Metal Ions and Complexes in Organic Reactions. Part XI.[1] Reactions in Pyridine between Copper Species and Aryl Halides, in particular between Copper(I) Oxide and 2-Bromonitrobenzene

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The main result of reaction between 2-bromonitrobenzene and copper(I) oxide in boiling pyridine was Ullmann-type coupling, giving up to 70% of 2,2′-dinitrobiphenyl; other products were 2-nitrophenol (0—40%), nitrobenzene (0—70%), and bis-2-nitrophenylamine (*ca.* 1%), formed *via* 2-nitroaniline resulting from opening of the pyridine ring. Brief reaction of 1-bromo- or 1-chloro-2,4-dinitrobenzene under similar conditions produced 2,4-dinitroaniline. Reactions like those of 2-bromonitrobenzene were shown by some other *ortho*-nitro-substituted aryl bromides or iodides, and by methyl *ortho*-iodobenzoate. If the appropriate element was added to reaction mixtures, biaryl formation (ArHal ⟶ ArAr) was suppressed in favour of formation of the aryl derivatives Ar_2Hg, Ar_2Se_2 (or Ar_2Se), and Ar_2Te. Good yields of the biaryl were produced by use of copper metal or copper(I) sulphide (also giving Ar_2S) in place of the oxide, but not by copper(I) halides. Effects of various additives are reported and a mechanistic scheme is suggested.

In the traditional procedure for biaryl preparation by the Ullmann coupling reaction (1),[2] an aryl bromide, iodide, or (if sufficiently activated by substituents) chloride, is heated at *ca.* 150—300° with copper, sometimes in the presence of an organic solvent:

$$2\mathrm{ArHal} + 2\mathrm{Cu} \longrightarrow \mathrm{ArAr} + 2\mathrm{CuHal} \qquad (1)$$

It is conceivable, though apparently not supported by evidence in the extensive literature of the reaction,[2] that the single-electron transfer occurring in this reductive process ($\mathrm{Cu} \longrightarrow \mathrm{Cu}^+ + e$) could be reinforced by a second single-electron transfer ($\mathrm{Cu}^+ \longrightarrow \mathrm{Cu}^{2+} + e$) in reaction (2), involving the copper(I) halide produced in (1):

$$2\mathrm{ArHal} + 2\mathrm{CuHal} \longrightarrow \mathrm{ArAr} + 2\mathrm{CuHal}_2 \qquad (2)$$

However, in view of the customary excess of copper employed, any occurrence of reaction (2) would be likely to go undetected, because of the ready regeneration of copper(I) by the disproportionation process, $\mathrm{Cu}^{2+} + \mathrm{Cu} \longrightarrow 2\mathrm{Cu}^+$.

This paper demonstrates that Ullmann-type coupling reactions can be achieved with copper(I), but the species found effective were the oxide and the sulphide, and not the halides. Moreover, the applicability of these copper(I) compounds was observed only in special circumstances, namely, with aryl bromides or iodides substituted by NO_2 (or in some cases by CO_2R) in an *ortho*-position, and with pyridine as the reaction medium, at or near its b.p. (*ca.* 95—115°). Circumstances leading to this investigation were explained in a preliminary note,[3] in which comment was made on the sensitivity of the process to adventitious impurities. The only well established precedent for the use of copper(I) oxide in halide coupling reactions is the intramolecular conversion of *oo*′-di-iodobiaryls, at *ca.* 350°, into biphenylenes.[4] Here too the success of the operation tends to be erratic, depending upon the sample of oxide employed. Copper metal is traditionally regarded as ineffective for biphenylene preparations, but this belief has lately been challenged.[5]

The present investigation was mainly concerned with 2-bromonitrobenzene, which should undergo coupling as in equation (3). Reaction gave the expected copper(II)

$$2\ o\text{-}\mathrm{O_2N{\cdot}C_6H_4Br} + \mathrm{Cu_2O} \longrightarrow (o\text{-}\mathrm{O_2N{\cdot}C_7H_4})_2 + \mathrm{CuO} + \mathrm{CuBr_2} \qquad (3)$$

species and 2,2′-dinitrobiphenyl (in yields of up to *ca.* 70%), but the biaryl was accompanied by 2-nitrophenol and by nitrobenzene, in yields (0 to *ca.* 40% and 0 to *ca.* 70%, respectively) which varied as changes were made in the experimental conditions. A minor by-product (*ca.* 1%) was bis-2-nitrophenylamine. Also, by inclusion of the appropriate element, reaction could be diverted from coupling to the production of the species Ar_2Hg, Ar_2Se_2 ($+Ar_2Se$), and Ar_2Te (Ar = 2-nitrophenyl), in yields of *ca.* 10—70%. The conventional Ullmann method is reported to afford 2,2′-dinitrobiphenyl in yields of up to 75% from 2-bromonitrobenzene and up to 99% from 2-iodonitrobenzene.[2] Although the process (3) thus lacks practical advantage, investigation was of interest in relation to the general topic of copper-promoted reactions of aryl halides.[6]

