The Chemistry of Nitro-compounds. Part II.[1] The Scope and Mechanism of the Base-catalysed Transformations of Some *NN*-Disubstituted *o*-Nitrobenzamides

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In reactions explicable by the intermediate formation of 2-cyanoquinazolone *N*-oxides (2), hot ethanolic sodium ethoxide converts the *N*-cyanomethyl-*o*-nitrobenzamides (1a—c) in high yield into the *N*-hydroxyquinazolinediones (3a—c). In contrast, treatment of the *N*-benzoylmethyl-amide (6a) or the *N*-ethoxycarbonylmethyl-amide (6b) with ethanolic sodium ethoxide affords the indazolone (13a). The indazolones (13a and b) are formed under similar conditions from the *N*-α-cyanoethyl-amides (8a and b). On the other hand, hot aqueous ethanolic sodium carbonate converts the amide (8a) into a mixture of the indazolone (13a) and *NN'*-diphenylazobenzene-2,2'-dicarboxamide (15a); similar treatment of the amide (8b) affords the corresponding azoxybenzene derivative (16b) and benzaldehyde 2-carboxyphenylhydrazone (20). Mechanisms for the base-catalysed transformations of the amides (6a and b) and (8a and b) are discussed.

THE base-catalysed cyclisation of α-substituted *o*-nitroacetanilides provides valuable synthetic routes to otherwise inaccessible heterocyclic *N*-oxides.[2] These reactions exemplify a type of cyclisation in which an aromatic nitro-group functions as the electrophilic centre in an intramolecular aldol-type condensation.[3] In such reactions condensation may involve the intact nitro-group or may be preceded by rearrangement to an *aci*-nitro-tautomer. *aci*-Nitro intermediates have been postulated in certain photochemical,[4] thermal,[5] and acid-catalysed[6] cyclisations of *o*-nitrobenzene derivatives. On the other hand, unequivocal support for the alternative mode of condensation, involving the intact nitro-group, is almost entirely lacking. Indirect evidence is provided by the base-catalysed cyclisations of *N*-cyanomethyl-*o*-nitrobenzamide to 2-alkoxy-1-hydroxyquinazolones,[7] reactions which cannot involve *aci*-nitro-intermediates. However, the precise course of these reactions is made uncertain by the low yields of cyclised products and by the intervention of side reactions, features which can be attributed[7] to the presence of the NH group in the side chain. We now report a study † of the base-catalysed reactions of *NN*-disubstituted *o*-nitrobenzamides which lack the offending NH group. The products of these reactions are explicable only on the basis of direct condensation between the unmodified nitro-group and the methylene centre in the *ortho*-side-chain.

The amides studied [(1a—c), (6a and b), and (8a—c)] were prepared in satisfactory yield by the base-catalysed condensation of *o*-nitrobenzoyl chloride with the appropriate amino-compounds. Sodium acetate in acetic acid proved to be a suitable catalyst for the preparation of the amides (1a—c) and (6a and b) but failed to catalyse the formation of the methyl derivatives (8a—c) and (8; R = H). These compounds were eventually obtained in moderate yield by carrying out the condensation in the presence of an excess of the amino-component, which also functions as the catalyst. When heated under reflux with ethanolic sodium ethoxide, the amides (1a—c) were converted in excellent yield (70—90%) into acidic products assigned the structures (3a—c) on the basis of the following evidence. Their i.r. spectra lacked bands due to a cyano-group or a nitro-group but contained broad absorption at *ca.* 2700 cm^{-1} and carbonyl bands at 1700 and *ca.* 1650 cm^{-1} attributable to the 1-hydroxyquinazoline-2(1*H*),4(3*H*)-dione nucleus.[7] They dissolved unchanged in aqueous sodium hydrogen carbonate and gave deep red solutions with iron(III) chloride,[7,8] and in further support of their cyclic hydroxamic acid structures they afforded monoacetyl derivatives (4a—c) showing carbonyl i.r. absorption at 1800 cm^{-1} (cyclic :N·OAc).[7,8] Dithionite reduction of the *N*-hydroxy-compounds (3a—c) or hydrogenolysis of the derived acetoxy-derivatives (4a—c) yielded the known[9-11] quinazolinediones (5a—c), which were identical with samples synthesised by condensing the appropriate *N*-substituted *o*-aminobenzamide derivative with urea.

The base-catalysed conversions of the amides (1a—c) into the *N*-hydroxyquinazolinediones (3a—c) can be rationalised by a course [(1) ⟶ (2) ⟶ (3)] involving a direct aldol condensation across space between the nitro-group and the methylene centre in the *ortho*-side-chain. The observed products (3) are then plausibly explained by loss of cyanide ion (see Scheme) from hydrates (21a) produced by nucleophilic attack by hydroxide ion (liberated in the initial ring-forming step) at the reactive 2-position in the initially formed 2-cyanoquinazolone *N*-oxides (2). The detection of free cyanide ion in the reaction mixtures and the readiness

† Preliminary account, *Chem. Comm.*, 1969, 195.

[1] T. W. M. Spence and G. Tennant, *J. Chem. Soc.* (*C*), 1971, 3712.

[2] G. Tennant, *J. Chem. Soc.* (*C*), 1966, 2285, and references cited therein; R. Fusco and S. Rossi, *Gazzetta*, 1964, **94**, 3.

[3] J. D. Loudon and G. Tennant, *Quart. Rev.*, 1964, **18**, 389.

