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REACTIONS OF PHENYLCOPPER WITH IODOARENES

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On the basis of investigations by Costa and co-workers of the preparation and characterization of phenylcopper, it is now possible to study its reactions in some detail. Phenylcopper is rather reactive but can be kept unchanged under nitrogen or in a vacuum for some days.$^{(1)}$ Decomposition of phenylcopper in ether-xylene mixtures at 35-80° gives biphenyl (reaction 1) and some benzene.$^{(2)}$

$$2\ \text{Ar-Cu} \longrightarrow \text{Ar-Ar} + 2\ \text{Cu} \qquad (1)$$

Arylcopper compounds have been discussed as intermediates in the Ullmann biaryl synthesis.$^{(3,4)}$ Lewin and Cohen have reported evidence for the existence of an organocopper intermediate in the reaction of p-iodotoluene with metallic copper in 8-methylquinoline and have shown that reaction 1 is important.$^{(5)}$ However, 2-thienylcopper reacts with iodobenzene in quinoline at 160° to give 2-phenylthiophene (reaction 2).$^{(6)}$

$$\text{Ar-Cu} + \text{Ar}'\text{-I} \longrightarrow \text{Ar-Ar}' + \text{CuI} \qquad (2)$$

The decarboxylative couplings of 2-nitrobenzoic, 2-thenoic or 2-furoic acids with iodoarenes using copper(I) oxide are carried out in quinoline, as are the related couplings of m-dinitrobenzene.$^{(7-9)}$ It seems probable that these reactions proceed via organocopper intermediates stabilized by the solvent.

The present work is an exploration of the relative importance of the dimerisation of phenylcopper and its reactions with iodoarenes. First the thermal decomposition of phenylcopper (ca. 0.8 g) in dry dimethylformamide (DMF), pyridine or quinoline (25 ml) was studied at 50° under nitrogen. Small samples were withdrawn at intervals during the reaction and injected into a mixture of benzene and hydrochloric acid. The organic phase was analysed by gas chromatography using naphthalene as internal standard. In DMF, phenylcopper was largely present as a suspension. Pyridine and quinoline gave initially homogeneous solutions. The formation of biphenyl was essentially complete after 3 h in DMF and after 13 h in pyridine. The yields of biphenyl after 30 h and the relative rates of its formation were: DMF, 75 %, 10; pyridine, 92 %, 2.5; and quinoline, 70 %, 1. The reaction between phenylcopper and iodobenzene was then investigated. Phenylcopper (0.2 g) and an equivalent amount of 4-deuteroiodobenzene (70 % deuterated according to mass spectrum) in DMF, pyridine or quinoline (25 ml, 50°) gave biphenyl. This was isolated and investigated by mass spectrometry. Metallic copper was formed in DMF, whereas copper(I) iodide was formed in pyridine and quinoline. The reaction times, yields of biphenyl (based on phenylcopper + iodobenzene) and the product distribution among the deuterated biphenyls are shown in Table 1.

TABLE 1

	Reaction time h	Total yield of biphenyl %	Relative product distribution		
			Biphenyl	4-*d*-biphenyl	4,4'-d_2-biphenyl
DMF	5	35	94	6	0
Pyridine	20	60	40	50	10
Quinoline	25	55	41	49	10
Calculated random distribution	-	-	42	46	12

The predominant formation of undeuterated biphenyl in DMF shows that there is little reaction between phenylcopper and iodobenzene in this solvent and that reaction 1 is favoured. The agreement between the observed and calculated product distribution, together with the formation of copper(I) iodide, shows that metal-halogen exchange (reaction 3) and unsymmetric coupling (reaction 2) must dominate in pyridine and quinoline solutions.

$$\text{Ar-Cu} + \text{Ar'-I} \longrightarrow \text{ArI} + \text{Ar'-Cu} \qquad (3)$$

The reactions of phenylcopper with some other iodoarenes provided further evidence for the copper-halogen exchange and unsymmetric coupling in quinoline solutions. Equivalent amounts of phenylcopper and 2,6-dimethoxyiodobenzene (5.7 mmole) in quinoline (25 ml, 50°, 25 h) gave iodobenzene, biphenyl, 2,6-dimethoxybiphenyl and 2,2',6,6'-tetramethoxybiphenyl. The products were separated and identified by IR and m.p. (iodobenzene by GLC only). The reaction was followed by GLC with naphthalene as internal standard (Fig. 1). The presence of *m*-dimethoxybenzene is interpreted as due to the accumulation and slow disappearance of 2,6-dimethoxyphenylcopper formed through metal-halogen exchange. Analogous results were obtained from the reaction between phenylcopper and *o*-iodoanisole in quinoline (20-40°, 135 h). The reaction was followed by GLC with the sum of *o*-methoxyphenyl groups as internal standard. 2-Methoxyphenylcopper, observed as