In boiling pyridine (Table 1) coupling occurred at a temperature well below the range customary for Ullmann reactions.[2] Only a low degree of coupling had been observed [3] in 2,4,6-collidine or dimethylacetamide; little or none was achieved in boiling α-picoline or quinoline. In pyridine, under standard conditions, the rate of formation of 2,2′-dinitrobiphenyl (the yield of which reached *ca.* 70% in 25—70 hr.) depended on the sample employed; the slower reactions occurred with the purer samples. With a particular sample of pyridine ('Batch A'), under standard conditions, the yield of 2,2′-dinitrobiphenyl showed reasonably good reproducibility for a heterogeneous reaction, *i.e.* 35 ± 3%, in 24 hr. for 17 experiments.

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[1] Part X, R. G. R. Bacon and J. R. Wright, *J. Chem. Soc.* (*C*), 1969, 1978.

[2] P. E. Fanta, *Chem. Rev.*, 1946, **38**, 139; 1964, **64**, 613.

[3] R. G. R. Bacon, Seetar G. Seeterram, and O. J. Stewart, *Tetrahedron Letters*, 1967, 2003.

[4] M. P. Cava and M. J. Mitchell, 'Cyclobutadiene and Related Compounds,' Academic Press, New York, 1967, p. 255.

[5] J. C. Salfeld and E. Baume, *Tetrahedron Letters*, 1966, 3365.

[6] R. G. R. Bacon and H. A. O. Hill, *Quart. Rev.*, 1965, **19**, 95.

Since trace impurities in the pyridine influence the reaction, selected additives were tested, at low concentrations (Table 1); some showed a moderate catalytic or inhibitive effect on the coupling. If various hydrogen donors were added, in concentrations comparable to that of the halide, there was a major diversion of reaction in favour of the reductive substitution (ArBr ⟶ ArH), to which 2-nitrobromobenzene is very susceptible.[7]

TABLE 1

Effect of varying experimental conditions on the products [a] from reaction between 2-bromonitrobenzene (ArBr) (0·01 mole) and copper(I) oxide (0·01 mole) in pyridine (40 ml.) at *ca.* 115°, under nitrogen, for 24 hr.

Experimental conditions	ArAr (%)	ArH (%)	ArOH (%)	Other data
Standard conditions (as above, in 'Batch A' pyridine)	32—37	0	7—18	*ca.* 10% ArAr in 10 hr.; *ca.* 60% in 70 hr.
Variation in pyridine:				
(i) 'Batch B'	70 [b]	17		(i) 17% ArAr at 96°
(ii) 'Batch B', purified	35—45	0	0—20	(ii) purified by cerium(IV) oxidation or *via* $ZnCl_2$ complex
(iii) AnalaR	25	0		
Effects of various added compounds:				
(i) catalytic (*ca.* 0·0003 mole)	44—48	0—4	15—20	(i) phenylhydrazine, n-octylamine
(ii) relatively ineffective	31—39	0—6	9—35	(ii) see Experimental
(iii) inhibitive (*ca.* 0·01 mole)	25—27	0—3	0—19	(iii) 2-picoline, tetrahydrothiophen
Addition of water (0·5, 5, or 10 ml.)	20, 8, 6	24, 35, 40	24, 18, 26	
Variation in atmosphere:				
(i) nitrogen plus varying proportions of air	0—37	0—20	0—20	
(ii) oxygen	0—6	0—3	2—72	
(iii) hydrogen	29	13	39	
(iv) nitric oxide	0—6	0—8	52—54	(iv) also tarry products
(v) sulphur dioxide	22	24	7	(v) also Ar_2S (6%)
Addition of radicals (*ca.* 0·0003 mole):				
(i) diphenylpicrylhydrazyl	35	0	11	
(ii) azobisisobutyronitrile	37	2	17	
Addition of chlorinated hydrocarbons (0·05 mole):				
(i) chloroform	0	26	0	(i) gave ArCl (65%)
(ii) carbon tetrachloride	0	0	0	(ii) gave ArCl (85%)
Addition of hydrogen-donating compounds:				
(i) phenylhydrazine (0·01 mole)	0	80	0	
(ii) 1,2-bisdimethylaminoethane (used as solvent)	0	54	0	(ii) b.p. 120°
(iii) 2-nitrophenol (0·01 mole)	16	41		
(iv) benzyltrimethylammonium hydroxide (0·01 mole)	2	61	12	
Addition of elements (0·02—0·04 g. atom):				
(i) mercury	0	0	0—12	(i) gave 32—56% Ar_2Hg
(ii) selenium	0			(ii) gave 9—72% Ar_2Se_2 + 0—3% Ar_2Se
(iii) tellurium	7—30	8		(iii) gave 21% Ar_2Te
(iv) sulphur	0	0	0	(iv) gave blue product (also in absence of ArBr)
(v) arsenic, antimony, tin, lead	26—44	0—15	0—35	(v) no metal aryls were identified

[a] Also, bis-2-nitrophenylamine (*ca.* 1%) was isolated in some experiments. [b] This yield % appeared to be around the maximum; longer reaction times resulted in a decline in yield.