[4] P. de Mayo and S. T. Reid, *Quart. Rev.*, 1961, **15**, 393.

[5] G. V. Garner and H. Suschitzky, *Tetrahedron Letters*, 1971, 169, and references cited therein.

[6] R. Fielden, O. Meth-Cohn, D. Price, and H. Suschitzky, *Chem. Comm.*, 1969, 772.

[7] G. Tennant and K. Vaughan, *J. Chem. Soc.* (*C*), 1966, 2287.

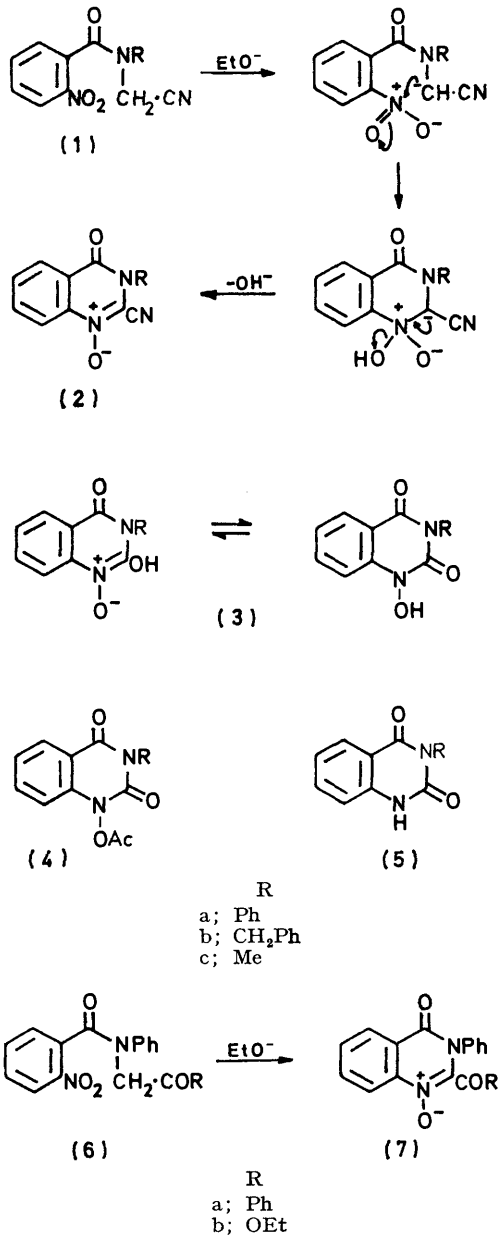
[8] J. D. Loudon and I. Wellings, *J. Chem. Soc.*, 1960, 3470.

[9] W. Abt, *J. prakt. Chem.*, 1889, **39**, 140.

[10] T. Kappe, W. Steiger, and E. Ziegler, *Monatsh.*, 1967, **98**, 214; R. P. Staiger and E. C. Wagner, *J. Org. Chem.*, 1953, **18**, 1427.

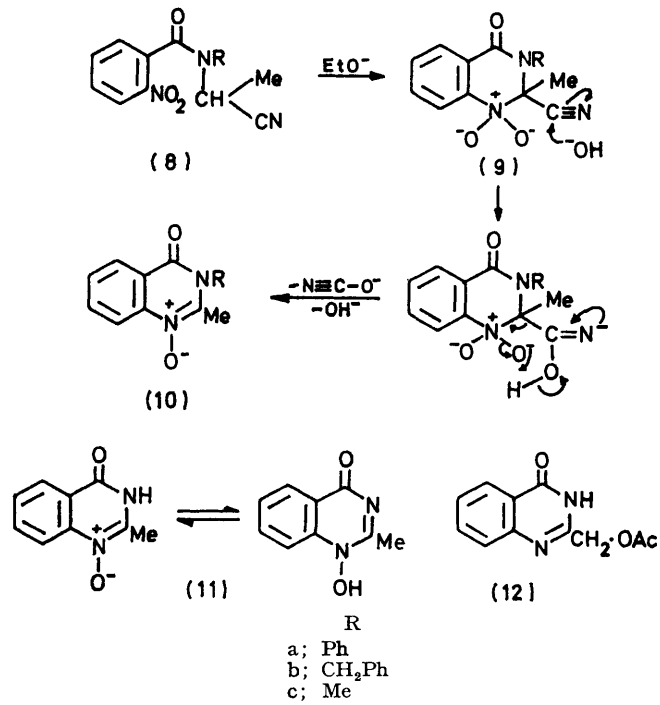
[11] B. Taub and J. B. Hino, *J. Org. Chem.*, 1961, **26**, 5238.

with which the cyano-group in 2-cyanoquinazolines [12] undergoes nucleophilic displacement, lend support to



this mechanism. Attempts to isolate the proposed *N*-oxide intermediates (2) were unsuccessful, however. Thus, treatment of the amide (1a) with various basic catalysts under a variety of conditions either failed to effect condensation or yielded the *N*-hydroxyquinazolone (3a) in high yield. The enhanced yields of cyclised products obtained from the amides (1a—c) compared with the low yields obtained from the amide (1; R = H) [7] can be attributed to the absence of an enolisable centre in the side chain and consequently the greater methylene reactivity of the former compounds.

