# Reactions of Phenylcopper with Iodobenzenes

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Phenylcopper reacts with iodobenzenes at moderate temperature in pyridine or quinoline to form unsymmetrical biphenyls and copper(I) iodide. Simultaneously, copper-iodine exchange occurs giving iodobenzene and an arylcopper compound. Further coupling reactions lead to the formation of biphenyl and symmetrically substituted biphenyls also. Strongly electron-attracting groups such as nitro- or methoxycarbonyl *ortho* to iodine in the iodobenzene increase the reaction rates significantly. The influence of the solvent on the reactions is discussed together with some possible reaction mechanisms.

Phenylcopper was first obtained as an impure product from phenyl-magnesium bromide and copper(I) iodide.[1] Recently, Costa and co-workers have prepared it in almost pure form and characterised it by infrared spectroscopy.[2] Phenylcopper is sensitive to air and moisture. It decomposes slowly at room temperature to biphenyl and copper (reaction 1).

$$Ph-Cu \longrightarrow 1/2\ Ph-Ph + Cu \tag{1}$$
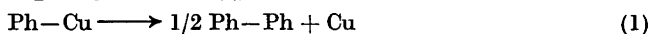
Phenylcopper reacts with acid chlorides or allyl bromide to form new carbon-carbon bonds and copper(I) halide.[3]
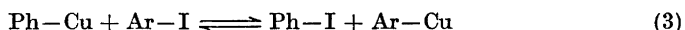
Arylcopper compounds have been suggested as intermediates in the Ullmann reaction [4] and other copper-promoted reactions involving iodo-arenes.[5,6] We have therefore investigated the reactions between phenylcopper and iodobenzenes. Part of the work has been reported briefly.[7]

Phenylcopper is soluble in pyridine or quinoline. In these solvents it decomposes slowly at 50° to copper and biphenyl. This reaction is markedly faster in dimethylformamide suspension.[7]

Phenylcopper reacts with iodobenzenes in pyridine or quinoline forming unsymmetrical biphenyls and copper(I) iodide (reaction 2).

$$Ph-Cu + Ar-I \longrightarrow Ph-Ar + Cu-I \tag{2}$$

Simultaneously, copper-iodine exchange occurs (reaction 3) giving products

$$Ph-Cu + Ar-I \rightleftharpoons Ph-I + Ar-Cu \tag{3}$$

which may react further. Both iodobenzene and intermediate arylcopper compounds have been observed during the reaction, the latter as the hydrolysis products, Ar—H.

In the present work we have investigated reactions between phenylcopper and 4-iodoanisole, 2-chloroiodobenzene, 2-iodonitrobenzene and some methyl halogenobenzoates in pyridine solutions at 25 to 50°.

## RESULTS

Reactions of phenylcopper with substituted iodobenzenes in all cases led to formation of three biphenyls. The experimental results are summarised in Table 1. Copper(I) iodide was the only copper-containing end-product ob-

*Table 1.* Yields (%) of products from reactions between phenylcopper and iodobenzenes in pyridine (p) or quinoline (q). The starred yields are based on GLC measurements.
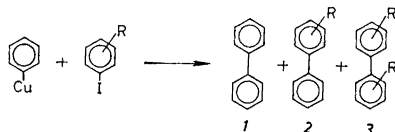
| R | 1 | 2 | 3 | Temp. | Solvent |
|---|---|---|---|---|---|
| 4-D | 15 | 30 | 15 | 50 | p, q |
| 2-OCH$_3$ | 15* | 33* | 38* | 25—40 | q |
| 4-OCH$_3$ | 36 | 36 | 10 | 50 | p |
| 2,6-(OCH$_3$)$_2$ | 10* | 60* | 14* | 50 | q |
| 2-F | not isolated | 26 | 59 | 40 | q |
| 2-Cl | 23* | 44* | 31* | 50 | p |
| 2-NO$_2$ | 48 | 18 | 49 | 25 | p |
| 2-COOCH$_3$ | 33 | 28 | 36 | 25 | p |
| 4-COOCH$_3$ | 12 | 29 | 7 | 25 | p |

served except for the formation of some metallic copper in the reaction with 4-iodoanisole. Reactions 2 and 3 are thus important but reaction 1 can compete when an unreactive iodobenzene is used. Some of the reactions were followed by GLC and arylcopper compounds and iodobenzene resulting from metal-halogen exchange could be observed. This has been reported for the reactions with 2-iodoanisole and 2,6-dimethoxyiodobenzene.[7] A similar result was also obtained from the reaction between phenylcopper and 2-chloroiodobenzene (Fig. 1).