The examples of hydrogen donors in the Table are: (i) phenylhydrazine, a known reductant;[7] (ii) 1,2-bisdimethylaminoethane, which has been recommended as solvent for other copper-promoted reactions;[8] (iii) 2-nitrophenol, which has shown abnormality when tested for copper-catalysed preparations of diaryl ethers;[9] and (iv) a quaternary ammonium hydroxide, included (for comparison with water) as a potential means of producing 2-nitrophenol. The observed effects of adding water (Table 1) are considered to be due to hydrolysis of the halide to 2-nitrophenol and hydrogen transfer from the phenol to unchanged halide, in copper-catalysed reactions.

Homolytic features of copper-promoted reactions of aryl halides [1,7] may be involved in the reductive substitution and possibly also in other effects shown in Table 1, *i.e.* suppression of coupling by oxygen or nitric oxide, by carbon tetrachloride or chloroform, and by some elements. In the case of runs involving nitric oxide, it was considered, in view of known examples of copper-catalysed nitrosation,[10] that 2-nitronitrosobenzene might be formed, but a sample of this compound was found to be unstable

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

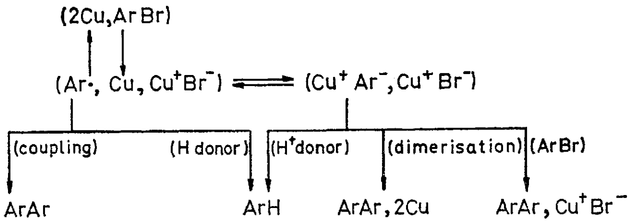
[8] A. S. Hay, *J. Org. Chem.*, 1962, **27**, 3320.

[9] R. G. R. Bacon and O. J. Stewart, *J. Chem. Soc.*, 1965, 4953.

[10] W. Brackman and P. J. Smit, *Rec. Trav. chim.*, 1965, **84**, 357, 372.

in the reaction system. Known reactions of carbon tetrachloride include copper-catalysed decomposition by pyridine [11] and by other amines.[12] In the experiments shown in the Table, the predictable effect [6] of the resulting chloride ion was to cause halide exchange, ArBr ⟶ ArCl. Alternatively, homolytic abstraction (CCl_4 + Ar• ⟶ ArCl) may have occurred.[13] Production of the mercury, selenium, and tellurium derivatives may reasonably be attributed to combination of the elements with aryl radicals. Analogous effects are well known from studies of diazonium-salt decompositions.[13] The production of mercury biaryls by reactions of diazonium salts with a mercury(II) salt and copper [6] seems to be mechanistically related.

The unexpected appearance of bis-2-nitrophenylamine among the reaction products is attributed to intermediate formation of 2-nitroaniline, which may then undergo nucleophilic or reductive substitution in copper-catalysed reactions with unchanged halide. 2-Nitroaniline probably arises from hydrolytic fission of an intermediate pyridinium salt, $(2\text{-}O_2N\cdot C_6H_4)(C_5H_5N)^+Br^-$. This would represent a variation of Zincke's method of opening the pyridine ring, in which $[2,4\text{-}(NO_2)_2C_6H_3](C_5H_5N)^+Cl^-$ gives 2,4-dinitroaniline with water at 150°, or by successive treatment with aqueous alkali and acid.[14]



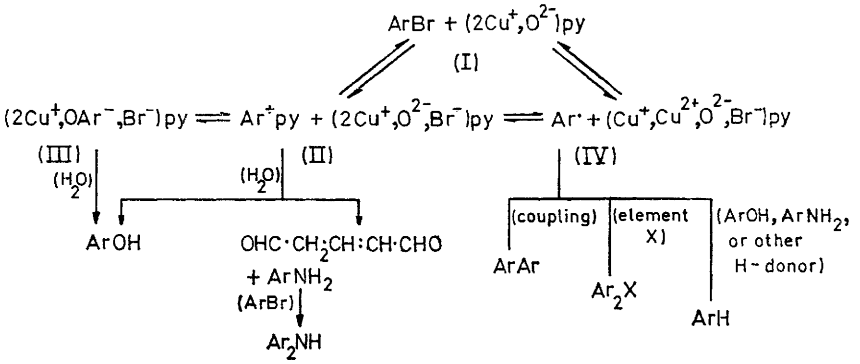
SCHEME 1

When 1-chloro- or 1-bromo-2,4-dinitrobenzene was treated with copper(I) oxide in pyridine for a short period (Table 2), a little 2,4-dinitroaniline was isolated. Another product of the ring-opening reactions should be glutaconaldehyde, the presence of which would further complicate the system.

