Metal Ions and Complexes in Organic Reactions. Part XII.[1] Copper-catalysed Reaction between 2-Bromonitrobenzene and Diphenylamine

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Copper-catalysed nucleophilic substitution of the type $NHAr_2 + Ar'Br \longrightarrow NAr_2Ar'$ occurred in dimethylacetamide between diphenylamine and *o*-bromonitrobenzene, giving *NN*-diphenyl-*o*-nitroaniline (*ca.* 50%), accompanied by nitrobenzene (up to 50%), a compound of probable structure $o\text{-}NO_2\cdot C_6H_4\cdot NPh\cdot C_6H_4\cdot NPh_2$ (up to 3%), and only traces of 2,2'-dinitrobiphenyl. Methyl *o*-bromobenzoate was less reactive, and *m*- and *p*-bromonitrobenzene were unreactive. Heterogeneous copper catalysts (preferable Cu_2O) were much superior to homogeneous catalysts (CuHal) for this particular nucleophilic substitution.

THE preparation of triarylamines from aryl halides and diarylamines is known to require copper catalysis. Published procedures, summarised in equations (1), (2), and (3), respectively involve small amounts (*e.g.* 1%) of copper metal,[2] or larger amounts of copper(I) iodide [3] or copper(II) oxide: [4]

$$NHAr_2 + Ar'I + 0{\cdot}5K_2CO_3 \xrightarrow[(ca.\ 210^\circ)]{Cu\text{-}PhNO_2} NAr_2Ar' + KI + 0{\cdot}5CO_2 \qquad (1)$$

$$LiNAr_2 + Ar'I \xrightarrow[(ca.\ 140-170^\circ)]{CuI\text{-}(C_4H_9)_2O \text{ or } (C_5H_{11})_2O} NAr_2Ar' + LiI \qquad (2)$$

$$NHAr_2 + Ar'I \xrightarrow[(210-220^\circ)]{CuO\text{-}KF} NAr_2Ar' + (?) \qquad (3)$$

The traditional method (1) is an adaptation of Ullmann's procedure [5] for preparing carboxydiarylamines, *e.g.*:

$$PhNH_2 + o\text{-}HalC_6H_4\cdot CO_2H \longrightarrow o\text{-}PhNH\cdot C_6H_4\cdot CO_2H$$

These copper-catalysed diarylamine preparations, which have found extensive application in syntheses of acridines,[6] sometimes suffer from competition by reductive dehalogenation, RHal ⟶ RH (ref. 6, pp. 157—160).

Copper-catalysed reductive dehalogenation of aryl bromides, effected by a variety of aromatic hydrogen donors, was recently studied here.[7] Diphenylamine proved to be exceptional, at least among the nitrogeneous compounds tested as donors, because it acted moderately efficiently as a nucleophile, yielding a triarylamine (Ar' being $o\text{-}NO_2\cdot C_6H_4$ in the case examined) under the conditions shown in equation (4):

$$NHAr_2 + Ar'Br + 0{\cdot}5Cu_2O \xrightarrow[(165^\circ)]{Me_2NAc} NAr_2Ar' + CuBr + 0{\cdot}5H_2O \qquad (4)$$

In a further examination of this reaction, we have not obtained *NN*-diphenyl-*o*-nitroaniline in yields exceeding *ca.* 50%, and the process is therefore inferior to the traditional procedure (1), which is reported [2] to give yields of 80—95%. However, the results (see Table and Scheme) show the following features, which are of interest in relation to the varying pattern of reactivity observed in liquid-phase systems containing halide, nucleophile, copper species, and solvent.

(*a*) The nucleophilic substitution product (I) was accompanied by substantial but variable amounts of the reduction product, nitrobenzene, and by only traces of the Ullmann-type coupled product, 2,2'-dinitrobiphenyl, which has been obtained with copper(I) oxide in good yield under other circumstances.[1] A significant by-product was a crystalline compound, $C_{30}H_{23}N_3O_2$,

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[1] Part XI, R. G. R. Bacon and Seetar G. Pande, preceding paper.

