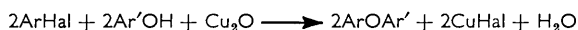


912. *Metal Ions and Complexes in Organic Reactions. Part IV.¹
Copper-promoted Preparations of Diaryl Ethers and Competing
Hydrogen-transfer Processes*

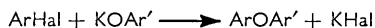
By R. G. R. BACON and O. J. STEWART

Diaryl ethers have been prepared, *e.g.*, in collidine or dimethylacetamide solution at $\sim 170^\circ$, by the reaction:



in which a suspension of copper(I) oxide functions as reagent and catalyst; copper or copper(II) oxide may also be used. The process has preparative value and may be superior to the conventional Ullmann condensation. With an alkali-metal phenoxide the copper oxide is not consumed and reaction may be faster than with the phenol, particularly in dimethylacetamide. Pronounced solvent effects were observed. Halide reactivity was in the order $\text{ArI} > \text{ArBr} > \text{ArCl}$. Substituent effects were studied. Copper-catalysed substitutive reduction, $\text{ArHal} \longrightarrow \text{ArH}$, was a common competing reaction, and was sometimes a major effect with an efficient hydrogen acceptor, *e.g.*, *o*-bromonitrobenzene, or with an efficient hydrogen donor, *e.g.*, *o*-nitrophenol. Sources of transferred hydrogen may be a substituent group, *e.g.*, OH or NH_2 , or an aromatic or heterocyclic nucleus. Other side-reactions included decarboxylation, halogen exchange, coupling of the halide to a biaryl, and substitution of the halide by a nucleophile other than the phenol.

ULLMANN and his co-workers discovered² that small amounts of copper catalyse the formation of diaryl ethers in the reaction:



Their method was to heat the halide, usually at about 200° , with a small excess of the potassium phenoxide and with copper powder (~ 0.02 g.-atom per mole); yields of 70–90% were claimed from numerous combinations of reagents. The experience of later workers³

¹ Part III, R. G. R. Bacon and H. A. O. Hill, *J.*, 1964, 1112.

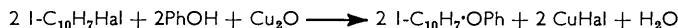
² F. Ullmann *et al.*, 1905, **38**, 2211; 1906, **39**, 622; *Annalen*, 1906, **350**, 83.

³ (a) P. A. Sartoretto and F. J. Sowa, *J. Amer. Chem. Soc.*, 1937, **59**, 603; (b) *Org. Synth.*, Coll. Vol. II, 445; (c) *ibid.*, Coll. Vol. III, 566.

confirms that when certain nitro-substituted halides are used reaction occurs readily (at $\sim 150^\circ$) and yields of ethers are high, but when methyl- or methoxy-substituted halides or phenols are used the best yields (at $\sim 200^\circ$) are 50–60%.

When, with the object of synthesising naturally occurring diaryl ethers,⁴⁻⁶ it has been necessary to use polyfunctional reagents, with substituents including carboxylic ester groups, low or negligible yields have resulted. In one such investigation⁵ the method was improved by the use of 1 g.-atom of copper per mole; copper(I) oxide, but not copper(II) oxide was an alternative catalyst. A variation, recently used for a kinetic study of the reaction,⁷ involved phenol, potassium hydroxide, and an excess of various halides, with copper(II) chloride as catalyst (~ 0.015 mole per mole of phenol), in diethylene glycol dimethyl ether as solvent, at 160° . The results were considered to resemble those from non-catalysed nucleophilic aromatic substitutions, and copper(I) was suggested as the effective catalytic species. A further variation was demonstrated here⁸ when copper(I) oxide (0.5 mol.) was used to catalyse reactions of aryl halides with certain nucleophiles in dimethylformamide or collidine at $150\text{--}170^\circ$; both phenol and sodium phenoxide were effective in this system, producing diaryl ethers in good yield. This procedure, with free phenols as reagents, has since proved advantageous for syntheses of diaryl ethers containing carboxylic ester groups.⁶ An evaluation of the method is described in this Paper.

Table I shows effects of varying the reagent concentrations, and the nature of the copper species, halide, and solvent, for the reaction



conducted under nitrogen, at temperatures around 170° . The standard of reference was the system (A), in which 1-bromonaphthalene and phenol were used in equimolar quantities in collidine solution, and copper(I) oxide, which was largely dissolved during the reaction, was supplied in the half-molar proportion required by the above equation. The oxide was used in the form of laboratory-grade cuprous oxide, which contains $\sim 90\%$ Cu_2O , substantial amounts of CuO , and small amounts of water and ionic impurities.