Mechanism.—The reaction system needs to be compared with that of the conventional Ullmann process, in which biaryl formation has been variously attributed to coupling of radicals, ' dimerisation ' of copper(I) aryl, or interaction of aryl halide with copper(I) aryl.[2,6,15] These alternatives, together with reductive side-reactions, are collectively represented in Scheme 1.

A tentative view of reactions occurring in the $o\text{-}O_2N\cdot C_6H_4Br\text{-}Cu_2O\text{-}C_5H_5N$ system is shown in Scheme 2. Here Ar represents $o\text{-}O_2N\cdot C_6H_4$; symbols in parentheses represent ionic species in the original copper(I) oxide lattice, or in its various transformation products; and py represents pyridine in a pyridinium salt or associated with copper species. The participation of pyridine ligands has parallels in some other copper-assisted aromatic reactions.[16]

Unlike Scheme 1, Scheme 2 does not include the anion Ar^-, which is unlikely to exist simultaneously with Cu^{2+}. On the other hand, reaction (I) ⟶ (II) may generate the pyridine-stabilised cation Ar^+, leading to 2-nitroaniline by pyridine ring-opening, or to 2-nitrophenol by reaction with adventitious water. The content of water in the laboratory supply of pyridine would have sufficed, on this basis, to produce the phenol in *ca.* 20% yield (or the amine in *ca.* 10% yield); this water was not completely removed by routine drying procedures. Moisture in the copper(I) oxide might have contributed up to about 2% to the yield of the phenol. Alternatively, the reaction (II) ⟶ (III) may be considered as a source of pyridine-stabilised copper(I) phenoxide, yielding the phenol by hydrolysis in the work-up.



SCHEME 2

The radical Ar• might be formed by electron transfer

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[11] P. Karrer, W. Wehrli, E. Biedermann, and M. dalla Vedova, *Helv. Chim. Acta*, 1928, **11**, 233.

[12] N. H. Cromwell, P. W. Foster, and M. M. Wheeler, *Chem. and Ind.*, 1959, 228; G. J. Beichl, J. E. Colwell, and J. G. Miller, *ibid.*, 1960, 203; A. Asscher and D. Vofsi, *J. Chem. Soc.*, 1961, 2261.

[13] W. A. Waters, *J. Chem. Soc.*, 1937, 2007; 1939, 864.

[14] E. N. Shaw, ' Pyridine and its Derivatives,' Part II, ed. E. Klingsberg, Interscience, New York, 1961, p. 58; H. S. Mosher, ' Heterocyclic Compounds,' vol. I, ed. R. C. Elderfield, Wiley, New York, 1950, p. 428.

[15] Recent investigations: *e.g.*, A. H. Lewin and T. Cohen, *Tetrahedron Letters*, 1965, 4531; M. Nilsson, *ibid.*, 1966, 675, 679; 1968, 3307.

[16] *E.g.*, T. Ito and K. Watanabe, *J. Chem. Soc., Japan*, 1968, **41**, 419; A. S. Hay, *J. Polymer Sci.*, 1962, **58**, 581; G. F. Endres and J. Kwiatek, *ibid.*, 1962, **58**, 593; *J. Org. Chem.*, 1963, **28**, 1300.

from copper(I), either to the halide, as in (I) ⟶ (IV), or to the cation, as in (II) ⟶ (IV). Coupling of the radical would give the biaryl; hydrogen abstraction from a suitable donor would give nitrobenzene; and combination with appropriate elements would give their aryl derivatives.

Variation in Aryl Halide.—Examples are shown in Table 2. As expected, 2-iodonitrobenzene gave a higher yield of 2,2′-dinitrobiphenyl than the bromo-compound, whilst the chloro-compound showed negligible response. The Table includes two further examples of *o*-nitroaryl bromides undergoing coupling. On the other hand, reduction was the only type of reaction identified in the case of 2-bromo-1-nitronaphthalene or 9-bromo-10-nitrophenanthrene. The reactivity of 1-chloro- and 1-bromo-2,4-dinitrobenzene has already been discussed. Ten aryl halides containing nuclear substituents other than NO_2 were tested; of these, only methyl *o*-iodobenzoate underwent coupling. Compounds in Table 2 provide further examples of features of the reaction system shown for 2-bromonitrobenzene in Table 1: *i.e.* there was a modest enhancement of coupling when particular amines were present; coupling was suppressed in favour of phenol formation under an atmosphere of nitric oxide; and coupling could be directed to the formation of selenium or mercury aryls.

TABLE 2

Reactions of various halides (ArHal) (0·01 mole) with copper(I) oxide (0·01 mole) in pyridine (40 ml.) at *ca.* 115°, under nitrogen, for 24 hr.