The base-catalysed transformations of the amides (6a and b) were next studied in an attempt to obtain more definite evidence for the intermediate formation of quinazoline *N*-oxides. It was hoped that, in contrast to the cyano-compounds (2), the primary products (7a and b) of aldol condensation in the amides (6a and b) would now be stable enough to permit their isolation. In practice, heating the amides (6a and b) with ethanolic sodium ethoxide yielded in both cases the same acidic

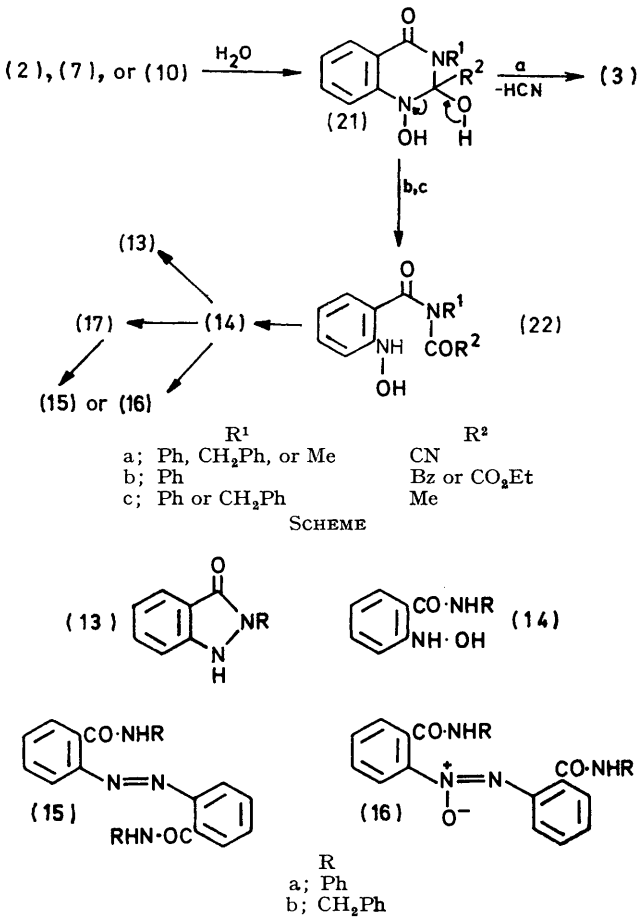


product, which gave analytical data consistent with the formula $C_{13}H_{10}N_2O$. Comparison with a sample synthesised unambiguously by reductive cyclisation of *o*-nitrobenzanilide in alkaline solution, identified this compound as 2-phenylindazolone (13a). The transformation of the amides (6a and b) into this product can be explained by courses (see Scheme) leading to the formation and cyclisation of the common intermediate *o*-hydroxyamino-*N*-phenylbenzamide (14a). The intermediate formation and base-catalysed cyclisation of the latter compound is implicit in the reduction of *o*-nitrobenzanilide in alkaline solution to the indazolone (13a). Ring opening of hydrates (21b) derived from quinazolone *N*-oxide intermediates (7a and b) and subsequent deacylation of the compounds (22b) formed then accounts for the conversion of the amides (6a and b) into the hydroxyamino-derivative (14a). An alternative course, based on the prior deacylation [13] of the acylquinazolones (7a and b) to the *N*-oxide (7; H for COR) is less likely since the corresponding hydrate (21b; H for Bz or CO_2Et) would be expected to be partly diverted by dehydration to 3-phenylquinazoline-2(1*H*),4(3*H*)-dione (5a) none of which could be detected in the reaction mixtures.

[12] E. Hayashi and T. Higashino, *Chem. and Pharm. Bull.* (*Japan*), 1964, **12**, 43 (*Chem. Abs.*, 1964, **60**, 9278); R. G. Shepherd and J. L. Fedrick, *Adv. Heterocyclic Chem.*, 1965, **4**, 373.

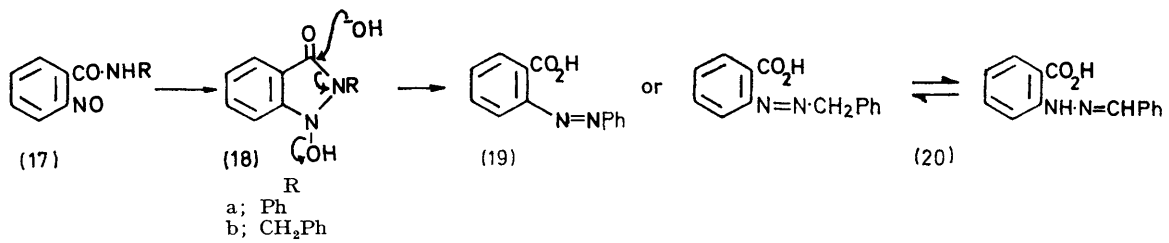
[13] G. Tennant, *J. Chem. Soc.*, 1963, 2428.

Further support for the presence of hydroxyamino-intermediates in the foregoing reactions was provided by the study of the base-catalysed transformations of