In general, good reproducibility has not been observed in these experiments with stirred suspensions of cuprous oxide or with other heterogeneous copper-containing systems. Repetition of preparations has sometimes shown a degree of reproducibility of $\pm 2\%$ in the yield figures, but the variation has commonly been substantially higher than this. It is evident (Tables 1, 3, and 4) that good or moderate yields of diaryl ethers are obtainable directly from phenols, but that yields are higher (or reactions are faster) if the phenol is first converted into the sodium phenoxide. Dimethylacetamide is the preferred medium for the phenoxide reactions, since it is a good solvent for these salts, whereas collidine is not. Little attention was paid to variation in the cation, but the reactivity of sodium and potassium phenoxides seemed to be comparable. The use of phenols in place of phenoxides represents a marked departure from traditional Ullmann procedure and has accordingly been explored in these experiments.

Ether production was improved (Table I) by raising the proportion of the halide, or the phenol, or cuprous oxide relative to the other two components. The relative response of naphthyl halides was in the order $\text{ArI} > \text{ArBr} > \text{ArCl}$, in agreement with results obtained elsewhere with copper-containing systems.^{2,7,8} No reaction was observed in the absence of a copper species, and under these conditions, or in systems where little reaction had occurred, the naphthyl halide was recovered nearly quantitatively. When, however, extensive reaction occurred, the recovery of halide, and also of undissolved copper species, was often a good deal lower than was expected from the yield of ether. In several cases

⁴ H. King, *J.*, 1939, 1157, 1165.

⁵ W. M. Whaley, L. Starker, and M. Meadow, *J. Org. Chem.*, 1953, **18**, 833.

⁶ J. R. Crowder, E. E. Glover, M. F. Grondon, and H. X. Kaempfen, *J.*, 1963, 4578.

⁷ H. Weingarten, *J. Org. Chem.*, 1964, **29**, 977, 3624.

⁸ R. G. R. Bacon and H. A. O. Hill, *Proc. Chem. Soc.*, 1962, 113; *J.*, 1964, 1108.

TABLE I

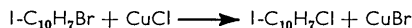
1-C₁₀H₇Hal + PhOH + Copper species + Solvent (48 hr.); halide, 0.4M (except in the second experiment)

Mol. ratio, halide : PhOH : Cu species	Halide	Copper species	Solvent	Temp.	1-C ₁₀ H ₇ ·OPh (yield, %) *	Special features
1 : 1 : 0	1-C ₁₀ H ₇ Br	None	2,4,6-Collidine	170°	0	
2 : 1 : 0.5	"	Cu ₂ O	"	"	61	
1 : 2 : 0.5	"	"	"	"	67	
1 : 1 : 1	"	"	"	"	57	
1 : 1 : 0.5 (A)	"	"	"	"	50	Reference system for the series
"	"	"	"	"	~60 †	NaOH (1 mol.) added or NaOPh (1 mol.) used
"	1-C ₁₀ H ₇ Cl	"	"	"	13	
"	1-C ₁₀ H ₇ I	"	"	"	69	Also gave C ₁₀ H ₈ (9%)
"	1-C ₁₀ H ₇ Br	Cu	"	"	23	
"	"	CuO	"	"	31	
"	"	Cu ₂ S	"	"	2	
"	"	CuCl	"	"	Trace	Gave 1-C ₁₀ H ₇ Cl (49%)
"	"	CuBr	"	"	"	
"	"	CuCl ₂	"	"	0	
"	"	Cu ₂ O	Quinoline	"	46	Also gave C ₁₀ H ₈ (12%)
"	"	"	Pyridine <i>N</i> -oxide	"	38	Also gave C ₁₀ H ₈ (36%)
"	"	"	Dimethylacetamide	166°	40	
"	"	"	"	"	77	NaOPh used
"	"	"	Ethylacetamide	"	5	
"	"	"	Diethylacetamide	"	3	
"	"	"	Diethylene glycol dimethyl ether	160°	5	
"	"	CuCl ₂	"	"	0	CuCl pptd. (cf. ref. 7)

* Yields refer to product isolated chromatographically; recovery on recrystallisation of these fractions was ~90%. † Erratic results, probably associated with poor solubility of NaOPh.

(see below) the important side-reaction which produced naphthalene accounted for some of the halide; no other crystalline by-products, such as binaphthyl, were detected.