ArHal	Time (hr.)	ArAr (%)	ArH (%)	ArOH (%)	Other data
$2\text{-}O_2N\cdot C_6H_4Cl$ [a]	24	0	16	0	
$2\text{-}O_2N\cdot C_6H_4Cl$	24	3	0	0	0·0003 mole $(CH_2\cdot NH_2)_2$ present
$2\text{-}O_2N\cdot C_6H_4I$ [a]	24	81	0	0	
$2\text{-}O_2N\cdot C_6H_4I$	48	27	6	53	atmosphere of NO used
$2\text{-}IC_6H_4\cdot CO_2Me$ [a]	24	9	0	0	
$1,4\text{-}Br_2,2\text{-}O_2N\cdot C_6H_3$	48	23	7	27	
$1,4\text{-}Br_2,2\text{-}O_2N\cdot C_6H_3$	48	37	4	16	0·0003 mole $n\text{-}C_8H_{17}\cdot NH_2$ present
$1,4\text{-}Br_2,2\text{-}O_2N\cdot C_6H_3$	24	0	0	0	0·04 g. atom Se present, giving Ar_2Se_2 (41%) and Ar_2Se (14%)
$1\text{-}Me,3\text{-}NO_2,4\text{-}BrC_6H_3$	24	18	0	3	
$1\text{-}Me,3\text{-}NO_2,4\text{-}BrC_6H_3$	24	25	0	4	0·0003 mole $n\text{-}C_8H_{17}\cdot NH_2$ present
$1\text{-}Me,3\text{-}NO_2,4\text{-}BrC_6H_3$	24	0	0	0	0·016 g. atom Hg present, giving Ar_2Hg (35%)
$1\text{-}Me,3\text{-}NO_2,4\text{-}BrC_6H_3$	24	0	0	0	0·04 g. atom Se present, giving Ar_2Se_2 (56%)
$1\text{-}Cl,2,4\text{-}(NO_2)_2C_6H_3$	0·25	0	0	0	gave $ArNH_2$ (11%) + tar
$1\text{-}Br,2,4\text{-}(NO_2)_2C_6H_3$	0·25	0	0	0	gave $ArNH_2$ (2%) + tar

[a] ‘Batch B’ pyridine (see Table 1) used in these cases, ‘Batch A’ pyridine used in other cases.

Variation in the Copper Species (Table 3).—Comparison with data in Table 1 shows that efficiency of coupling by copper bronze, copper(I) oxide, or copper(I) sulphide was broadly similar. Recorded yields indicate the reactivity order $Cu > Cu_2S > Cu_2O$, but this takes no account of probable differences in particle size or possible differences in response to varying catalytic or inhibitive influences in the reaction system. Nitric oxide appeared to have no inhibitive effect on coupling by copper or copper(I) sulphide. The metal seemed less sensitive to oxygen than were the oxide and sulphide. In the presence of the elements, coupling by the metal was similarly diverted to the formation of mercury or selenium aryls.

With copper(I) sulphide as reagent, the products included a little bis-2-nitrophenyl sulphide. This evidence of nucleophilic activity of S^{2-} ions in the Cu_2S lattice has relevance in connection with the possible contribution of O^{2-} to phenol formation, shown in Scheme 2. When copper(I) halides were tested in the system, no coupling occurred; there was some reduction to nitrobenzene, as observed with 2-bromonitrobenzene and copper(I) halides under other circumstances;[7,17] and there was the expected nuclear halogen-exchange:[6] ArBr + CuCl ⟶ ArCl + CuBr.

TABLE 3

Reactions of various copper species (0·01 g. atom or mole) with 2-bromonitrobenzene (ArBr) (0·01 mole) in pyridine (40 ml.) at *ca.* 115°, under nitrogen

Copper species	Special conditions	ArAr (%)	ArH (%)	ArOH (%)	Other products (%)
Cu bronze		55—70	3—8	0—4	
Cu bronze	O_2 atmos.	32	1	2	
Cu bronze	NO atmos.	57	4	5	
Cu bronze	SO_2 atmos.	51	9	5	
Cu bronze	+ Hg (0·03 g. atom)	28	0	3	Ar_2Hg (44)
Cu bronze	+ Se (0·04 g. atom)	0	0	0	Ar_2Se_2 (40)
Cu (pptd.)		7	27	0	
Cu_2S		50	19	0	Ar_2S (3)
Cu_2S	O_2 atmos.	7	29	32	Ar_2S (3)
Cu_2S	NO atmos.	52	15	7	Ar_2S (6)
Cu_2S	H_2 atmos.	52	16	7	Ar_2S (9)
CuO		6	0	0	
CuBr		0	50	0	
CuCl		0	12	4	ArCl (77)

EXPERIMENTAL

Reagents.—Particulars concerning the composition of the copper(I) oxide used (Hopkin and Williams Ltd.) have been reported.[18] The moisture content was *ca.* 0·25%. Analysis

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[17] R. G. R. Bacon and D. J. Maitland, following paper.