SCHEME

the methyl-substituted amides (8a—c). These compounds were chosen initially in the expectation that, despite the lower methylene reactivity, condensation would still take place to afford adducts (9) convertible by loss of the cyano-group into 2-methylquinazolone *N*-oxides (10). It was anticipated that these compounds would be sufficiently deactivated at the 2-position to inhibit their further transformation in the basic medium. In fact, the amide (8a) was converted by hot ethanolic sodium ethoxide into the indazolone (13a). The benzyl derivative (8b) similarly afforded 2-benzylindazolone [14] (13b), which was identified by its synthesis from *N*-benzyl-*o*-nitrobenzamide by reductive cyclisation. In contrast, the *N*-methyl compound (8c) was rapidly decomposed by hot ethanolic sodium ethoxide affording low yields of unidentified gums. Ring opening of hydrates (21c) derived from initially formed 2-methylquinazolone *N*-oxide intermediates (10a and b), followed by deacylation and subsequent cyclisation of the resulting *o*-hydroxyaminobenzamides (14a and b) accounts for indazolone formation from the amides (8a and b) (see Scheme). The intermediate formation of the *N*-oxides (10a and b) is supported by the conversion of the amide (8; R = H) in hot ethanolic sodium ethoxide into the tautomeric *N*-hydroxyquinazolone (11). The structure assigned to this product follows from its spectral properties and from its conversion in acetic anhydride into the known [15] acetoxymethylquinazolone (12). The stability of the compound (11) compared with the apparent instability of the proposed *N*-oxide intermediates (10a and b) is presumably associated with the additional deactivation of the 2-position towards nucleophilic attack, caused by enolisation of the adjacent amide group. Formation of the quinazolone (11) and of the intermediate *N*-oxides (10a and b) requires the loss of the cyano-group from an initially formed aldol condensate (9). Related transformations involving the loss of a cyano-group are known [3] but information on the mechanism of such processes is lacking. One possibility is that the cyano-group is eliminated in the form of isocyanate ion as shown [see (9) ⟶ ⟶ (10)]. The cyclisation of the *o*-hydroxyaminobenzamides (14a and b) to the indazolones (13a and b) is implicit in the formation of these compounds by reduction of *N*-benzyl-*o*-nitrobenzamide and *o*-nitrobenzanilide, thereby lending support to the role of the compounds (14a and b) as intermediates in the ethoxide-catalysed reactions of the amides (8a and b) (see Scheme). In support of this contention, hot aqueous ethanolic sodium carbonate converted the *N*-phenyl compound (8a) into a mixture of the indazolone (13a) and the azobenzene derivative (15a). The latter product was identified with a sample



prepared by condensing *o*-aminobenzamide with *o*-nitrosobenzanilide (17a),[16] and its formation from the amide (8a) indicates the presence in the reaction mixture of the hydroxyamino-derivative (14a). In contrast, the reaction of the benzyl compound (8b) with aqueous ethanolic sodium carbonate afforded a mixture of the known [14] hydrazone (20) and the azoxy-amide (16b).

[14] E. Fischer and R. Blochmann, *Ber.*, 1902, **35**, 2315.
[15] G. Tennant, unpublished work.
[16] F. Sachs and R. Kempf, *Ber.*, 1902, **35**, 2704.

The latter was identical with the product of the peroxy-acid oxidation of the azo-derivative (15b) obtained as a by-product in the reduction of *N*-benzyl-*o*-nitrobenzamide. The isolation of the azoxy-amide (16b) requires the additional presence in the reaction mixture of the nitroso-amide (17b) formed by mild oxidation of the corresponding hydroxylamine (14b). The oxidation of phenylhydroxylamines to nitrosobenzene derivatives in aqueous alkaline solution is well known.[17] Also, cyclisation of the nitroso-amide (17b) to the 1-hydroxyindazolone (18b) followed by ring scission accounts for the formation of the hydrazone (20). This course finds analogy in the base-catalysed scission [18] of 1-hydroxyindolinones to *N*-acylanthranilic acids, and was further substantiated by the demonstration that *o*-nitrosobenzanilide (17a) [16] (available from the photochemical rearrangement of *o*-nitrobenzylideneaniline) is converted in high yield into azobenzene-2-carboxylic acid (19) by treatment with aqueous sodium carbonate. Additionally, heating *o*-nitrosobenzanilide (17a) with aqueous ethanolic sodium hydroxide gave 2-phenylindazolone (13a), implying the intermediate formation and reduction of a 1-hydroxyindazolone intermediate (18a). However, the possibility that this reaction proceeds by initial reduction to the hydroxylamine (14a) followed by cyclisation (see before) cannot be excluded.

EXPERIMENTAL

I.r. spectra were recorded for Nujol suspensions with a Unicam SP 200 instrument. Molecular weights were measured with an A.E.I. MS 902 mass spectrometer.

Light petroleum had b.p. 60—80°. Alumina was Spence type H.

Unless otherwise stated, chloroform extracts were washed (aqueous sodium hydrogen carbonate, water) and dried ($MgSO_4$) prior to evaporation under reduced pressure.

Preparation of Amino-compounds.—A solution of sodium hydrogen sulphite (26·0 g) and acetaldehyde (11·0 g) in water (200·0 ml) was stirred at room temperature for 30 min and was then treated dropwise with stirring with aqueous 27·5% methylamine (28·0 g) or benzylamine (26·8 g). The mixture was stirred at 60—70° for 2 h, solid potassium cyanide (18·0 g) was added, and stirring was continued at 40° for a further 2 h. The oil which separated was recovered in chloroform and distilled to afford α-methylaminopropiononitrile (47%), b.p. 74° at 36 mmHg (lit.,[19] 78° at 34 mmHg) or α-benzylaminopropiononitrile (82%), b.p. 125° at 18 mmHg (lit.,[20] 137° at 18 mmHg).

Other amino-compounds were prepared by methods adequately described in the literature; anilinoacetonitrile (54%) had m.p. 45° (lit.,[21] 48°); α-anilinopropiononitrile (83%), had m.p. 91° (lit.,[22] 92°); benzylaminoacetonitrile hydrochloride (52%), had m.p. 168° (lit.,[23] 171°). α-Aminopropiononitrile was obtained as an oil and was used without further purification. It was characterised as the hydrochloride, m.p. 110° (lit.,[24] 117°); methylaminoacetonitrile hydrochloride was commercially available and was used without further purification.