Cuprous oxide was the most effective of the copper species examined. Its consumption during ether formation led to loss of catalytic activity in the system, since the dissolved copper(I) bromide which replaced it had negligible catalytic effect. This was also the case for copper(I) chloride, the only effect of which was to cause the previously reported⁹ halogen-replacement reaction:



Cuprous sulphide was a poor catalyst and was largely unchanged. Both copper and copper(II) oxide were quite good catalysts, and both were largely consumed during reaction. In the latter case copper(I) may well have been the effective species, produced by oxidative reaction of the oxide with phenol or solvent. The mode of reaction of the metal is more obscure; it probably functioned initially as an electron donor, as occurs (*e.g.*, with halides at ~200°) in the Ullmann reaction which produces biaryls, but subsequent steps in the process are unknown. Copper(II) chloride, which has been found effective in other circumstances,⁷ was ineffective under the conditions we employed; it was changed into copper(I) halide.

Table I shows three examples of an important competing process, substitutive reduction, 1-C₁₀H₇Br → C₁₀H₈, occurring as a major reaction in pyridine *N*-oxide and to a smaller extent in collidine (with naphthyl iodide) and quinoline. Similar reduction had been observed⁹ in the reaction between 1-bromonaphthalene and copper(I) chloride in pyridine

⁹ R. G. R. Bacon and H. A. O. Hill, *J.*, 1964, 1097.

N-oxide. Provided that these effects are not due to impurities in the solvents, they demonstrate the capacity of compounds containing a pyridine nucleus to act as donors in copper-catalysed hydrogen transfer to an aryl halide (cf. Tables 2 and 3).

TABLE 2

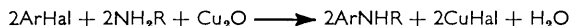
1-C₁₀H₇Br (0.4M) + PhOH (1 mol.) + Cu₂O (0.5 mol.) in basic solvents under N₂ (144°; 21 hr.)

Solvent	Yield of ether (%)	Solvent	Yield of ether (%)
Benzylamine	27 *	Di- <i>n</i> -butylamine	0—4
Pyridine <i>N</i> -oxide	20 †	Dicyclohexylamine	"
<i>n</i> -Octylamine	15 ‡	Tri- <i>n</i> -butylamine	"
Quinoline	15	<i>NN</i> -Diethylaniline	"
2,4,4-Trimethyl-2-pentylamine	10§	2,6-Lutidine	"
2,4,6-Collidine	10	* <i>N</i> -Methyl-2-pyrrolidone (<i>o</i> -Xylene)	0

* C₁₀H₈, 1-C₁₀H₇·NH·CH₂Ph, and PhCHO also produced. † C₁₀H₈ (33%) also produced. ‡ C₁₀H₈ (38%) and a liquid (?1-C₁₀H₇·NH·C₈H₁₇) also produced. § "Tertiary octylamine," at b. p. (142°).

It might be supposed, when solvents are compared, that ease of ether formation should increase with the basicity of the solvent, owing to an increasing extent of phenoxide-ion formation in the equilibrium: PhOH + B \rightleftharpoons PhO⁻ + BH⁺. This, however, appears to be a factor of small importance, since effective solvents differ very greatly in basicity, and a phenol, in any case, is not greatly inferior to its phenoxide under the conditions which we describe. Solvent effects are further illustrated in Table 2, which gives a comparison of basic solvents, employed under milder conditions than in Table 1, the yield of 1-naphthyl phenoxide in the collidine reference system being reduced to 10%. It is again evident that the yield of ether is not related in any simple way to the basicity of the solvent. It is also evident (Tables 1 and 2) that relatively small changes in the structure of solvent molecules have a profound effect upon the reaction; some of the amine and amide solvents were little better than the relatively non-polar solvent xylene.

The primary amines of aliphatic type (Table 2) were high in the order of effectiveness as solvents for ether formation, and in the cases of benzylamine and *n*-octylamine they also provided instances of the simultaneous occurrence of substitutive reduction of the halide as a major reaction. The simultaneous production of benzaldehyde when benzylamine was the solvent indicated that the group CH₂·NH₂ was the hydrogen donor. Reduction of bromonaphthalene was not observed in "tertiary octylamine," which has no hydrogen atom α to the NH₂ and is very resistant to dehydrogenation.¹⁰ The process was further complicated with benzylamine, and probably also with *n*-octylamine, by their acting as competing nucleophiles in copper-catalysed formation of *N*-alkylarylamines:



Substitutions of related type were first reported by Ullmann,¹¹ who described the condensation of primary aromatic amines with *o*-chlorobenzoic acid in the presence of copper or copper(I) chloride and potassium carbonate. His method has since been extensively applied to pairs of appropriately substituted aromatic compounds for syntheses of compounds with a central heterocyclic ring,¹²⁻¹⁴ but instances of copper-catalysed reactions of aryl halides with aliphatic amines are restricted to an industrial amination process¹⁵ or an occasional laboratory application.¹⁶

¹⁰ D. Stewart, unpublished experiments.