[2] I. Goldberg and M. Nimerovsky, *Ber.*, 1907, **40**, 2448; S. Gambarjan, *ibid.*, 1908, **41**, 3507; J. Piccard and L. M. Larsen, *J. Amer. Chem. Soc.*, 1917, **39**, 2006; J. Piccard and M. Kharasch, *ibid.*, 1918, **40**, 1074; J. Piccard, *ibid.*, 1926, **48**, 2878; J. Piccard, *Helv. chim. Acta*, 1924, **7**, 789; F. D. Hager, *Org. Synth.*, Coll. Vol. I, 2nd edn., 1948, p. 544.

[3] O. Neunhoeffer and P. Heitmann, *Chem. Ber.*, 1961, **94**, 2511.

[4] G. C. Yakobson, A. E. Ioffe, and N. N. Vorozhtsov, *Izvest. sibirsk. Otdel., Akad. Nauk, Ser. khim. Nauk.*, 1963, 156.

[5] F. Ullmann, *Ber.*, 1903, **36**, 2382; F. Ullmann and H. Kipper, *ibid.*, 1905, **38**, 2120; *cf.* P. E. Weston and H. Adkins, *J. Amer. Chem. Soc.*, 1928, **50**, 859.

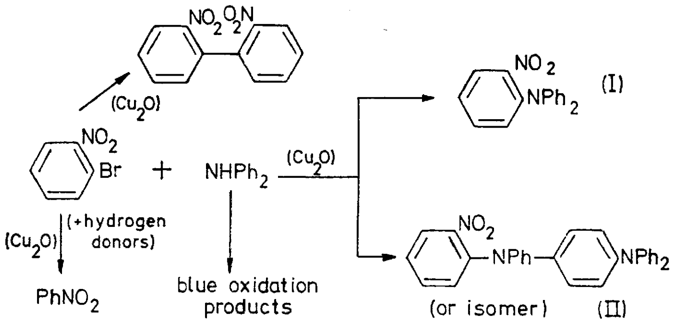
[6] R. M. Acheson, 'Acridines', Interscience, New York, 1956, pp. 122—161.

[7] R. G. R. Bacon and O. J. Stewart, *J. Chem. Soc.* (*C*), 1969, 301.

Reaction of *o*-bromonitrobenzene (0·0166 mole) with diphenylamine (0·0166 mole) and copper species (0·0083 mole) in refluxing dimethylacetamide (25—40 ml.) for 8 hr. under nitrogen.

Catalyst [a]	Method of product analysis	Triarylamine (I) (%)	$PhNO_2$ [f] (%)	Product (II) (%)	Biaryl (%)	Bromo-compound recovered (%)
Cu_2O [b,c]	Al_2O_3 column	45—50	10—15	1·6—3·0	<1	
Cu_2O	G.l.c.	60	32			
Cu [c]	G.l.c.	30	50			4
CuO	G.l.c.	37	45		2	13
Cu_2S	G.l.c.	6	26			80
CuBr	Al_2O_3 column	3	24			
CuBr	G.l.c.	6	32			58
CuCl [d]	G.l.c.	5	40			12
CuI [c,e]	G.l.c.	3	28			69

[a] In the absence of catalyst, halide and amine were unchanged. [b] Yields of (I) were 44—47% (recrystallised chromatographic fractions) when reaction time was varied from 2 to 16 hr. and were 58—64% (by g.l.c.) when the amount of copper(I) oxide was varied from 0·0083 to 0·025 mole. [c] In the presence of potassium carbonate (0·033 mole) the yields of (I) and nitrobenzene were respectively 12 and 64% with copper(I) oxide, 12 and 50% with copper, and 13 and 41% with copper(I) iodide. [d] Another product was *o*-chloronitrobenzene (50%). [e] Another product was *o*-iodonitrobenzene (4%). [f] 8% of nitrobenzene was obtained when diphenylamine was omitted from the reaction system.



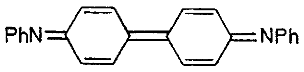
SCHEME

considered to be *N*-4-(or 3-, or 2-)diphenylaminophenyl-*N*-2-nitrophenylaniline, apparently resulting from dehydrogenative coupling between diphenylamine and the nitrotriphenylamine (I):

$$NO_2{\cdot}C_6H_4{\cdot}NPh{\cdot}C_6H_5 + NHPh_2 \xrightarrow{(-2H)} NO_2{\cdot}C_6H_4{\cdot}NPh{\cdot}C_6H_4{\cdot}NPh_2 \quad (5)$$

C–N coupling is a common result in homolytic oxidation of amines.[8] The structure assigned to (II) is supported by the value for the molecular weight and the fragmentation pattern given by mass spectrometry, and by the n.m.r. and i.r. spectral characteristics. Identical features, attributable to *ortho-* and *para*-protons in the nitro-substituted ring, were observed in compounds (I) and (II) (see Experimental section). This indicates, as shown in (5), that this ring is not involved in the coupling process which produces (II); *para*-coupling is suggested, but *ortho-* or *meta*-coupling cannot be excluded.