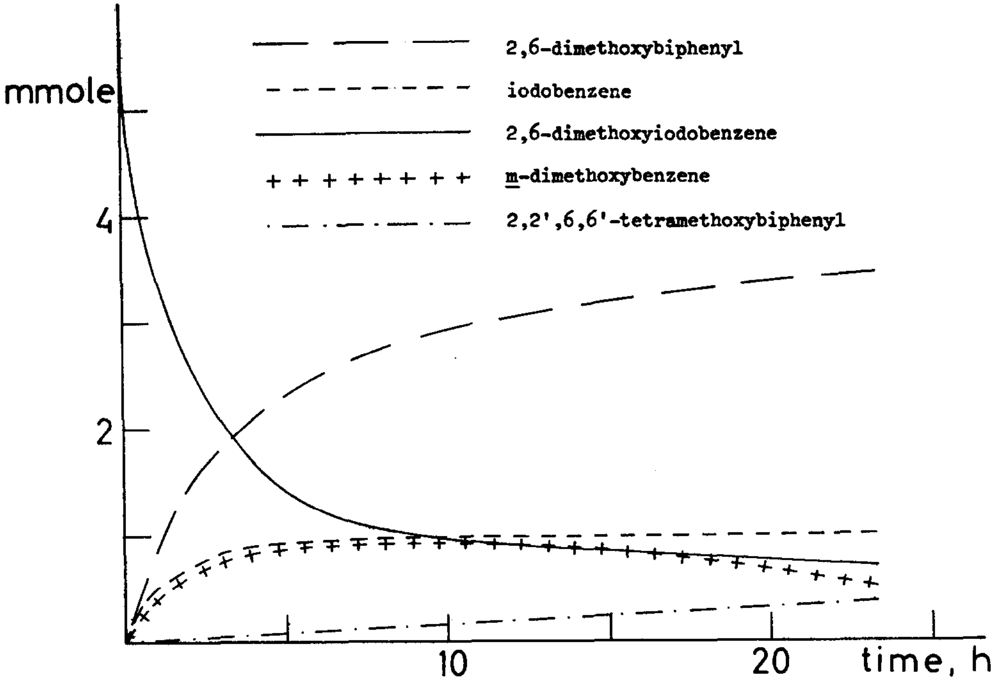

FIG. 1

Reaction between phenylcopper and 2,6-dimethoxyiodobenzene at 50° in quinoline.

anisole, was formed in parallel with iodobenzene, reached a maximum (30 % yield) after 75 h at 20°, and slowly disappeared when the temperature was raised. After the reaction was complete, the products were isolated by chromatography on silica gel and identified by comparison with authentic material (IR, GLC and, when possible, m.p. also). The products formed were: iodobenzene (40 %), biphenyl (13 %), 2-methoxybiphenyl (30 %) and 2,2'-dimethoxybiphenyl (40 %). The yields are based on GLC measurements. Phenylcopper and methyl o-iodobenzoate (10 mmole each, 20°, 20 h, quinoline) gave methyl 2-biphenylcarboxylate (1,7 mmole) and dimethyl diphenate (1.7 mmole). The products were separated on silica gel and identified by IR and m.p. or b.p. Essentially analogous results were obtained from the reaction between phenylcopper and 2-iodonitrobenzene in quinoline (identifications by GLC only). Phenylcopper and 2-fluoroiodobenzene (13.5 mmole each, 40°, 40 h, quinoline) gave 2-fluorobiphenyl (3.5 mmole) and 2,2'-difluorobiphenyl (4.0 mmole). The isolated products were identified by IR and m.p. Copper(I) iodide was the dominant copper-containing product in all reactions in pyridine and quinoline solutions. The main source of error could be the formation of benzene from phenylcopper. The yields obtained show that this error cannot be severe and will not affect the conclusions.

The experimental results show that the medium has a decisive influence on the reactions of phenylcopper. The dimerisation (reaction 1) is most marked in DMF and is less important in pyridine and quinoline solutions. The reactions of phenylcopper with iodoarenes which lead to unsymmetric coupling (reaction 2) and metal-halogen exchange (reaction 3) are clearly favoured in solvents, like pyridine and quinoline, which can be expected to solvate phenylcopper. The resulting complexes may be analogous to those described between phenylcopper and triphenylphosphine.(10) The simultaneous occurrence of metal-halogen exchange and coupling so far makes a comparison between these reactions difficult.

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