¹¹ F. Ullmann, *Ber.*, 1903, **36**, 2382; *Annalen*, 1907, **355**, 312.

¹² R. M. Acheson, "Acridines," Interscience, New York, 1956, p. 148.

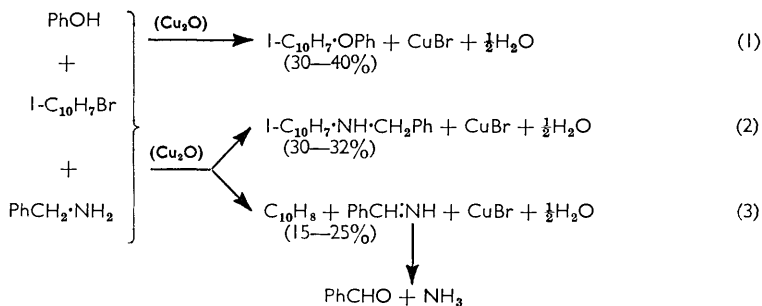
¹³ H. Gilman *et al.*, *J. Amer. Chem. Soc.*, 1944, **66**, 888; *J. Org. Chem.*, 1958, **23**, 1903; A. J. Saggiomo, P. N. Craig, and M. Gordon, *ibid.*, p. 1906.

¹⁴ G. E. Bonvicino, L. H. Yogodzinski, and R. A. Hardy, *J. Org. Chem.*, 1961, **26**, 2797.

¹⁵ E. C. Hughes, F. Veatch, and V. Elersich, *Ind. Eng. Chem.*, 1950, **42**, 787.

¹⁶ *E.g.*, J. M. McManus and R. M. Herbst, *J. Org. Chem.*, 1959, **24**, 1042.

The reactions occurring in benzylamine were further examined under conditions similar to those shown in Table 2, except that a period of 48 hours at 170° was used. The bromonaphthalene was accounted for to the extent of 90—100%, of which about 10% was due to unchanged halide, and the rest to the ether, alkylarylamine, and hydrocarbon, produced from the halide by the competing reactions (1), (2), and (3), respectively. Reactions



(2) and (3) also occurred in the absence of phenol, but yields were lower, which suggests some kind of interconnection with reaction (1) in the phenol-containing system. The yield of benzaldehyde was variable, and was partly due to an independent reaction, also found when the bromide was absent, in which the copper oxide or adventitious oxygen acted as oxidant. The inorganic residue contained some copper metal.

TABLE 3

I-C₁₀H₇Br (0.3—0.5M) + ArOH or ArONa (1 mol.) + Cu₂O (0.5 mol.), under N₂, in boiling collidine (170°) or dimethylacetamide (166°), for 48 hr.

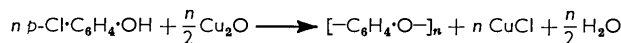
Phenol or phenoxide	Solvent	1-Naphthyl aryl ether (%)	Naphthalene (%)
<i>p</i> -Me·C ₆ H ₄ ·OH	Collidine	62 *	2
"	Dimethylacetamide	24	5
<i>p</i> -MeO·C ₆ H ₄ ·OH	Collidine	72 *	1
"	Dimethylacetamide	39	5
<i>p</i> -Cl·C ₆ H ₄ ·OH	Collidine	49 * †	
<i>p</i> -Cl·C ₆ H ₄ ·ONa	"	74 †	
<i>o</i> -CO ₂ H·C ₆ H ₄ ·OH	"	32 §	24
<i>p</i> -CO ₂ H·C ₆ H ₄ ·OH	"	11 §	24
<i>o</i> -NO ₂ ·C ₆ H ₄ ·OH	"	0	27
"	Dimethylacetamide	0	5
<i>o</i> -NO ₂ ·C ₆ H ₄ ·ONa	"	0	50
<i>m</i> -NO ₂ ·C ₆ H ₄ ·OH	Collidine	12 *	35
"	Dimethylacetamide	23	<1
<i>m</i> -NO ₂ ·C ₆ H ₄ ·ONa	"	38	20
<i>m</i> -NO ₂ ·C ₆ H ₄ ·OK	"	37	9
<i>p</i> -NO ₂ ·C ₆ H ₄ ·OH	Collidine	12 *	15
"	Dimethylacetamide	5	5
<i>p</i> -NO ₂ ·C ₆ H ₄ ·ONa	"	9	9

* New compounds. † Other products were I-C₁₀H₇Cl (32%) and I-C₁₀H₇OPh (3%). ‡ The result was inferior when *p*-Cl·C₆H₄·OH + NaOH was used. § This product was I-C₁₀H₇OPh.