Ethyl *N*-phenylglycine (68%) had m.p. 57° (lit.,[25] 58°); 2-anilinoacetophenone (79%) had m.p. 99° (lit.,[26] 93°).

NN-*Disubstituted* o-*Nitrobenzamides* (1a—c), (6a and b), (8a—c), *and* (8; R = H).—*Method* (*A*). A slurry of fused sodium acetate (11·3 g) in glacial acetic acid (68·0 ml) was stirred and treated in one portion at room temperature with methylaminoacetonitrile hydrochloride, benzylaminoacetonitrile hydrochloride, ethyl *N*-phenylglycine, or 2-anilinoacetophenone (0·03 mol), and then dropwise with *o*-nitrobenzoyl chloride (5·6 g, 0·03 mol). The mixture was stirred at room temperature for 3 h, evaporated under reduced pressure, and treated with water to yield the crude amide.

Method (*B*). Solutions of α-aminopropiononitrile and α-benzylaminopropiononitrile (0·06 mol) in anhydrous benzene (60·0 ml) were stirred and treated dropwise at room temperature with a solution of *o*-nitrobenzoyl chloride (0·03 mol) in anhydrous benzene (40·0 ml). The mixtures were stirred at room temperature for 48 h, then filtered, and the solids were washed with chloroform. Evaporation of the combined benzene filtrate and chloroform washings gave the oily amides, which solidified directly in contact with benzene–light petroleum, or after chromatography over alumina.

Method (*C*). α-Methylaminopropiononitrile or α-anilinopropiononitrile (0·02 mol) was heated with *o*-nitrobenzoyl chloride (1·9 g, 0·01 mol) at 100° for 10 min. The mixture was cooled, treated with water, and extracted with chloroform to yield the crude amide.

Method (*D*). A mixture of fused sodium acetate (19·0 g) and anilinoacetonitrile (6·6 g) in anhydrous benzene (113·0 ml) was treated dropwise with *o*-nitrobenzoyl chloride (9·3 g) and heated under reflux for 2 h. The oil obtained by evaporating the mixture was treated with water and extracted into chloroform. Evaporation of the chloroform extract gave an oil which crystallised on cooling to afford the crude amide.

The crude *NN*-disubstituted *o*-nitrobenzamides prepared by methods (A)—(D) were purified by crystallisation from methanol or ethanol; $\nu_{max.}$ 1660—1640 (CO) and 1530 and 1350 (NO_2) cm^{-1}. Yields, m.p.s, and analytical data are shown in the Table.

1-*Hydroxyquinazoline*-2(1H),4(3H)-*diones* (3a—c).—Solutions of the amides (1a—c) (0·01 mol) in absolute ethanol (25·0 ml) were heated under reflux with a solution of sodium (0·92 g) in absolute ethanol (25·0 ml) for 1 h. The salt, obtained by evaporating the mixture under reduced pressure, was dissolved in water, washed (chloroform), acidified (dilute aqueous sulphuric acid), and extracted with chloroform to afford the N-*hydroxyquinazolinediones*, $\nu_{max.}$ 3100sh and 2700sh (OH), and 1700 and 1670—1640 (CO) cm^{-1}. *Product* (3a) (76%) had m.p. 180° (from methanol) (Found: C, 65·8; H, 4·0; N, 11·3. $C_{14}H_{10}N_2O_3$ requires C, 66·1; H, 3·9; N, 11·0%); *product* (3b) (85%) had m.p. 237° (from glacial acetic acid) (Found: C, 67·4; H, 4·7; N, 10·4. $C_{15}H_{12}N_2O_3$ requires C, 67·2; H, 4·5; N, 10·4%); and product (3c) (93%) had m.p. 240° (from

[17] E. Bamberger, *Ber.*, 1894, **27**, 1548.
[18] G. Heller and W. Boessneck, *Ber.*, 1922, **55**, 474.
[19] P. L. DeBenneville, U.S.P. 2,743,291 (*Chem. Abs.*, 1956, **50**, 16,826).
[20] A. L. Langis and M. G. P. Stegen, U.S.P. 3,202,674 (*Chem. Abs.*, 1965, **63**, 14,872).
[21] E. Knoevenagel, *Ber.*, 1904, **37**, 4073.
[22] F. Tiemann and R. Stephan, *Ber.*, 1882, **15**, 2034.
[23] W. Baker, W. D. Ollis, and V. D. Poole, *J. Chem. Soc.*, 1949, 307.
[24] N. Zelinsky and G. Stadnikoff, *Ber.*, 1908, **41**, 2061.
[25] P. J. Mayer, *Ber.*, 1875, **8**, 1152.
[26] A. Bischler, *Ber.*, 1892, **25**, 2860; R. Mohlau, *ibid.*, 1881, **14**, 171.

methanol) (lit.,[27] 245°) (Found: C, 56·5; H, 4·5; N, 14·6. Calc. for $C_9H_8N_2O_3$: C, 56·3; H, 4·2; N, 14·6%). They dissolved in aqueous sodium hydrogen carbonate and were recovered (quantitatively) on acidification, and gave deep red solutions with iron(III) chloride in ethanol.

