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## o-Nitroaniline Derivatives. Part I. The Preparation and Stability of o-Nitroanils

By R. Marshall, D. J. Sears, and D. M. Smith,\* Department of Chemistry, University of St. Andrews, St. Andrews, Scotland

The formation of Schiff bases by treatment of benzaldehyde with *o*-nitroaniline and its derivatives proceeds best in the presence of an excess of aldehyde, under conditions which permit removal of water as soon as it is formed. The products obtained from the corresponding reactions with substituted benzaldehydes depend on the nature of the substituents.

AROMATIC primary amines normally react readily with aromatic aldehydes, in alcoholic solution or in the absence of a solvent, to give Schiff bases. *o*-Nitroaniline and its derivatives, however, do not form readily isolable Schiff bases with most aldehydes under these conditions; the usual products of such reactions are either *NN*-arylmethylenebis-*o*-nitroanilines (II),<sup>1,2</sup> corresponding to the addition of a further molecule of *o*nitroaniline to the anil (I), or, with longer reaction periods or at higher temperatures, 2-aryl-1-hydroxybenzimidazoles (III).<sup>1,3</sup>



N-Benzylidene-o-nitroaniline (IV), first isolated from a direct condensation of benzaldehyde and o-nitroaniline in ethanol,<sup>4</sup> was subsequently prepared in acceptable yield by the reaction of o-nitroaniline with Nbenzylideneaniline,<sup>1</sup> the equilibrium being displaced in

<sup>1</sup> G. W. Stacy, B. V. Ettling, and A. J. Papa, J. Org. Chem., 1964, 29, 1537.

<sup>3</sup> Merck and Co. Inc., Netherlands Pat. 6,517,255 (Chem. Abs., 1967, 66, 2565).

favour of the required product by removal of the aniline under reduced pressure (Scheme 2). Neither of these



methods has proved satisfactory, however, as a convenient general route to N-arylmethylene-o-nitroanilines.

A recent preparation of the anil (IV) <sup>5</sup> involved the reaction of o-nitroaniline with an excess of benzaldehyde at 140°, the aldehyde acting as both solvent and reactant, and the water produced being removed by distillation. We have found, however, that in the absence of any solvent other than the excess of aldehyde, complete removal of water is difficult, and that addition of an inert solvent of b.p. *ca.* 140° (xylene) to assist removal of the water leads to the formation of 1-hydroxy-2-phenylbenzimidazole (III; Ar = Ph, X = H) rather than the anil (IV).

On the other hand, when toluene (b.p.  $110^{\circ}$ ) replaces xylene as solvent, the anil is obtained in satisfactory yield. A solution of *o*-nitroaniline and benzaldehyde (molar ratio 1:2.5) in toluene is heated under reflux in an apparatus connected to a Dean and Stark trap. As soon as the calculated volume of water has been collected, the mixture is cooled and diluted with dry light petroleum to precipitate the anil.

<sup>4</sup> O. H. Wheeler and P. H. Gore, J. Org. Chem., 1961, 26, 3298.

<sup>5</sup> Nasiruddin, E. Walker, and M. Latif, *Chem. and Ind.*, 1969, 51.

<sup>&</sup>lt;sup>2</sup> D. J. Sears and D. M. Smith, unpublished work.

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Benzylidene derivatives of 4-methyl- and 4-chloro-2nitroaniline are prepared similarly, in benzene and xylene respectively. In each case, the success of the synthesis depends on the choice of solvent, *i.e.* on the reaction temperature. If the b.p. of the chosen solvent is too low, reaction occurs very slowly or not at all, and in higher-boiling solvents the benzimidazole derivative (III) is the main product. The excess of benzaldehyde presumably helps to prevent addition of a further molecule of *o*-nitroaniline to the anils to give benzylidenebis-*o*-nitroanilines, *e.g.* (II).

The anils prepared by this route are very easily hydrolysed, even by atmospheric moisture. The mass spectrum of (IV) shows, in addition to a molecular ion at m/e 226, ions of m/e 243 and 244  $[(M + 17)^+$  and  $(M + 18)^+]$ , indicative of rapid addition of water to the anil. The anils are converted on storage into benzaldehyde and benzylidenebis-amines, e.g. (II).

Attempts to extend the synthesis to o-nitroanils of substituted benzaldehydes have proved unsuccessful.  $\phi$ -Chlorobenzaldehyde reacts with o-nitroaniline to give a little p-chlorobenzoic acid and an unresolvable mixture of products, the spectroscopic properties of which indicate the likely presence both of the anil and of NN*p*-chlorobenzylidenebis-*o*-nitroaniline. p-Nitrobenzaldehyde and o-nitroaniline do not apparently react in the absence of a catalyst even in boiling xylene; in the presence of acetic acid the reaction occurs readily, but the sole product is NN-p-nitrobenzylidenebis-o-nitroaniline (II; X = H,  $Ar = p - O_2 N \cdot C_6 H_4$ ). The reaction of p-methoxybenzaldehyde with o-nitroaniline, on the other hand, yields p-methoxybenzoic acid as the only identifiable organic product, even when acetic acid is present.