Reactions were then studied between various halides, phenols or phenoxides, and suspensions of cuprous oxide, in refluxing collidine or dimethylacetamide. The stated yields (Tables 3 and 4) are generally the average of two to four experiments, but, in view of the poor reproducibility often encountered, small differences in yields from different pairs of reagents are not highly significant.

In reactions of 1-bromonaphthalene with substituted monocyclic phenols (Table 3), methyl, methoxyl, or chloro-substituents either had no appreciable effect on ease of ether

formation, or slightly enhanced it, but the reaction was markedly depressed by a nitro- or carboxyl group in the phenol. Ether formation was accompanied by the substitutive reduction, $1\text{-C}_{10}\text{H}_7\text{Br} \longrightarrow \text{C}_{10}\text{H}_8$, on which substituents had the reverse effect; it occurred weakly with methyl- or methoxy-substituted phenol, but was dominant when nitro- or carboxyl groups were present. Hence, phenols, particularly if they carry electron-attracting substituents, provide another class of effective hydrogen donors for the copper-catalysed reduction of aryl halides. The presence of a little 1-phenoxynaphthalene among the products from bromonaphthalene and *p*-chlorophenol showed that such reduction could also occur with the chlorine in this phenol or in the ether derived from it. The production in the same reaction of a substantial amount of 1-chloronaphthalene indicates halogen exchange with copper(I) chloride,⁹ a possible source of which is the polycondensation:



which is a reaction of known type.¹⁷ A further complication, observed for the hydroxybenzoic acids, was copper-catalysed decarboxylation, which may have occurred before or after ether formation. Decarboxylation had been observed for salicylic acid under conventional Ullmann conditions.²

TABLE 4

ArHal (0.3—0.5M) + Ar'OH or Ar'ONa (1 mol.) + Cu₂O (0.5 mol.), under N₂, in boiling collidine (170°) or dimethylacetamide (DMA) (166°)

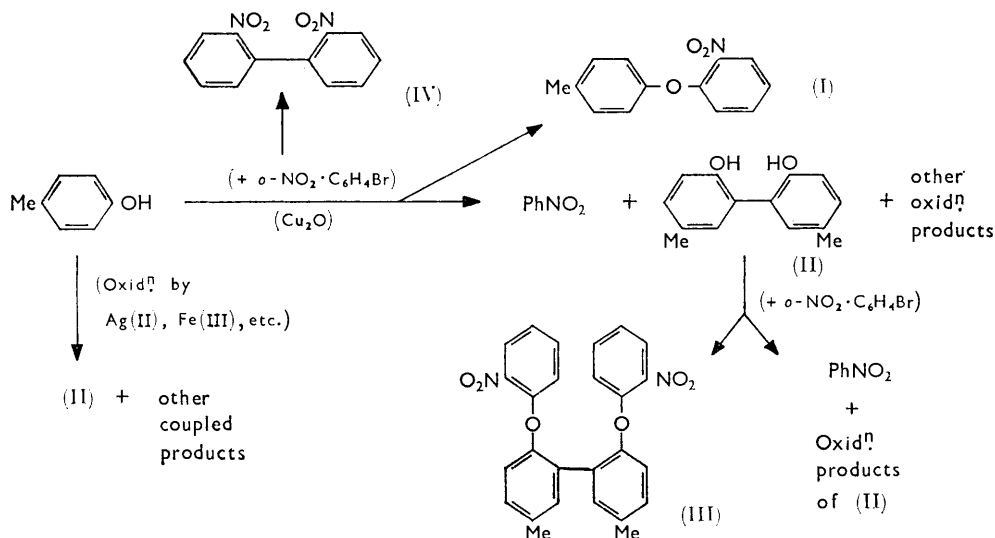
Halide	Phenol or phenoxide	Solvent	Time (hr.)	Diaryl ether (%)	Other products (%)
C ₆ H ₅ Br	<i>p</i> -Me·C ₆ H ₄ ·OH	Coll.	16	43	
"	<i>o</i> -MeO·C ₆ H ₄ ·OH	"	48	96	
<i>o</i> -Me·C ₆ H ₄ Br	<i>p</i> -Me·C ₆ H ₄ ·OH	"	16	42	
<i>p</i> -Me·C ₆ H ₄ Br	"	"	16	41	
"	<i>o</i> -MeO·C ₆ H ₄ ·OH	"	48	96	
<i>p</i> -MeO·C ₆ H ₄ Br	<i>p</i> -Me·C ₆ H ₄ ·OH	"	16	54	
<i>o</i> -NO ₂ ·C ₆ H ₄ Br	"	"	16	48	PhNO ₂ (22), 2,2'-dinitrobiphenyl (3), diether (III) (3)
"	2,2'-Dihydroxy-5,5'-dimethylbiphenyl (II)	"	16	30 †	PhNO ₂ (50)
"	None	"	16	—	PhNO ₂ (12), 2,2'-dinitrobiphenyl (8)
"	None ‡	None	20	—	2,2'-Dinitrobiphenyl (13)
<i>p</i> -NO ₂ ·C ₆ H ₄ Br	<i>p</i> -Me·C ₆ H ₄ ·OH	Coll.	16	81	
<i>p</i> -Me·C ₆ H ₄ Br	<i>p</i> -Me·C ₆ H ₄ ·ONa	DMA	36	81	
<i>p</i> -NO ₂ ·C ₆ H ₄ Br	"	DMA	16	85	