Besides the expected products shown in Table 1 and Fig. 1 minor amounts of three terphenyls and three quaterphenyls were formed. These products are probably *o*-terphenyl, 2-chloro-*o*-terphenyl, 2,2″-dichloro-*o*-terphenyl, *o,o′*-quaterphenyl, 2-chloro-*o,o′*-quaterphenyl and 2,2‴-dichloro-*o,o′*-quaterphenyl. The unexpected formation of terphenyls and quaterphenyls
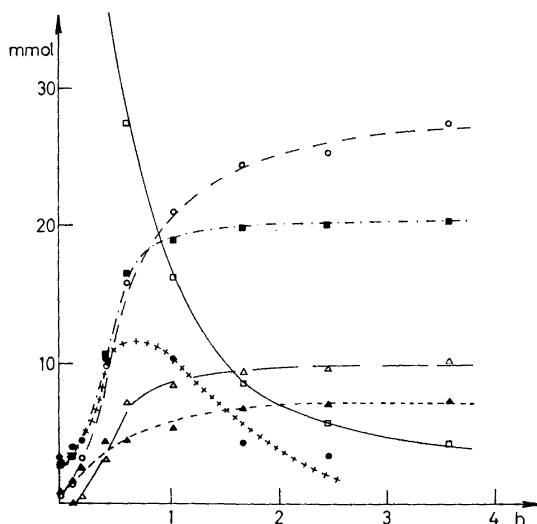
*Fig. 1.* Reaction between equimolar amounts (65 mmol) of phenylcopper and 2-chloro-iodobenzene in pyridine (150 ml) at 50°.
○ 2-chlorobiphenyl, ■ iodobenzene, △ 2,2'-dichlorobiphenyl, ▲ biphenyl, □ 2-chloro-iodobenzene, ● 2-chlorophenylcopper.

indicates that coupling occurs between phenylcopper or 2-chlorophenylcopper and a halogenoarene. However, no reaction product except biphenyl was observed from phenylcopper and *o*-dichlorobenzene or 2,2''-dichlorobiphenyl. Reactions of benzyne, formed by elimination of copper(I) chloride from 2-chlorophenylcopper, could also lead to polyphenyls. The formation of these complex products is reminiscent of complications in the Ullmann reaction of 2-chloroiodobenzene[4] and may warrant further investigation.

Nitro- and methoxycarbonyl groups *ortho* to the halogen in halobenzenes increase the reaction rates significantly. Similar *ortho* effects are well known in the Ullmann reaction[4] and also in copper-catalysed halogen exchange in haloarenes.[8] The same groups in the *para* position have only a moderate effect on the rates of these reactions. The influence of *ortho* and *para* substituents was further compared by a competetive reaction between equimolar amounts of phenylcopper, methyl 2-iodobenzoate and methyl 4-iodobenzoate. Phenyl-copper reacted almost selectively with the *ortho* isomer to methyl 2-biphenyl-carboxylate, dimethyl diphenate, and dimethyl 2,4-biphenyldicarboxylate. Here, however, in contrast to earlier cases, 2-methoxycarbonylphenylcopper or iodobenzene could not be detected and thus, if formed, did not accumulate.

Surprisingly large amounts of biphenyl are formed in the reactions with 2-iodonitrobenzene or methyl 2-iodobenzoate. Phenylcopper also reacts slowly with methyl 2-bromobenzoate to give biphenyl, methyl 2-biphenyl-carboxylate and traces of dimethyl diphenate. Copper(I) bromide and metallic copper were formed. We did not observe any reaction between phenylcopper and methyl 2-chlorobenzoate.

## DISCUSSION

Little is known about the mechanisms of arylcopper reactions. Decompositions of phenylcopper and 4-tolylcopper in ether-xylene mixtures to copper and biphenyls have been suggested to proceed *via* free radicals,[9] whereas copper(II) species have been proposed as intermediates in thermal and oxidative coupling reactions of the more stable fluorinated arylcopper compounds.[10] 4-Tolylcopper has also been reported as a long-lived intermediate in the Ullmann reaction of 4-iodotoluene in 8-methylquinoline at 190°;[11] such a high stability of an organocopper compound is, however, in contrast to other findings and may be questioned.

