a white crystalline product, identified as 2-(3-*methoxyphenylmethyl*)*quinazolin*-4(3H)-*one* (17) (0.15 g, 30%), m.p. 178—180 °C (Found: C, 71.9; H, 5.3; N, 10.6. $C_{16}H_{14}N_2O_2$ requires C, 72.2; H, 5.3; N, 10.5%); δ($CDCl_3$) 8.20 (d, *J* 8 Hz, quinaz. 5-H), 7.7—7.2 [m, NH (exch. D_2O), quinaz. 6-, 7-, and 8-H), 7.2—6.7 (m, phenyl 2-, 4-, 5-, and 6-H), 4.10 (s, CH_2), and 3.70 (s, OMe); $\nu_{max.}$ 3 160w, 1 680s, 1 605s, 1 250s, 1 150m, 1 040m, 910m, 770m, and 690m cm^{-1}.

Oxidation of Compound (14).—A similar oxidation to that above using (14) (0.5 g) also gave a black tar. Sublimation (160 °C; 0.3 mmHg) gave 2-(4-methoxyphenylmethyl)-quinazolin-4(3*H*)-one (16) (0.18 g, 36%) as colourless crystals, m.p. 178—180 °C, δ($CDCl_3$) 8.20 (d, *J* 8 Hz, quinaz. 5-H), 7.7—7.3 [m, NH (exch. D_2O), quinaz. 6-, 7-, and 8-H, 7.2—6.7 (AA'BB', phenyl 2-, 3-, 5-, and 6-H), 4.00 (s, CH_2), and 3.76 (s, OMe); $\nu_{max.}$ 3 160m, 1 680s, 1 605s, 1 510s, 1 250s, 1 170m, 770s, and 690m cm^{-1}.

Oxidation of 3-*Amino*-2-[2-(3-*methoxyphenyl*)*ethyl*]*quinazolin*-4(3H)-*one* (5) *in the Presence of Styrene*.—The general procedure above was followed using (5) (0.22 g, 0.75 mmol), but with prior addition of styrene (0.39 g, 3.73 mmol) to the dichloromethane (2.2 ml) before addition of lead tetra-acetate (0.33 g, 0.75 mmol). After separation of lead di-acetate the solution was washed with saturated aqueous sodium hydrogen carbonate solution, then water, and evaporated. Excess of styrene was removed from the residual oil by trituration with light petroleum and the insoluble solid separated. Crystallisation from ethanol gave 2-[2-(3-*methoxyphenyl*)*ethyl*]-3-(2-*phenylaziridin*-1-*yl*)-*quinazolin*-4(3*H*)-*one* (24) (47%), as pale yellow crystals, m.p. 131—133 °C (Found: C, 75.55; H, 5.8; N, 10.6. $C_{25}H_{23}N_3O_2$ requires C, 75.55; H, 5.8; N, 10.6%); δ($CDCl_3$) 8.20 (d, *J* 8 Hz, quinaz. 5-H), 7.7—7.0 (m, 10 × ArH), 6.6—6.4 (m, 2 × ArH), 3.66 (s, OMe; + dd, *J* 7.5 and 6 Hz, C*H*Ph), 3.0—3.2 (m, $[CH_2]_2$, azir. H *trans* to Ph), and 2.85 (dd, *J* 6 and 2 Hz, azir. H *cis* to Ph); $\nu_{max.}$ 1 680s, 1 595s, 1 260m, 1 030m, 770s, and 690s cm^{-1}; *m/z* 397, 305, 293, 280, 279 (base), 260, 186, 173, 160, 121, 104, and 91.

Oxidation of 3-*Amino*-2-[2-(4-*methoxyphenyl*)*ethyl*]*quinazolin*-4(3H)-*one* (6) *in the Presence of Styrene*.—The oxidation was carried out as in the previous experiment using (6) (0.5 g, 1.7 mmol), styrene (0.53 g, 5.1 mmol), dichloromethane (5 ml), and lead tetra-acetate (0.75 g, 1.7 mmol). Trituration with ether of the residual oil obtained after removal of solvents gave the *aziridine* (25) (0.38 g, 56%), m.p. 138.5—140 °C (from acetonitrile) (Found: C, 75.5; H, 5.9; N, 10.7%); δ($CDCl_3$) 8.20 (d, *J* 8 Hz, quinaz.

5-H), 7.7—7.2 (m, 3 × ArH), 6.78 (AA'BB', 4 × ArH), 3.76 (s, OMe; + dd, *J* 7.5 and 6 Hz, C*H*Ph), 3.18 (m, 2 × CH_2; + dd, *J* 7.5 and 2.5 Hz, azir. H *trans* to Ph), and 2.86 (dd, *J* 6 and 2.5 Hz, azir. H *cis* to Ph); $\nu_{max.}$ 1 670s, 1 600m, 1 500m, 1 245m, 1 030m, and 770s cm^{-1}; *m/z* 397, 306, 293, 280, 263, 160, 134, 121 (base), 104, 91, and 77.

Oxidation of 3-Amino-2-(4-methoxyphenylmethyl)quinazolin-4(3H)-one (14) *in the Presence of Styrene*.—The oxidation was carried out as above using (14) (0.4 g), styrene (0.45 g), chloroform (3 ml), and lead tetra-acetate (0.63 g). Trituration with ether of the residual oil obtained after removal of solvents gave the *aziridine* (26) (0.17 g, 31%), m.p. 146—148 °C (from ethanol) (Found: C, 75.1; H, 5.55; N, 10.9. $C_{24}H_{21}N_3O_2$ requires C, 75.2; H, 5.5; N, 10.95%); δ(CD_3COCD_3) 8.08 (d, *J* 8 Hz), 7.8—6.7 (m, 12 × ArH), 4.3 (s, CH_2), 4.04 (dd, *J* 7.5 and 5.5 Hz, C*H*Ph), 3.75 (s, OMe), 3.23 (dd, *J* 7.5 and 2 Hz, azir. H *trans* to Ph), and 2.91 (dd, *J* 5.5 and 2 Hz, azir. H *cis* to Ph); $\nu_{max.}$ 1 662s, 1 591s, 1 244m, 776s, and 766 cm^{-1}.

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