* ArBr increased to 2 mol. and Cu₂O to 2 mol. † Diether (III); new compound. ‡ At 195°.

Bromobenzene and methyl- or methoxy-substituted bromobenzene formed ethers, *e.g.*, with *p*-cresol, to comparable extents, whereas a *p*-nitro-group in the halide markedly enhanced reaction (Table 4). Two examples in the Table (reaction of guaiacol with bromobenzene or *p*-bromotoluene) show that by modifying the relative proportions of the reagents and prolonging the reaction period, typical condensations can be effected practically quantitatively; the yields under conventional Ullmann conditions^{3c} are 55—65%.

Results of particular interest emerged from the use of *o*-bromonitrobenzene, which is in various respects an exceptionally reactive halide. With *p*-cresol it gave a moderate yield of the expected ether (I) together with three by-products as shown in the annexed scheme:

¹⁷ G. P. Brown and A. Goldman, Amer. Chem. Soc., Abstracts of 145th Meeting, New York, 1963, p. 2U.



One product was 2,2'-dinitrobiphenyl (IV), resulting from the Ullmann biaryl coupling reaction,¹⁸ for which copper, not cuprous oxide, is the reagent normally necessary. A somewhat higher yield of the biaryl resulted when the phenol was omitted, but it was not increased much further by omitting the solvent also and raising the temperature. A second product, formed in substantial amounts, was nitrobenzene, resulting from substitutive reduction of the halide. The transfer of hydrogen occurred by dehydrogenation of the phenol, since a third by-product was the diether (III), formed by catalysed condensation of the halide with the biphenyl derivative (II), which is a known product from reactions of *p*-cresol with homolytic oxidants, and is believed to be formed by *ortho*-coupling of *p*-cresoxy-radicals. The compound (II) is available, *e.g.*, as one of the products formed by treatment of *p*-cresol¹⁹ with the aqueous oxidant $\text{S}_2\text{O}_8^{2-}\text{-Ag}^+$. Thus obtained, it was used in place of *p*-cresol with *o*-bromonitrobenzene, when it likewise gave the diether (III), together with nitrobenzene; the formation of the latter shows that the coupled phenol (II) is also a hydrogen donor for the nitro-halide. When the biaryl (IV) was produced in the absence of the phenol, it was accompanied by some nitrobenzene. The formation of the latter suggests that the solvent collidine functions as a subsidiary source of hydrogen for reduction of the nitro-halide. There were no indications of reduction of the other monocyclic halides by a phenol; no anisole was found, but benzene and toluene, if produced, would probably have escaped detection.

Two main conclusions may be drawn. First, the system $\text{ArHal-Ar'OH-Cu}_2\text{O-solvent}$, or variations on it described in this Paper, has practical value in syntheses, and may be found superior to the conventional Ullmann method, at least in the absence of substituents which favour side-reactions. Secondly, the transfer of hydrogen to an aryl halide from a substituent group such as OH or NH_2 , or from an aromatic or heterocyclic nucleus, must be recognised as a common manifestation of the catalytic activity of copper species. The extent of its occurrence depends upon the relative ability of components of the system to function as hydrogen donors and acceptors. Reductions of this type have from time to time been observed as side-reactions when conventional Ullmann conditions have been applied to the coupling of aryl halides,²⁰ and to their condensation with phenols,^{4,5,21} or with

¹⁸ P. E. Fanta, *Chem. Rev.*, 1946, **38**, 139; 1964, **64**, 613.

¹⁹ R. G. R. Bacon, R. Grime, and D. J. Munro, *J.*, 1954, 2275.

²⁰ *E.g.*, W. R. H. Hurlley, *J.*, 1929, 1870; M. S. Lesslie and E. E. Turner, *J.*, 1932, 281; R. S. W. Braithwaite and P. F. Holt, *J.*, 1959, 3025; R. G. R. Bacon and R. Bankhead, *J.*, 1963, 839.