Phenylcopper can possibly be regarded as a co-ordination polymer and is insoluble in most solvents. Tertiary phosphines such as tributyl- and triphenylphosphine have a moderately stabilising and markedly solubilising effect on phenylcopper and probably reduce the polymer to lower aggregates.[12]

Phenylcopper dissolves exothermally in pyridine or quinoline. These solvents seem to stabilise phenylcopper with respect to decomposition (reaction 1) and to increase its reactivity towards halogenobenzenes and polynitroarenes.[13] This seems to be analogous to the effect of strong complexing agents such as tetramethylethylenediamine on the reactivity of organolithium compounds.[14] The basic ligands have been considered to polarise the lithium-carbon bond and thus to increase the nucleophilic character of the carbon atom. Another suggestion is that complexing agents favour the monomeric organolithium compounds in solution and this increases the reactivity.[15] Analogous explanations could also be considered for the influence of "soft" bases on phenylcopper reactions. As phenylcopper is prepared from phenyllithium, lithium contamination could affect some of the results.

Further insight into the solvent effect can be obtained by the following reasoning. If reaction 1 is subtracted from reaction 2 the result will be the Ullmann biaryl synthesis (reaction 4). This reaction is usually run at 150—250° with or without solvents. It is reasonable to assume that the free energy

$$Ar-I + Cu \longrightarrow 1/2Ar-Ar + Cu-I \qquad (4)$$
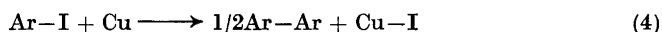
change for the reaction is negative even at room temperature and thus that reaction 2 is energetically more favoured than reaction 1. However, a complexing solvent is needed for reaction 2 which leads to the conclusion that the dominating effect of the solvent is to reduce the free energy of activation for the reaction rather than to reduce the energy of the products by forming complexes with them.

Substituents in the iodobenzene affect the reaction rates markedly. The approximate order of increasing reactivity towards phenylcopper for various substituents is: 4-methoxy, 2,6-dimethoxy, 2-methoxy, none, 2-chloro, 2-fluoro, 4-methoxycarbonyl, 2-methoxycarbonyl, and 2-nitro. Essentially the same order has been observed in reactions between 2-thienylcopper and iodobenzenes.[16]

The position of equilibrium for the reversible metal-halogen exchange reaction depends on the thermodynamic stabilities of the arylcopper compounds as well as of the halogenobenzenes. Stabilisation by interaction between

copper and a hetero atom seems to be important in 2-thienylcopper,[16] 2-methoxyphenylcopper,[17] and 2,6-dimethoxyphenylcopper.[13] A similar effect has been observed for fluorinated organocopper compounds.[10] Determination of the relative stabilities of arylcopper compounds is important in predicting the outcome of metal-halogen exchange with halogenobenzenes. For synthesis of unsymmetrical biaryls the reactants may then be chosen so as to reduce the metal-halogen exchange and thus to increase the yields. Extreme cases are pentafluorophenylcopper [10] and 2-thienylcopper [16] which react almost selectively with iodoarenes to unsymmetrical biaryls (reaction 2).

The high reactivity of positions *ortho* to nitro and methoxycarbonyl groups in copper-promoted reactions indicates that short-range interactions between the substituents and the copper species are important. Such interactions may decrease the energy of he transition state. The latter may be similar to a $\sigma$-complex. In fact arylcopper compounds react with *m*-dinitrobenzene and 1,3,5-trinitrobenzene to intensely coloured, rather stable $\sigma$-complexes.[13]

Unsymmetrical coupling (reaction 2) and copper-iodine exchange (reaction 3) are both favoured by solvents such as pyridine or quinoline. It is possible that these reactions proceed *via* a common intermediate or similar transition states in which interactions between copper and the aromatic $\pi$-electrons are important. It is tempting to speculate about the nature of such intermediates. One plausible geometry for the transition state would be a tetrahedron (Fig. 2). Such a model may account also for the influence of *ortho* substituents.
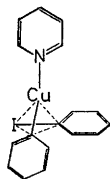


Fig. 2. One plausible geometry for the transition state in the reaction between phenylcopper and iodobenzenes in pyridine.