The *N*-hydroxyquinazolinedione (3c) was also obtained (85—95%) (*a*) by heating the amide (1c) under reflux with 10% w/v ethanolic or aqueous sodium or potassium hydroxide for 30 min, or (*b*) by stirring the amide (1c) with ethanolic sodium ethoxide at room temperature for 30 min; the mixtures were worked up as described before. The amide (1c) was unchanged (recovery 94%) after being heated under reflux (1 h) with piperidine in ethanol.

1-*Acetoxyquinazoline*-2(1H),4(3H)-*diones* (4a—c).—The appropriate *N*-hydroxyquinazolinedione (3a—c) (0·001 mol) was warmed on a steam-bath with acetic anhydride (0·5 ml) until the suspended solid dissolved. The solution was heated for a further 30 min and the excess of acetic anhydride was removed by evaporation under reduced pressure. The solid obtained was crystallised to yield the *acetoxy-derivative*, $\nu_{max.}$ 1800—1790 (cyclic :N·OAc), and 1720 and 1680—1670 (CO) cm^{-1}. *Product* (4a) (93%) had m.p. 202° (from ethanol) (Found: C, 65·0; H, 4·0; N, 9·6. $C_{16}H_{12}N_2O_4$ requires C, 64·9; H, 4·1; N, 9·5%); *product* (4b) (90%) had m.p. 151° (from benzene–light petroleum) (Found: C, 65·2; H, 4·4; N, 9·3. $C_{17}H_{14}N_2O_4$ requires C, 65·8; H, 4·5; N, 9·0%); and *product* (4c) (92%) had m.p. 132° (from benzene–light petroleum) (Found: C, 56·5; H, 4·6; N, 11·8. $C_{11}H_{10}N_2O_4$ requires C, 56·4; H, 4·3; N, 12·0%).

Quinazoline-2(1H),4(3H)-*diones* (5a—c).—The quinazolinediones (5a—c) were obtained (70—90%) (*a*) by heating the *N*-hydroxyquinazolinediones (3a—c) (0·001 mol) under reflux in 70% v/v aqueous ethanol (20·0 ml) with twice their weight of dithionite for 1 h or (*b*) by hydrogenating the acetoxy-compounds (4a—c) in ethanol over 10% palladium–charcoal. Crystallisation of the solids isolated by evaporating the filtered mixtures afforded the pure quinazolinediones: (5a), m.p. 282° (from methanol) (lit.,[11] 281°), (5b), m.p. 229° (from methanol) (lit.,[10] 227°), and (5c), m.p. 235° (from methanol) (lit.,[9] 234°), $\nu_{max.}$ 3100sh and 2700sh (OH) and 1725—1710 and 1665—1660 (CO) cm^{-1}, which were identical (mixed m.p. and i.r. spectrum) with samples synthesised as described in (*c*).

(*c*) Intimate mixtures of urea (0·01 mol) with *o*-aminobenzanilide,[28] *o*-amino-*N*-benzylbenzamide,[29] and *o*-amino-*N*-methylbenzamide [30] (0·01 mol) were heated (1—1·5 h) at 200° (oil-bath) until the evolution of ammonia had ceased. The dark melts were cooled and crystallised from methanol to yield the quinazolinediones: (5a) (77%), (5b) (52%), and (5c) (34%), which were identical (m.p., mixed m.p., and i.r. spectrum) with samples prepared in (*a*) and (*b*).

1-*Hydroxy*-2-*methylquinazolin*-4-(1H)-*one* (11).—A solution of the amide (8; R = H) (0·44 g) in absolute ethanol (30·0 ml) was heated under reflux with a solution of sodium (0·18 g) in absolute ethanol (10·0 ml) or with a solution of sodium hydroxide (0·32 g) in water (3·2 ml) for 1 h. The mixture was concentrated under reduced pressure and diluted with water. The acidified (dilute aqueous sulphuric acid) solution was washed with chloroform to remove unchanged amide (0·05 g), neutralised, and extracted with chloroform to afford the N-*hydroxyquinazolone* (11) (0·14 g), m.p. 247° (from dimethylformamide), $\nu_{max.}$ 2600br and 2150br (OH) and 1615—1600 (CO) cm^{-1} (Found: C, 61·4; H, 4·4; N, 16·6. $C_9H_8N_2O_2$ requires C, 61·4; H, 4·6; N, 15·9%), which gave a deep red colour with iron(III) chloride in ethanol. Heated under reflux (5 min) with acetic anhydride, the *N*-hydroxyquinazolone (11) afforded the acetoxymethylquinazolone (12), m.p. 198° (from ethanol) (lit.,[15] 198°), $\nu_{max.}$ 3150—2700br (OH) and 1750 and 1680 (CO) cm^{-1}, which was identical (mixed m.p. and i.r. spectrum) with an authentic sample.[15]