²¹ H. E. Nursten, *J.*, 1955, 3081; see also an example in F. Ullmann, *Annalen*, 1909, **366**, 79.

amines.¹² In the systems described in this Paper such reductions have occurred very commonly, and examples have appeared in which the centre providing the hydrogen could be clearly located. Further aspects of copper-catalysed hydrogen transfer are under investigation.²²

EXPERIMENTAL

General Procedures.—Halides and solvents were redistilled; phenols and copper compounds were dried. Amides used as solvents were stored over Linde molecular sieve, type 5A; heterocyclic bases used as solvents were stored over potassium hydroxide. To prepare dry phenoxides, a slight excess of the phenol, dissolved in the minimum amount of methanol, was treated with the appropriate alkali, dissolved in the minimum amount of 85% aqueous methanol; solvent was evaporated, in the presence of successively added portions of benzene to remove water; the residue was powdered, and dried at 80°/15 mm. and then at 20°/0.1 mm.

Mixtures of the solvents (20—45 ml.) and the reagents specified in the Tables were stirred and heated for the times stated, while a slow stream of nitrogen circulated through the flask. When the reaction temperature was not that of the refluxing solvent, it was attained by use of a vapour bath provided by boiling collidine (170°), dimethylacetamide (166°), or *o*-xylene (144°). The solution generally darkened considerably as reaction proceeded, and the cuprous oxide (or cupric oxide, or copper) largely disappeared from suspension. After reaction, undissolved material was filtered off, and solvent was in some cases removed by distillation, but generally by adding the solution to an excess of dilute (2—6*N*) hydrochloric acid, from which the precipitated organic material was isolated by ether extraction. Tarry by-products, which were particularly prominent when reduction had occurred, sometimes caused troublesome emulsions at this stage. The crude extract was normally purified by chromatography on alumina (150 g.; Peter Spence type H). The first fractions contained unchanged halide, frequently mixed with naphthalene from naphthyl halides (or with nitrobenzene from *o*-bromonitrobenzene). Later fractions contained the fairly pure diaryl ether. Fractions containing naphthyl halide and naphthalene were mixed and were analysed quantitatively at 125—140° in a Pye Argon Chromatograph containing Apiezon—Celite columns. Gas-chromatographic analytical methods were also developed for investigating some halide-diaryl ether mixtures which were difficult to separate cleanly on alumina. Melting points were recorded with a Kofler hot-stage apparatus.

1-Phenoxy-naphthalene.—Chromatography of the crude reaction products (Tables 1 and 2) yielded unchanged halide, sometimes mixed with naphthalene, on elution with light petroleum (b. p. 30—40°). Further elution with light petroleum (b. p. 60—80°) gave 1-phenoxy-naphthalene, needles, m. p. 55° (from propan-2-ol or aqueous ethanol). Continued elution failed to give any binaphthyl.

In the case of the reactions carried out in benzylamine (Table 2), the ether extract containing the mixed products was shaken with saturated aqueous sodium pyrosulphite to remove benzaldehyde. The yield of the latter was determined by adding an excess of aqueous sodium carbonate to the pyrosulphite extract, removing the aldehyde by steam-distillation, and oxidising it to benzoic acid with aqueous permanganate. Bromonaphthalene, naphthalene, and 1-phenoxy-naphthalene were determined chromatographically as described above, and further elution from the alumina yielded *N*-benzyl-1-naphthylamine, m. p. 66—67° (lit.,²³ 67°), identical with a sample prepared by a procedure described²⁴ for other *N*-substituted naphthylamines (Found: C, 87.3; H, 6.6; N, 5.7. Calc. for C₁₇H₁₅N: C, 87.5; H, 6.5; N, 6.0%); it gave the same 1,3,5-trinitrobenzene adduct,²⁵ m. p. 174—175°.

Other Aryl 1-Naphthyl Ethers.—The preparations with 1-bromonaphthalene, summarised in Table 3, yielded products as follows. Reaction with *p*-cresol gave 1-4'-methylphenoxy-naphthalene, eluted by 1 : 1 light petroleum (b. p. 60—80°)-ether, and obtained as prisms, m. p. 38.5—39.5° (from ethanol) (Found: C, 87.4; H, 6.1. C₁₇H₁₄O requires C, 87.2; H, 6.0%.) *p*-Methoxyphenol gave 1-4'-methoxyphenoxy-naphthalene, similarly eluted and obtained as needles, m. p. 77° (from ethanol) (Found: C, 81.3; H, 5.7. C₁₇H₁₄O₂ requires C, 81.6; H, 5.6%).