Electron-attracting substituents in the aldehydederived ring of the anil thus appear to increase the electrophilicity of the benzylic carbon to such an extent that, in the case of the p-nitrobenzylidene compound, the step (ii) (Scheme 1) is very easily reversible, and, in this and the case of the p-chlorobenzylidene compound, the anil, once formed, undergoes addition of o-nitroaniline [step (iii)] even in the presence of excess of aldehyde.

The failure of p-methoxybenzaldehyde to give an isolable o-nitroanil is more difficult to explain. It may be that the electron-releasing methoxy-substituent diminishes the reactivity of the aldehydic carbonyl group towards attack by the feebly nucleophilic o-nitroaniline so that condensation does not take place; alternatively, the anil may indeed be formed but be subsequently converted under the reaction conditions into some other, as yet unidentified, product. In any event, the oxidation-reduction process implicit in the production of p-methoxybenzoic acid—a process which is paralleled in the p-chlorobenzaldehyde reaction—remains to be investigated.

In contrast, N-o-nitrobenzylidene-o-nitroaniline <sup>6</sup> (V)

\* The CH=N proton in N-benzylideneaniline resonates at  $\tau$  1.64. 4  $\rm E$  is comparatively stable. It may be prepared under 'normal' conditions by heating equimolar amounts of the aldehyde and amine in ethanol, and is resistant to hydrolysis by aqueous acid, although it is hydrolysed under basic conditions. Its stability is possibly due to interaction of the electron-deficient benzylic carbon with an oxygen of the adjacent nitro-group, as shown in Scheme 3, such interaction making this carbon atom less susceptible to nucleophilic attack.



EXPERIMENTAL

'Light petroleum' refers to the fraction of b.p.  $40-60^{\circ}$ . I.r. spectra were recorded for Nujol mulls. N.m.r. spectra were recorded with tetramethylsilane as internal reference.

N-Benzylidene-o-nitroaniline (IV).—A solution of onitroaniline (13.8 g., 0.1 mole) and benzaldehyde (26.5 g., 0.25 mole) in toluene (50 ml.) was heated under reflux in an apparatus connected to a Dean and Stark trap. As soon as the calculated volume (1.8 ml.) of water had been collected (6 hr.), the solution was cooled and diluted with light petroleum (50 ml.). The precipitated solid was recrystallised from benzene-light petroleum, to give Nbenzylidene-o-nitroanaline (IV) (10.2 g., 45%), m.p. 78—79° (lit.,<sup>1</sup> 76—78°) (Found: C, 68.7; H, 4.3; N, 12.5. Calc. for C<sub>18</sub>H<sub>10</sub>N<sub>2</sub>O<sub>2</sub>: C, 69.0; H, 4.45; N, 12.4%),  $v_{max}$ . (C=N) 1630 cm.<sup>-1</sup>,  $\tau$  (CDCl<sub>3</sub>) 1.62 (1H, s, CH=N) \* and 2.0—3.1 (9H, m, aromatic).

N-Benzylidene-4-methyl-2-nitroaniline, m.p. 74—76°, was similarly obtained (66%) from the reaction of 4-methyl-2-nitroaniline (11·1 g.) with benzaldehyde (19·4 g.) in benzene (50 ml.) (Found: C, 70·1; H, 5·0; N, 11·7.  $C_{14}H_{12}N_2O_2$  requires C, 70·0; H, 5·0; N, 11·7%),  $\nu_{max}$  (C=N) 1630 cm.<sup>-1</sup>,  $\tau$  (CCl<sub>4</sub>) 1·75 (1H, s, CH=N), 2·1—3·3 (8H, m, aromatic), and 7·64 (3H, s, ArMe).

N-Benzylidene-4-chloro-2-nitroaniline, obtained (61%) from the reaction of 4-chloro-2-nitroaniline (17·2 g.) with benzaldehyde (26·5 g.) in xylene (50 ml.) had m.p. 75—77° (from benzene-light petroleum) (Found: C, 60·1; H, 3·3; N, 10·6. C<sub>13</sub>H<sub>9</sub>ClN<sub>2</sub>O<sub>2</sub> requires C, 59·9; H, 3·5; N, 10·75%)  $\nu_{max}$ , (C=N) 1630 cm.<sup>-1</sup>,  $\tau$  (CCl<sub>4</sub>) 1·70 (1H, s, CH=N) and 2·05—3·15 (8H, m, aromatic).