NN-Disubstituted *o*-nitrobenzamides

	Method	Yield (%)	M.p. (°C)	Found (%) C	Found (%) H	Found (%) N	Formula	Required (%) C	Required (%) H	Required (%) N
(1a)	D	69	101	63·6	4·1	14·9	$C_{15}H_{11}N_3O_3$	64·1	3·9	14·9
(1b)	A	71	113	64·6	4·7	14·2	$C_{16}H_{13}N_3O_3$	65·1	4·4	14·2
(1c)	A	76	113	54·7	4·2	19·3	$C_{10}H_9N_3O_3$	54·8	4·1	19·2
(6a)	A	52	124	69·5	4·6	8·0	$C_{21}H_{16}N_2O_4$	70·0	4·5	7·8
(6b)	A	66	108	62·4	5·0	8·9	$C_{17}H_{16}N_2O_5$	62·2	4·9	8·5
(8a)	C	56	136	65·2	5·1	14·2	$C_{16}H_{13}N_3O_3$	65·1	4·4	14·2
(8b)	B	58	92	65·7	4·7	13·8	$C_{17}H_{15}N_3O_3$	66·0	4·9	13·6
(8c)	C	74	158	56·5	4·8	18·2	$C_{11}H_{11}N_3O_3$	56·7	4·7	18·0
(8; R = H)	B	31	110	55·0	4·2	19·1	$C_{10}H_9N_3O_3$	54·8	4·1	19·2

Base-catalysed Reactions of the NN-*Disubstituted* o-*Nitrobenzamides* (8a—c).—(*a*) The amide (8a or b) (0·002 mol) in absolute ethanol (15·0 ml) was heated under reflux with a solution of sodium (0·18 g) in absolute ethanol (10·0 ml) for 1 h. Removal of the solvent under reduced pressure gave a semi-solid which was dissolved in water, washed (chloroform), acidified (dilute aqueous sulphuric acid), and extracted with chloroform to afford the indazolone: (13a) (76%), m.p. 206° (from benzene) (lit.,[31] 212°); (13b) (66%), m.p. 179° (from ethanol) (lit.,[14] 180°), identical (mixed m.p. and i.r. spectrum) with samples prepared as described later.

(*b*) A solution of the amide (8a) (2·7 g) in ethanol (130·0 ml) was heated under reflux with aqueous N-sodium carbonate (70·0 ml) for 1 h. The mixture was evaporated under reduced pressure, treated with water, and extracted with chloroform. The red semi-solid recovered by evaporating the chloroform extract was chromatographed over alumina: 1 : 1 benzene–ether successively eluted unchanged amide (8a) (1·1 g) and NN′-*diphenylazobenzene*-2,2′-*dicarboxamide* (15a) (0·4 g), m.p. 262° (decomp.) (from glacial acetic acid), $\nu_{max.}$ 3300 (NH) and 1650 (CO) cm^{-1} (Found: C, 73·8; H, 5·0; N, 13·6%; M^+, 420. $C_{26}H_{20}N_4O_2$ requires C, 74·3; H, 4·8; N, 13·3%; *M*, 420), which was identical (mixed m.p. and i.r. spectrum) with a sample

[27] L. Capuano and W. Ebner, *Chem. Ber.*, 1969, **102**, 1480.
[28] H. Kolbe, *J. prakt. Chem.*, 1884, **30**, 467.
[29] R. H. Clark and E. C. Wagner, *J. Org. Chem.*, 1944, **9**, 55.
[30] A. Weddige, *J. prakt. Chem.*, 1887, **36**, 141.
[31] G. Heller, *Ber.*, 1916, **49**, 2751.

synthesised later. Further elution, with 1 : 1 ether–chloroform gave the indazolone (13a) (0·27 g), m.p. 206° (from benzene), identical (mixed m.p. and i.r. spectrum) with a sample prepared later.

(*c*) The amide (8b) (0·6 g) was heated under reflux (1 h) with aqueous N-sodium carbonate (8·0 ml) in ethanol (50·0 ml). The oil obtained by evaporating the mixture under reduced pressure was treated with water and chloroform, and the deep red aqueous layer was set aside. The oil obtained from the chloroform layer was chromatographed over alumina; 1 : 1 benzene–chloroform eluted unchanged amide (8b) (0·09 g) followed by NN′-*dibenzyl-azoxybenzene-2,2′-dicarboxamide* (16b) (0·23 g), m.p. 172° (from ethanol), $\nu_{max.}$ 3300 (NH) and 1640 (CO) cm^{-1} (Found: C, 72·3; H, 5·4; N, 12·5%; M^+, 464. $C_{28}H_{24}N_4O_3$ requires C, 72·4; H, 5·2; N, 12·1%; *M*, 464), identical (mixed m.p. and i.r. spectrum) with a sample synthesised later.

Acidification of the dark red aqueous phase (see before) and extraction with chloroform yielded the hydrazone (20) (0·16 g), m.p. and mixed m.p. 228° (from benzene) (lit.,[14] 228°), $\nu_{max.}$ 3300 (NH), 3150sh and 2700br (OH), and 1670 (CO) cm^{-1}, i.r. spectrum identical with that of an authentic sample.[14]

(*d*) The amide (8c), warmed with ethanolic sodium ethoxide or sodium carbonate as described in (*a*) and (*b*), gave low yields of unidentified gums.

2-*Phenylindazolone* (13a).—(*a*) Solutions of the amides (6a and b) (0·01 mol) in absolute ethanol (30·0 ml) were heated under reflux (1 h) with solutions of sodium (1·4 g) in absolute ethanol (20·0 ml). The mixtures were worked up as described before to afford the indazolone (13a) (50%), which was identical (m.p., mixed m.p., and i.r. spectrum) with a sample synthesised in (*c*).

(*b*) A suspension of *o*-nitrosobenzanilide (17a) (0·06 g) in ethanol (2·0 ml) was heated on a steam-bath for 10 min with a solution of sodium hydroxide (0·05 g) in water (0·5 ml). Acidification of the diluted and filtered mixture gave the indazolone (13a) (0·05 g), which was identified by comparison (m.p. and i.r. spectrum) with a sample synthesised as described in (*c*).