Stable complexes between copper(I) chloride, triphenylphosphine and organic halides have been reported recently.[18] Similar interactions between arylcopper compounds and organic halides should be considered when mechanisms for such copper-promoted reactions are discussed.

### EXPERIMENTAL

Solvents were freshly distilled before use, ether from lithium aluminium hydride, pyridine (AR) and quinoline (purified) from phosphorus pentoxide. Quinoline was purified from neutral impurities *via* acid extraction.

Phenylcopper was prepared essentially according to Costa *et al.*[2] and handled under dry oxygen-free nitrogen.

*General procedure.* Equimolar amounts of phenylcopper and halogenoarenes were dissolved in cooled pyridine or quinoline under vigorous stirring. A two-necked flask flushed with nitrogen and equipped with a silicon rubber membrane was used as reaction vessel. The temperature was maintained by a termostated oil bath.

Usually small aliquots were withdrawn from the reaction mixture by a syringe, hydrolyzed with dilute acid and extracted with benzene. The organic phase was analyzed by gas chromatography.

After completion of the reaction the mixture was diluted with ether and the copper(I) halide filtered off. The basic solvent was removed by acid extraction. The ether phase was dried over anhydrous sodium sulphate and the solvent evaporated. The residue was separated by chromatography on silica gel with mixtures of light petroleum (b.p. 40—60°) and toluene. The products were identified by comparison with authentic samples (m.p. and IR).

*4-Iodoanisole.* Phenylcopper (2.05 g) and 4-iodoanisole (2.60 g) were allowed to react for 47 h at 50° in 50 ml pyridine. Isolated products were: biphenyl (0.40 g, 36 %), 4-methoxybiphenyl (0.74 g, 36 %), 4,4'-dimethoxybiphenyl (0.12 g, 10 %) and unreacted 4-iodoanisole (0.65 g, 25 %).

*2-Iodonitrobenzene.* Phenylcopper (1.49 g) and 2-iodonitrobenzene (2.0 g) were allowed to react for 20 h at 25° in 40 ml pyridine. The exothermal reaction was, however, completed in 5 min. Isolation and separation of the reaction mixture gave biphenyl (0.39 g, 48 %), 2-nitrobiphenyl (0.28 g, 18 %) and 2,2'-dinitrobiphenyl (0.48 g, 49 %).

*Methyl 2-iodobenzoate.* Phenylcopper (1.31 g) and methyl 2-iodobenzoate (2.10 g) were allowed to react for 20 h at 25° in 40 ml pyridine. Analysis of small samples withdrawn during the reaction showed that the reaction was complete in one hour. Biphenyl (0.19 g, 33 %), methyl 2-biphenylcarboxylate (0.48 g, 28 %) and dimethyl diphenate (0.39 g, 36 %) were isolated.

*Methyl 4-iodobenzoate.* Phenylcopper (0.91 g) and methyl 4-iodobenzoate (1.69 g) were allowed to react for 20 h at 25° in 25 ml pyridine. Isolation of the products gave: biphenyl (0.06 g, 12 %), methyl 4-biphenylcarboxylate (0.40 g, 29 %), dimethyl 4,4-biphenyldicarboxylate (0.06 g, 7 %) and unreacted methyl 4-iodobenzoate (0.46 g, 27 %).

*Methyl 2-bromobenzoate.* Phenylcopper (4.75 g) and methyl 2-bromobenzoate (7.13 g) were allowed to react for 24 h at 50° in 150 ml pyridine. Biphenyl (0.55 g, 21 %), methyl 2-biphenylcarboxylate (2.0 g, 28 %), dimethyl diphenate (0.15 g, 3 %) and unreacted methyl 2-bromobenzoate (2.9 g, 41 %) were isolated from the reaction mixture.