Reaction of p-Chlorobenzaldehyde with o-Nitroaniline.—A solution of o-nitroaniline (6.9 g.) and p-chlorobenzaldehyde (17.5 g.) in toluene (50 ml.) was heated under reflux, in an apparatus connected to a Dean and Stark trap, for 1 hr.,

<sup>6</sup> W. Borsche and F. Sell, Chem. Ber., 1950, 83, 78; W. Ried and M. Wilk, Annalen, 1954, 590, 91.

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after which time water (0.8 ml.) had been collected. p-Chlorobenzoic acid (0.84 g.), m.p. and mixed m.p. 238—240°, crystallised from the cooled solution and was filtered off. The toluene was evaporated off and most of the excess of aldehyde was removed by sublimation *in vacuo*. Fractional crystallisation of the residue from benzene-light petroleum gave a yellow solid (3.3 g.), m.p. 65—67° (with partial resolidification and remelting at *ca.* 140°) [Found: C, 59.5; H, 4.1; N, 13.0.  $C_{13}H_9ClN_2O_2$  (the anil) requires C, 59.9; H, 3.5; N, 10.75%;  $C_{19}H_{15}ClN_4O_4$  (the arylmethylenebis-amine) requires C, 57.2; H, 3.8; N, 14.0%],  $v_{max}$ . (N-H) 3370 cm.<sup>-1</sup>,  $\tau$  (CCl<sub>4</sub>) 1.69 (s, CH=N) and 1.8—3.4 (m, aromatic and NH) (ratio of integrals *ca.* 1: 15).

Reaction of p-Nitrobenzaldehyde with o-Nitroaniline.—A solution of p-nitrobenzaldehyde (7.5 g.) and o-nitroaniline (4.5 g.) in xylene (30 ml.) containing acetic acid (0.5 ml.) was heated under reflux for 6 hr. in an apparatus connected to a Dean and Stark trap. Water (0.4 ml.) was collected. The solvent was evaporated off and the residue was washed with benzene and recrystallised from dimethylformamide-ethanol to give NN-p-nitrobenzylidenebis-o-nitroaniline (2.3 g., 35%), m.p. 118—120° (Found: C, 56.05; H, 3.7; N, 17.4. C<sub>19</sub>H<sub>15</sub>N<sub>5</sub>O<sub>6</sub> requires C, 55.75; H, 3.7; N, 17.1%),  $\nu_{max}$ . (N–H) 3380 cm.<sup>-1</sup>,  $\tau$  [(CD<sub>3</sub>)<sub>2</sub>SO] 1.4—3.3 (m, aromatic and NH). The benzene washings gave on evaporation unchanged p-nitrobenzaldehyde. In the absence of acetic acid, no reaction was observed.

Reaction of p-Methoxybenzaldehyde with o-Nitroaniline. p-Methoxybenzaldehyde (17.5 g.) and o-nitroaniline (6.9 g.) in boiling xylene, with or without acetic acid, gave after 3 hr. water (0.8 ml.). Dilution of the mixture with light petroleum gave p-methoxybenzoic acid (yield ca. 7%), identical (mixed m.p. and i.r. spectrum) with an authentic specimen. Concentration of the solution *in vacuo* gave a viscous oily residue, from which p-methoxybenzaldehyde was recovered by further distillation. No other product was isolated.

N-(o-Nitrobenzylidene)-o-nitroaniline (V).—A solution of o-nitroaniline (5.5 g.) and o-nitrobenzaldehyde (6.0 g.) in ethanol (40 ml.) was heated under reflux for 3.5 hr. The solvent was evaporated off, and the residue was triturated with a little fresh solvent and set aside to crystallise. Recrystallisation from benzene gave the anil (3.6 g., 35%), m.p. 180—182° (lit.,<sup>6</sup> 179—180°) (Found: C, 57.9; H, 3.4; N, 15.65. Calc. for  $C_{13}H_9N_3O_4$ : C, 57.6; H, 3.3; N, 15.5%),  $v_{max.}$  (C=N) 1640 cm<sup>-1</sup>,  $\tau$  (ClCH<sub>2</sub>·CH<sub>2</sub>Cl) 1.10 (s, CH=N).\*

The anil was recovered unchanged from an attempted hydrolysis with aqueous (2M) sulphuric acid and acetic acid at 100°. Hydrolysis was effected by boiling a mixture of the anil (0.81 g.) and AnalaR sodium carbonate (0.66 g.) in methanol (10 ml.) and water (4 ml.) for 1 hr. The crude product, recovered by extraction with ether, showed strong i.r. carbonyl absorption, and was treated with 2,4dinitrophenylhydrazine (0.60 g.) in methanol containing a little concentrated hydrochloric acid, to give *o*-nitrobenzaldehyde 2,4-dinitrophenylhydrazone (0.70 g., 70%), m.p. and mixed m.p. 246—247°.

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\* The CH=N proton in N-(o-nitrobenzylidene) aniline resonates at  $\tau$  1.18.