(*c*) Solutions of *o*-nitro-*N*-phenylbenzamide[32] (4·8 g) in methanol (50·0 ml) and sodium hydroxide (3·3 g) in water (75·0 ml) were mixed, treated with zinc dust (2·7 g) and heated under reflux for 13 h. The mixture was filtered hot to remove inorganic material, concentrated, and diluted with water. The solution obtained was cooled in ice, filtered to remove unchanged *o*-nitro-*N*-phenylbenzamide (0·76 g), and acidified (dilute aqueous sulphuric acid). Extraction with chloroform gave the indazolone (13a) (1·6 g), needles, m.p. 206° (from benzene) (lit.,[31] 212°), $\nu_{max.}$ 3050sh and 2700sh (NH) and 1640br (CO) cm^{-1} (Found: C, 74·2; H, 5·1; N, 13·2. Calc. for $C_{13}H_{10}N_2O$: C, 74·3; H, 4·8; N, 13·3%), which was further characterised by conversion in warm acetic anhydride into the monoacetyl derivative (13a; Ac for H), m.p. 90° (from light petroleum) (lit.,[33] 91°), $\nu_{max.}$ 1700br (CO) cm^{-1}.

[32] W. B. Van Horssen, *Rec. Trav. chim.*, 1936, **55**, 245.
[33] K. Auwers, *Ber.*, 1896, **29**, 1255.
[34] R. Anet and S. Somasekhara, *Canad. J. Chem.*, 1960, **38**, 746.

Reduction of N-*Benzyl-o-nitrobenzamide*.—*N*-Benzyl-*o*-nitrobenzamide[34] (5·0 g) was heated under reflux with zinc dust in aqueous methanolic sodium hydroxide for 13 h as described before. The mixture was filtered, diluted with water, and cooled in ice to yield NN′-*dibenzylazobenzene-2,2′-dicarboxamide* (15b) (0·74 g), m.p. 209° (from ethanol–water), $\nu_{max.}$ 3300 (NH) and 1635 (CO) cm^{-1} (Found: C, 75·5; H, 5·2; N, 13·1. $C_{28}H_{24}N_4O_2$ requires C, 75·0; H, 5·4; N, 12·5%). Acidification (dilute aqueous sulphuric acid) of the aqueous mother liquors afforded 2-benzylindazolone (13b) (3·6 g), m.p. 179° (from ethanol) (lit.,[14] 180°), $\nu_{max.}$ 3100sh and 2700sh (NH) and 1660br (CO) cm^{-1}.

NN-*Dibenzyl-azoxybenzene-2,2′-dicarboxamide* (16b).—A solution of the azo-compound (15b) (0·1 g) in glacial acetic acid (40·0 ml) was stirred and treated dropwise over 2 h at room temperature with aqueous 30% hydrogen peroxide (3·6 ml). Further portions (2 ml) of aqueous hydrogen peroxide (total 6·0 ml) were added with stirring in the course of a further 4 h. The mixture was diluted to 125 ml with water and the solid was collected, washed (aqueous sodium hydrogen carbonate, water), dried *in vacuo*, and crystallised to yield the azoxy-amide (16b) (0·05 g), m.p. 172° (from ethanol), identical (mixed m.p. and i.r. spectrum) with a sample prepared before.

o-*Nitrosobenzanilide* (17a).—A solution of *o*-nitrobenzylideneaniline[35] (9·9 g) in anhydrous benzene (200·0 ml) was irradiated (quartz filter; 450 W Hanovia medium-pressure mercury-arc lamp) under nitrogen for 18 h. The colourless solid was collected and combined with solid material obtained by evaporating the washed (aqueous 10% w/v sodium hydroxide) and dried ($MgSO_4$) filtrate. The crude product was washed with ethanol to remove unchanged *o*-nitrobenzylideneaniline (3·4 g) and crystallised to afford *o*-nitrosobenzanilide (17a) (3·3 g), m.p. 171° (from benzene) (lit.,[16] 171°), $\nu_{max.}$ 3300 (NH) and 1660 (CO) cm^{-1}.

Acidification of the alkaline washings (see before) and recovery in chloroform yielded the azo-acid (19) (1·1 g), m.p. 91° (from ethanol), identical (mixed m.p. and i.r. spectrum) with an authentic sample.[36]

NN′-*Diphenylazobenzene-2,2′-dicarboxamide* (15a).—A mixture of *o*-nitrosobenzanilide (0·23 g) and *o*-aminobenzanilide[28] (0·21 g) in glacial acetic acid (150·0 ml) was stirred at room temperature for 48 h. The mixture (containing a solid) was diluted with water and filtered to afford the azo-compound (15a) (0·14 g), m.p. 262° (from glacial acetic acid), identical (mixed m.p. and i.r. spectrum) with a sample prepared before.

Azobenzene-2-carboxylic Acid (19).—*o*-Nitrosobenzanilide (0·23 g) was heated under reflux with aqueous N-sodium carbonate (10·0 ml) for 3 h. The mixture was diluted with water, washed with chloroform, and acidified with dilute aqueous sulphuric acid to yield the azo-acid (19) (78%), m.p. 91° (from ethanol) (lit.,[36] 91°), identical (mixed m.p. and i.r. spectrum) with a synthetic sample.[36]

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[35] E. Knoevenagel, *Ber.*, 1898, **31**, 2596.
[36] M. P. Freundler, *Bull. Soc. chim. France*, 1911, **9**, 657.