[18] R. G. R. Bacon and S. C. Rennison, *J. Chem. Soc.* (*C*), 1969, 308.

by atomic-absorption spectrometry gave: Cu, 85·85% (Calc. for Cu_2O: 88·82%), plus traces of Pb, Zn, and Mg. After the oxide had been treated with boiling water and organic solvents and dried under vacuum, analyses showed Cu, 86·0—86·5%. An oxide sample, prepared in the laboratory by reduction of hot aqueous copper(II) acetate with glucose, gave results similar to those obtained with the commercial oxide in reaction with 2-bromonitrobenzene. Copper bronze (B.D.H. Ltd.) gave the following results on analysis by atomic-absorption spectrometry: Cu, 97·7; Zn, 0·3; Pb, 0·0004%; Mg, trace. After the metal had been treated with boiling water and organic solvents, analyses showed Cu, 98·1—98·5%. 'Activation' of copper(I) oxide or copper bronze according to described methods[19] did not significantly affect yields of 2,2′-dinitrobiphenyl.

Pyridine was 'redistilled laboratory' grade from B.D.H. Ltd., and the designations 'Batch A' and 'Batch B' refer to consignments received from the supplier on different occasions. The initial water content of the former sample (Karl Fischer method) was 0·098%. Before use, the pyridine was heated under reflux with solid potassium hydroxide and distilled at 114—116°. In a typical case, this reduced the water content to 0·034%. The suppliers stated in correspondence that their pyridine was wholely derived from coal-tar sources and that its purity was about 99%, the remaining 1% being essentially α-picoline. It contained traces (*ca.* 0·01—0·05%) of other impurities, one of which was likely to be tetrahydrothiophen (equivalent to a sulphur content of about 50 p.p.m.). Some experiments (Table 1) were carried out with AnalaR pyridine (B.D.H.) and with 'Batch B' pyridine purified by oxidation with cerium(IV) sulphate[20] or by formation and decomposition of the zinc chloride complex.[21]

Reaction of 2-Bromonitrobenzene with Copper Species.—(a) *Standard conditions*. Reaction mixtures with the compositions shown in Tables 1 and 3 were stirred under a slow stream of dry nitrogen. Insoluble material, consisting of unchanged copper(I) oxide, mixed with black copper(II) oxide and green crystals of pyridine-complexed copper(II) bromide, was then filtered off. The filtrate, which contained more copper(II) bromide, was treated with 5N-hydrochloric acid and the precipitated organic material was extracted into methylene chloride. Emulsions were not troublesome unless tarry products were present. Products subsequently isolated from the extract were characterised by m.p. (Kofler hot-stage), by analysis, and spectroscopically.

Treatment of the methylene chloride solution with aqueous sodium hydroxide removed 2-nitrophenol, which was recovered, after acidification and steam distillation, as yellow needles, m.p. 43—44°. Evaporation of methylene chloride then gave a red-brown liquid residue, which was chromatographed on alumina (Spence type H) with light petroleum (b.p. 30—40°), progressively reinforced with anhydrous diethyl ether. Fractions eluted by light petroleum–ether mixtures in the composition range 7 : 3—6 : 4 contained nitrobenzene, not separable from accompanying unchanged 2-bromonitrobenzene. The composition of these mixtures was determined by g.l.c. analysis (Griffin and George S91—350 Chromatograph), on a column (2 m.) of silicone oil (10%) on Celite, at 124°, with a nitrogen flow rate of 60 ml./min.; retention times for nitrobenzene and 2-bromonitrobenzene were 2 and 11 min. respectively. Later chromatographic fractions, eluted by light petroleum–ether mixtures in the composition range 4 : 6—2 : 8, contained 2,2′-dinitrobiphenyl, as cream-coloured needles, m.p. 124—125° (from ethanol) (lit.,[22] 123·5—124·5°). Further elution yielded impure orange crystals (*ca.* 0·02 g.), which furnished bis-2-nitrophenylamine, m.p. 170—171° (lit.,[23] 171—171·5°) after two recrystallisations from ethanol (Found: C, 55·8; H, 3·9; N, 16·7. Calc. for $C_{12}H_9N_3O_4$: C, 55·5; H, 3·5; N, 16·2%; parent peak at *m/e* 259 in the mass spectrum). If 2-nitrophenol had not been removed by alkaline extraction, it reacted with alkali in the alumina at the top of the column, giving a strongly adsorbed orange-red band of the sodium salt, which could be slowly eluted with methanol.

Total recovery of the main reaction products, plus unchanged 2-bromonitrobenzene, was 79 ± 15% in about 70 experiments. There were additional resinous products, eluted in the last stages of the chromatography. As a check on product stability and isolation procedure, a mixture of 2,2′-dinitrobiphenyl, nitrobenzene, and 2-nitrophenol was stirred with copper(I) oxide in refluxing pyridine for 24 hr.; recoveries were 99, 94, and 86%, respectively, of the amounts added.