(*b*) The amount of diphenylamine recovered was consistently less than would be expected from the yield of triarylamine. Some of the reagent is utilised in forming the product (II) and it could also be a hydrogen donor for the production of nitrobenzene. Isolation of products was hindered by the presence of deep blue tarry materials. These are characteristic of diphenylamine oxidations, and are attributed to dehydrogenatively coupled quinonoid products with structures such



(III)

as (III).[9] As expected,[7] reduction of the halide to nitrobenzene occurred to a small extent even in the absence of diphenylamine (see footnote to Table), the hydrogen donor being either the solvent or the nitro-compound itself.

(*c*) Solutions of copper(I) halides were much inferior to suspensions of copper(I) oxide, copper(II) oxide, or copper, in catalysing the nucleophilic substitution. This is the opposite to what has been observed in reactions of aryl halides with lithium salts of amines, as in equation (2),[3] or with sodium methoxide,[10] or with potassium phthalimide.[11] Since the superiority of copper(I) halides as catalysts appears to be associated with reactions of anionic nucleophiles, an intermediate step in such cases may be complex formation of well-known type: $CuHal + X^- \rightleftharpoons CuHalX^-$. Halogen exchange ($ArHal + CuHal' \rightleftharpoons ArHal' + CuHal$) occurred in the expected manner[12] (see Table) when copper(I) chloride or copper(I) iodide was employed as catalyst.

(*d*) Compared with many other nucleophiles which have been examined under similar conditions to those shown for the process (4), the reactivity of diphenylamine is low, and the presence of an activating *ortho*-substituent appears to be necessary in the halide. Neither *m*- nor *p*-bromonitrobenzene reacted, whilst methyl *o*-bromobenzoate gave only a 10% yield of methyl *NN*-diphenylanthranilate, accompanied by some methyl benzoate.

EXPERIMENTAL

Typical Procedure for Copper(I) *Oxide-catalysed Reaction between* o-*Bromonitrobenzene and Diphenylamine* (for variations see Table).—The reaction vessel was charged with *o*-bromonitrobenzene (0·0166 mole), diphenylamine (0·0166 mole), dried copper(I) oxide (0·0083 mole), and dried, redistilled dimethylacetamide (25 ml.). The mixture was stirred for 8 hr. under nitrogen, while the temperature was maintained at 165° by a vapour bath of boiling dimethylacetamide. The colour changed from red-brown to dark blue-green. Filtration of the cooled mixture, and washing

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[8] *E.g.* W. A. Waters, 'Mechanisms of Oxidation of Organic Compounds,' Methuen, London, 1964, p. 148; G. Engelsma and E. Havinga, *Tetrahedron*, 1958, **2**, 289; B. C. Saunders and V. R. Holland, *ibid.*, 1966, **22**, 3345 and earlier papers.

[9] Sidgwick's 'Organic Chemistry of Nitrogen,' 3rd edn., ed. I. T. Millar and H. D. Springall, Clarendon, Oxford, 1966.

[10] R. G. R. Bacon and S. C. Rennison, *J. Chem. Soc.* (*C*), 1969, 312.

[11] R. G. R. Bacon and Amna Karim, *Chem. Comm.*, 1969, 578.

[12] R. G. R. Bacon and H. A. O. Hill, *J. Chem. Soc.*, 1964, 1097.

the material on the filter with ether and with water, left a grey-brown powder (1·1—1·4 g.). Dilution of the filtrate with water (250 ml.), and treatment with ether for 24 hr. in an apparatus for continuous extraction, yielded an isoluble blue-grey powder (0·4—0·6 g.) and ether-soluble red-brown semi-solid material (5·6—5·8 g.); chromatography of this product furnished a total of *ca.* 4·0 g. of eluted material.