²² R. G. R. Bacon, S. C. Rennison, and O. J. Stewart, *Proc. Chem. Soc.*, 1964, 409, and unpublished results.

²³ L. Zechmeister and J. Truka, *Ber.*, 1930, **63**, 2883.

²⁴ H. H. Hodgson and E. Marsden, *J.*, 1938, 1181.

²⁵ J. J. Sudborough and S. H. Beard, *J.*, 1910, **97**, 773.

The first chromatographic fractions of the product from *p*-chlorophenol, eluted by light petroleum (b. p. 30–40°), were found by gas chromatography⁹ to be mainly 1-chloronaphthalene, with a little 1-bromonaphthalene and a trace of naphthalene. Further elution with light petroleum gave liquid ether fractions, shown by gas chromatography to contain a little 1-phenoxy-naphthalene; two distillations yielded 1-4'-chlorophenoxy-naphthalene, b. p. 148–149°/0.1 mm., n_D^{18} 1.6460 (Found: C, 75.6; H, 4.5. $C_{18}H_{11}ClO$ requires C, 75.4; H, 4.3%). The only product isolated by chromatography after reactions with *o*- or *p*-hydroxybenzoic acid was 1-phenoxy-naphthalene; in the case of the *ortho*-acid a blue colour preceded the usual darkening during reaction. The product from *m*-nitrophenol or sodium *m*-nitrophenoxide gave a yellow oil when eluted by 7:3 light petroleum (b. p. 40–60°)-ether; two distillations of it yielded 1-3'-nitrophenoxy-naphthalene, b. p. 178–180°/0.3 mm. (Found: C, 72.7; H, 4.2; N, 5.6. $C_{16}H_{11}NO_3$ requires C, 72.4; H, 4.2; N, 5.3%). From corresponding reactions with the *para*-isomer, 1-4'-nitrophenoxy-naphthalene was similarly eluted and obtained in yellow needles, m. p. 141–142° (from ethanol) (Found: C, 72.4; H, 4.1; N, 5.6%).

Substituted Diphenyl Ethers.—The following compounds were prepared as shown in Table 4. Phenyl *p*-tolyl ether,^{3a} b. p. 140°/13 mm., di-*p*-tolyl ether, m. p. 50° (lit.,²⁶ 50°), *o*-tolyl *p*-tolyl ether,^{3a} b. p. 144°/14 mm., and *p*-methoxyphenyl *p*-tolyl ether, m. p. 45–46° (lit.,²⁷ 47–48°) were best isolated by extending the time of reaction to 72 hr. and purifying by recrystallisation or distillation, when yields of >80% resulted. Products obtained at lower yields were difficult to separate chromatographically on alumina from unchanged bromide, and the resulting mixtures were analysed by gas chromatography. The product from guaiacol and bromobenzene gave excess of halide, when eluted from alumina with light petroleum, and phenyl *o*-methoxyphenyl ether, eluted by 9:1 light petroleum-ether, and obtained as needles (from ethanol), m. p. 78° (lit.,^{3c} 77–78°). The same procedure was used for *o*-methoxyphenyl *p*-tolyl ether, obtained as prisms (from ethanol), m. p. 53° (lit.,²⁷ 50–51°). *p*-Nitrophenyl *p*-tolyl ether was eluted by 8:2 light petroleum-ether as light yellow crystals (from ethanol), m. p. 69° (lit.,²⁸ 69°). The product from *p*-cresol and *o*-bromonitrobenzene, eluted by 9:1 light petroleum (b. p. 60–80°)-ether, gave nitrobenzene, followed by *o*-nitrophenyl *p*-tolyl ether, obtained in yellow crystals (from ethanol), m. p. 48° (lit.,²⁹ 49°). Subsequent elution, with ether alone, gave a mixture, which was separated by further chromatography and by recrystallisation from ethanol into 2,2'-dinitrobiphenyl, m. p. 124°, and the less soluble 5,5'-dimethyl-2,2'-di-*o*-nitrophenoxybiphenyl (III), obtained as cream coloured leaflets, m. p. 186–188° (Found: C, 68.3; H, 4.5; N, 5.8. $C_{26}H_{20}N_2O_6$ requires C, 68.4; H, 4.4; N, 6.1%). The latter compound showed the expected 7:3 ratio of nuclear hydrogen to methyl hydrogen in its n.m.r. spectrum, and was identical (m. p., infrared spectrum) with a sample prepared (Table 4) from 2,2'-dihydroxy-5,5'-dimethylbiphenyl¹⁹ and *o*-bromonitrobenzene.

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