(b) *Reactions in the Presence of Catalysts, Inhibitors,* etc. In the presence of either carbon tetrachloride or chloroform (Table 1) the reaction mixture became black and there was copious deposition of dark grey, water-soluble crystals, whether or not 2-bromonitrobenzene was present. Much tar accompanied the products when chloroform was used. The following compounds were ineffective as catalysts or inhibitors for biaryl formation under the conditions employed: acetic acid, aniline, 4-methyl-2,6-di-t-butylphenol, dimethylacetamide, ethylenediaminetetra-acetic acid, gelatine [present in commercial copper(I) oxide;[18] here used with a laboratory-prepared oxide sample], n-octanol, tri-n-butylamine, and triphenylmethane.

For examination of effects of oxygen, hydrogen, or nitric oxide (Tables 1 and 3), the magnetically stirred reaction system was connected to a gas burette. Volume contractions during reaction periods corresponded with consumption of 0·002—0·004 mole of gas, but the results were erratic. Solutions became green, and showed other colour changes, both with oxygen and with nitric oxide in the burette. Tests with an authentic sample of 2-nitronitrosobenzene[24] showed that it could be eluted from a silica-gel chromatography column (responding very similarly to 2,2′-dinitrobiphenyl), but none was thus isolable if the compound had previously been stirred with copper(I) oxide in refluxing pyridine.

To examine effects of sulphur dioxide (Tables 1 and 3), the gas was passed through the vessel during reaction between 2-bromonitrobenzene and copper(I) oxide in pyridine. The mixture became black, and the crude products contained much tar. Chromatographic fractions included yellow crystals of bis-2-nitrophenyl sulphide, m.p. 122—123°

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(lit.,[25] 122—123°), eluted from alumina by light petroleum–ether mixtures in the composition range 2 : 8—1 : 9, and identical with an authentic sample (Found: C, 52·4; H, 2·9; N, 10·1; S, 11·7. Calc. for $C_{12}H_8N_2O_4S$: C, 52·1; H, 2·9; N, 10·1; S, 11·6%). No 2-nitrobenzenesulphinic acid was found; an authentic sample [26] could not be isolated after it had been tested, as before, similarly to 2-nitronitrosobenzene. In reactions (not involving sulphur dioxide) carried out with copper(I) sulphide (Table 3), bis-2-nitrophenyl sulphide was isolated chromatographically with 3 : 7 light petroleum–ether mixtures on silica gel.

(c) *Reactions in the Presence of Elements*. The procedure described in (a) was modified by inclusion of the appropriate element in the stirred reaction mixture (Table 1).

Mercury was preferably used in finely divided form.[27] When a methylene chloride solution of the crude product was concentrated, most of the bis-2-nitrophenylmercury crystallised out. A further quantity was obtained by chromatography of the remaining material on alumina, with ether or chloroform as eluant. The mercury compound was usually obtained as pale yellow needles (from chloroform or benzene), m.p. 205—207° (Found: C, 32·5; H, 1·8; N, 7·0. Calc. for $C_{12}H_8HgN_2O_4$: C, 32·5; H, 1·8; N, 7·0%), and was identical with a sample, m.p. 206—208° (lit., 206—207°), prepared in low yield by a known method.[28] Samples were several times obtained melting in the range 215—222°; a preparation giving a product, m.p. 220—230°, has been reported.[29] No reaction occurred between 2-bromonitrobenzene and mercury in the absence of copper(I) oxide.

After reactions had been carried out involving selenium, the filtered pyridine solution deposited bis-2-nitrophenyl diselenide; more was obtained by evaporation. Recrystallisation from benzene gave the diselenide as a yellow powder, m.p. 210—213° (lit.,[30] 215°) [Found: C, 35·9; H, 2·2; N, 7·0; Se (ref. 31), 39·1. Calc. for $C_{12}H_8N_2O_4Se$: C, 35·8; H, 2·0; N, 7·0; Se, 39·2%]; it was identical with an authentic sample.[31] Residual solution and solvent washings, chromatographed on alumina, yielded more of the diselenide, which was eluted by 3 : 7 light petroleum–ether. Later fractions, eluted by light petroleum–ether mixtures of higher ether content, or by ether–chloroform, consisted largely of bis-2-nitrophenyl monoselenide, but recrystallisation failed to remove diselenide from it completely, as was indicated by imperfect analytical data and by its m.p. being below the recorded [32] value of 143°. The monoselenide likewise appeared as a by-product in a preparation of the diselenide carried out by a reported method.[31]

After reactions had been carried out involving tellurium, the filtered solution was concentrated, diluted with water, and extracted with methylene chloride, and the extract was chromatographed on alumina. Fractions containing bis-2-nitrophenyl telluride (not previously reported) were eluted by light petroleum–ether mixtures in the composition range 4 : 6—2 : 10. These fractions also contained 2,2′-dinitrobiphenyl, and they could not be completely purified by recrystallisation from benzene, which raised the m.p. to 144—146° and gave the telluride as dark red needles. Attempted preparation by a method described for other diaryl tellurides [33] was unsuccessful.