The chromatography was carried out on alumina (Spence type H; 100—200 mesh; 150 g.) and yielded the products shown in the Table. Elution with light petroleum (b.p. 40—60°) gave nitrobenzene. Further elution, with 49 : 1 light petroleum–ether gave diphenylamine as colourless crystals, m.p. 49—51°, followed by the main product as an impure fraction (3·1 g.), which, on trituration with cold methanol, gave *NN*-diphenyl-*o*-nitroaniline (I) as orange crystals (2·46 g., 51%), m.p. 100—103°; recrystallisation from light petroleum yielded 2·12 g. (44%), m.p. 102—103° (lit.,[13] 102—103°). Further elution, with 3 : 1 light petroleum–ether, gave red solid (227 mg.) which, on trituration with cold ether, gave the compound (II), m.p. 151—153°, not raised by recrystallisation from ether. Continued elution of the column with the same solvent mixture furnished traces of 2,2′-dinitrobiphenyl, m.p. and mixed m.p. 122—123°, identical (i.r. spectrum) with an authentic sample.[1]

G.l.c. Analysis of Mixed Reaction Products.—Analyses were carried out with a Perkin-Elmer F11 gas chromatograph, fitted with linear temperature programmer, electronic recorder, and integrator. A Versamid 930 column (2 m.) containing a polyamide stationary phase was used. The column was initially at 140° and was raised at 30° per min. to a temperature of 230° at which it was maintained. Calibration was carried out with mixtures of nitrobenzene, *o*-bromonitrobenzene, diphenylamine, *NN*-diphenyl-*o*-nitroaniline, and 2,2′-dinitrobiphenyl (retention times 1—20 min.), and correction factors were then applied to results from mixed reaction products.

Compound (II).—The mass spectrum contained a parent peak at *m*/*e* 457, corresponding with the molecular formula $C_{30}H_{23}N_3O_2$ (Found: C, 78·3; H, 5·1; N, 9·0. $C_{30}H_{23}N_3O_2$ requires C, 78·7; H, 5·1; N, 9·2%). Also included in the spectrum were peaks at $M - 30$ (loss of NO), $M - 46$ (loss of NO_2), $M - 213$ (loss of $NO_2{\cdot}C_6H_4{\cdot}NPh$), 168 ($NPh_2$), and 77 (Ph). The i.r. spectrum indicated the absence of an $\rangle$NH group. The n.m.r. spectrum showed signals at τ 2·24 (1H, d, H *ortho* to NO_2), 2·51 (1H, t, H *para* to NO_2), and 2·60—3·10 (m, other aromatic protons). The n.m.r. spectra of related compounds showed signals as follows: NPh_3 τ 2·64—3·4 (m); *o*-$O_2N{\cdot}C_6H_4{\cdot}NPh_2$ τ 2·21 (1H, d, H *ortho* to NO_2), 2·50 (1H, H *para* to NO_2), and 2·6—3·08 (12H, m); *o*-$MeO_2C{\cdot}C_6H_4{\cdot}NPh_2$ τ 2·40 (1H, d, H *ortho* to CO_2Me), 2·67 (1H, t, H *para* to CO_2Me), and 2·76—3·26 (12H, m).

Other Reactions.—Experiments with *m*- or *p*-bromonitrobenzene, under conditions described for the *ortho*-isomer, furnished only unchanged reagents when the products were chromatographed. A reaction carried out similarly with methyl *o*-bromobenzoate gave chromatographic fractions (from alumina) containing unchanged reagents and methyl benzoate, followed by methyl *NN*-diphenylanthranilate (10%), which was eluted by 9 : 1 light petroleum–ether, and was obtained from methanol as almost colourless needles, m.p. 131—132° (lit.,[14] 132·5—133°) (Found: C, 79·6; H, 5·8; N, 4·85%; M^+, 303. Calc. for $C_{20}H_{17}NO_2$: C, 79·2; H, 5·65; N, 4·6%; *M*, 303). Only traces of the corresponding acid were obtained when *o*-bromobenzoic acid was used for the reaction.

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[13] J. Forrest, *J. Chem. Soc.*, 1960, 581.

[14] G. M. Kosolapoff and C. S. Schoepfle, *J. Amer. Chem. Soc.*, 1954, **76**, 1276.