*Methyl 2-iodobenzoate and methyl 4-iodobenzoate.* Phenylcopper (2.44 g), methyl 2-iodobenzoate (4.54 g) and methyl 4-iodobenzoate (4.54 g) were allowed to react for 20 h at 25° in 50 ml pyridine. Some methyl 4-iodobenzoate (2.6 g) was recovered after evaporation of the ether. The residue was separated by chromatography on silica gel to give: biphenyl (0.1 g, 7 %), methyl 2-biphenylcarboxylate (1.38 g, 38 %), a mixture of dimethyl diphenate and dimethyl 2,4-biphenyldicarboxylate (0.9 g) and a mixture of unreacted methyl iodobenzoates (0.5 g). The ester mixtures were hydrolysed with ethanolic alkali and the acids were separated by crystallisation from ethanol-water. Diphenic acid (0.35 g, 17 %) and 2,4-biphenyldicarboxylic acid (0.23 g, 11 %), m.p. 292—94° subl.) were isolated. The structure of the latter was checked by NMR spectroscopy. Of the added methyl 4-iodobenzoate 60 % could be recovered (as acid or ester) whereas the corresponding figure for methyl 2-iodobenzoate was 8 %.

*2-Chloroiodobenzene.* Phenylcopper (9.2 g) and 2-chloroiodobenzene (15.6 g) were allowed to react for 20 h at 50° in 150 ml pyridine. Naphthalene (0.50 g) was added as internal standard. Samples from the reaction mixture were analysed by gas chromatography and the peak areas calculated electronically using an automatic digital integrator.

The products were separated on a silica gel column into four fractions. The first contained iodobenzene and unreacted 2-chloroiodobenzene, identified by thin layer and gas chromatography. The second fraction contained three components identified as biphenyl, 2-chlorobiphenyl and 2,2'-dichlorobiphenyl by thin layer and gas chromatography. This was confirmed by mass spectral data from analysis of the mixture on a combined gas chromatograph-mass spectrometer (LKB). The last two fractions (1.37 g and 0.45 g) consisted each of three components. Mass spectra were consistent with three terphenyls and three quaterphenyls with none, one, and two chlorine atoms, respectively. IR spectra of the unsubstituted terphenyl and quaterphenyl isolated by micro-preparative gas chromatography were compared with reported spectra of o-terphenyl and o,o'-quaterphenyl.[19] Our spectra were rather weak but identical with those reported with respect to the strong peaks. The positions of the chlorine atoms have not been proved but it seems most reasonable that they are attached in the 2-positions of the phenyl end groups.

## REFERENCES

1. Reich, R. *Compt. Rend.* **177** (1923) 322.
2. Costa, G., Camus, A., Gatti, L. and Marsich, N. *J. Organometal. Chem.* **5** (1966) 568.
3. Gilman, H. and Straley, J. M. *Rec. Trav. Chim.* **55** (1936) 821.
4. Fanta, P. E. *Chem. Rev.* **64** (1964) 613.
5. Björklund, C. and Nilsson, M. *Acta Chem. Scand.* **22** (1968) 2338.
6. Björklund, C. and Nilsson, M. *Acta Chem. Scand.* **22** (1968) 2585.
7. Nilsson, M. and Wennerström, O. *Tetrahedron Letters* **29** (1968) 3307.
8. Bacon, R. G. R. and Hill, H. A. O. *J. Chem. Soc.* **1964** 1097.
9. Hashimoto, H. and Nakano, T. *J. Org. Chem.* **31** (1966) 891.
10. Cairncross, A. and Sheppard, W. A. *J. Am. Chem. Soc.* **90** (1968) 2186.
11. Lewin, A. H. and Cohen, T. *Tetrahedron Letters* **50** (1965) 4531.
12. Costa, G., Camus, A., Marsich, N. and Gatti, L. *J. Organometal. Chem.* **8** (1967) 339.
13. Björklund, C., Nilsson, M. and Wennerström, O. *To be published.*
14. Coates, G. E., Green, M. L. H. and Wade, K. *Organometallic Compounds*, Methuen, London 1967, Vol. 1, p. 18.
15. Brown, T. M. *Advan. Organometal. Chem.* **3** (1965) 392.
16. Nilsson, M. and Ullenius, C. *Acta Chem. Scand. In press.*
17. Camus, A. and Marsich, N. *J. Organometal. Chem.* **14** (1968) 441.
18. Wada, K. and Hashimoto, H. *Bull. Chem. Soc. Japan* **42** (1969) 562.
19. Dale, J. *Acta Chem. Scand.* **11** (1957) 640.