Reactions of Other Aryl Halides with Copper Species.—The following particulars refer to products (characterised by analysis and spectroscopically) obtained under conditions shown in Table 2.

The products from methyl 2-iodobenzoate included methyl benzoate. Chromatography gave dimethyl biphenyl-2,2′-dicarboxylate, eluted with 3 : 7 light petroleum–ether, m.p. 71—73° (from methanol) (lit.,[34] 73—74°).

The coupling reaction with 1,4-dibromo-2-nitrobenzene yielded: 4-bromo-2-nitrophenol, m.p. 89° (from ethanol) (lit.,[35] 89°); 3-bromonitrobenzene, eluted by 6 : 4 light petroleum–ether; and 4,4′-dibromo-2,2′-dinitrobiphenyl, eluted by 3 : 7 light petroleum–ether, m.p. 149° (from ethanol) (lit.,[36] 150°). In the presence of selenium, 1,4-dibromo-2-nitrobenzene yielded a yellow powder, which was taken up in a little benzene and chromatographed on alumina. Elution by 5 : 5 light petroleum–ether gave a trace of starting material; 4 : 6 light petroleum–ether gave the diselenide; solvent mixtures varying from 3 : 7 light petroleum–ether to 5 : 5 ether–chloroform gave a mixture of di- and mono-selenide; subsequent elution gave tars. Further purification of fractions, by chromatography and recrystallisation from benzene, gave bis-4-bromo-2-nitrophenyl diselenide, as yellow prisms, m.p. 188—190° (lit.,[37] 178°) (Found: C, 26·1; H, 1·2; Br, 28·7; N, 5·0. Calc. for $C_{12}H_6Br_2N_2O_4Se_2$: C, 25·7; H, 1·4; Br, 28·6; N, 5·0%); and *bis-4-bromo-2-nitrophenyl selenide*, as yellow needles, m.p. 174—176° (Found: C, 30·1; H, 1·3; Br, 33·3; N, 5·8. $C_{12}H_6Br_2N_2O_4Se$ requires C, 30·0; H, 1·3; Br, 33·2; N, 5·8%).

The coupling reaction with 4-bromo-3-nitrotoluene yielded: 4-methyl-2-nitrophenol; unchanged halide (68%), eluted with 4 : 6 light petroleum–ether; and 4,4′-dimethyl-2,2′-dinitrobiphenyl, m.p. 138—140° (lit.,[38] 141°), eluted with 2 : 8 light petroleum–ether. When the reaction of 4-bromo-3-nitrotoluene was carried out in the presence of mercury, nearly all the derivative separated when the methylene chloride extract was concentrated; recrystallisation from nitromethane gave *bis-4-methyl-2-nitrophenylmercury* as pale yellow needles, m.p. 241—243° (Found: C, 35·4; H, 2·4; N, 5·8. $C_{14}H_{12}HgN_2O_4$ requires C, 35·5; H, 2·7; N, 5·9%). Chromatography gave unchanged halide (35%) and a trace of additional mercury derivative. When reaction was carried out in the presence of selenium, the sparingly soluble bis-4-methyl-2-nitrophenyl diselenide readily separated from organic solvents, and was obtained as a yellow powder, m.p. 178° (lit.,[39] 177—178°) (Found: C, 39·1; H, 2·8; N, 6·9; Se, 37·0. Calc. for $C_{14}H_{12}N_2O_4Se_2$: C, 39·0; H, 2·8; N, 6·5; Se, 36·5%). Chromatography yielded a further small amount of the diselenide, and unchanged halide (9%).

Attempts to effect coupling of 1-chloro- or 1-bromo-2,4-dinitrobenzene gave tarry products and 2,4-dinitro-

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aniline, eluted by 4 : 6 ether–chloroform, and obtained as orange needles, m.p. 178° (lit., 180°) (Found: C, 39·7; H, 3·0; N, 22·9; Calc. for $C_6H_5N_3O_4$: C, 39·4; H, 2·7; N, 22·9%; parent peak in mass spectrum at *m/e*, 183). Only unchanged halides were obtained when 3- or 4-bromonitrobenzene, 2-bromotoluene, or 2-bromoanisole were tested under the standard conditions; biphenyl-2,2′-iodonium iodide failed to give biphenylene, and 2-bromopyridine failed to give 2,2′-bipyridyl; 2-bromo-1-nitronaphthalene, 9-bromo-10-nitrophenanthrene, 2-iodobenzaldehyde, 2-iodobenzoic acid, and 2-iodobenzonitrile gave the unchanged halides, plus varying amounts of the reduced (*i.e.* dehalogenated) products; 2-bromo- or 2-iodo-1,4-dimethoxybenzene [1] [the latter of which was reported [5] to undergo Ullmann coupling with copper(I) oxide] were unchanged except for production of a trace of reduced product.

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