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ORGANOCOPPER INTERMEDIATES IN THE EXCHANGE REACTION OF ARYL HALIDES WITH SALTS OF COPPER(I). THE POSSIBLE ROLE OF COPPER(III)

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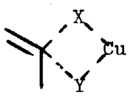
In 1966, Cohen and Lewin provided evidence that the newly discovered preparation of aryl and vinyl benzoates from aryl and vinyl halides by treatment with cuprous benzoate proceeds by an organocopper intermediate.[2] However, since that time, none of the mechanistic comment concerning the widely used exchange reaction of aryl and vinyl halides (RX) with the anions (Y^-) of copper(I) salts has mentioned organocopper intermediates.[3-10] Nearly all suggested mechanisms involve a 4-center transition state or intermediate (1)[11] leading directly to exchange products[3-6], or an organic radical intermediate[11] which accepts a ligand radical from a copper(II) salt.[5] The reduction product, arene, which frequently accompanies exchanged material has been attributed to hydrogen atom abstraction by the radical[5,7,8] or to displacement of the halide by a hydride ion.[7,9] We now provide strong evidence against 4-center and radical mechanisms and we demonstrate that these reactions involve an intermediate, almost certainly an organocopper, which may be protonated by acid to the arene or oxidized by Cu(II) to the exchanged material.

In the clean exchange of o-iodo-N,N-dimethylbenzamide (2; X = I) with CuCl and CuCN in refluxing DMF, the addition of benzoic acid results in the formation of N,N-dimethylbenzamide (2; X = H) as well as exchanged product (2; X = Cl or CN). In the CuCl reaction, added $CuCl_2$ counteracts the effect of benzoic acid; the ratio of aryl chloride to arene produced is directly proportional to $[CuCl_2]$ at constant $[C_6H_5CO_2H]$ and inversely proportional to $[C_6H_5CO_2H]$ at constant $[CuCl_2]$. The competitive protonation and chlorination of the intermediate was also illustrated by an experiment in which excess benzoic acid, but not cupric chloride, was present; the stoichiometry is such that $[CuCl_2]$ increases as the reaction progresses, and, as expected, the ratio of aryl chloride to arene produced increased throughout the experiment. An intermediate, other than an organocopper compound, which could display such behavior is very difficult to formulate. Arylcopper(I) compounds[12] (eg. 2; X = Cu) are known to become protonated by carboxylic acids[13] and we have now demonstrated the halogenation process by the chlorination and bromination of pentafluorophenylcopper[14] by CuCl$_2$ and CuBr$_2$, respectively. The presence of the intermediate precludes a direct 4-center exchange of nucleophiles.



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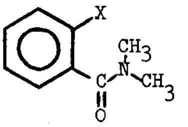

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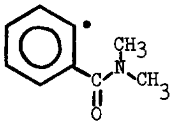

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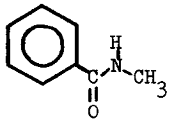

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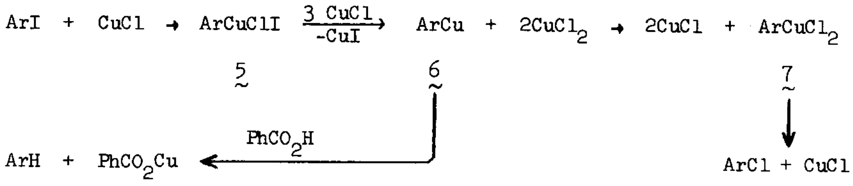
Radical intermediates are precluded by the absence of N-methylbenzamide (4) in the products of exchange of 2 (X = I) with CuCl, CuCN (both in DMF) and CuOBz (xylene) and of 2 (X = Br) with CuOBz (xylene).[15] Previously, it had been shown that the aryl radical 3 undergoes an extremely rapid hydrogen atom abstraction from the methyl group resulting in loss of the latter to give 4 and CH$_2$O.[16] When the radical 3 was generated in DMF by treatment of the corresponding diazonium (2; X = N_2^+) fluoborate[16] with CuCl in the presence of a concentration of CuCl$_2$ far exceeding the maximum possible in the exchange reaction of the iodide with CuCl, the product consisted of N-methylbenzamide (4; 80%), *o*-chloro-N,N-dimethylbenzamide (2, X = Cl; 15%), arising by chlorine abstraction from CuCl$_2$,[17] and some reduction product 2 (X = H). Thus, production of radical 3 during the exchange would certainly result in substantial formation of 4. The absence of a radical intermediate can also be inferred, with somewhat less certainty, from the retention of configuration observed in the exchange of vinyl halides with CuCN,[18] in view of the stereochemical instability of vinyl radicals.[19]

The two-electron reduction suffered by the carbon atom bearing the halogen upon conversion to an organocopper can not be readily explained by a pair of one-electron reductions of the aryl iodide without invoking production of an aryl radical. A two-electron reduction is thus indicated and it is thus probable that copper(I) is converted directly to copper(III)[20a] in this process. We propose the oxidative addition[20b] of the carbon-halogen bond to the cuprous chloride to form the copper(III) organometallic 5, reduction of which by cuprous chloride leads to an organometallic of lower oxidation state written here as the copper(I) species 6; oxidation of the latter by cupric chloride presumably occurs via the copper(III) compound 7 which could reductively eliminate[20b] cuprous chloride to produce the aryl chloride.[21]



$$\begin{tikzcd}[column sep=small] \mathrm{ArI} + \mathrm{CuCl} \arrow[r] & \underset{5}{\mathrm{ArCuClI}} \arrow[r, "3\,\mathrm{CuCl}", "-\mathrm{CuI}"'] & \underset{6}{\mathrm{ArCu}} \arrow[d, "\mathrm{PhCO_2H}"] + 2\mathrm{CuCl_2} \arrow[r] & 2\mathrm{CuCl} + \underset{7}{\mathrm{ArCuCl_2}} \arrow[d] \\ \mathrm{ArH} + \mathrm{PhCO_2Cu} & & \arrow[ll] & \mathrm{ArCl} + \mathrm{CuCl} \end{tikzcd}$$

There have been several recent suggestions of organocopper(III) intermediates,[17,22,23] some of them[22] formed by nucleophilic attacks which are essentially oxidative additions. In each of these latter cases, as is believed to be so with oxidative additions in general,[20b,21] the d electrons of the metal are believed to execute a nucleophilic attack on the substrate; such attack in the present case, with its consequent accumulation of negative charge on the ring and relief of crowding, could account in part for the great accelerating effect of the ortho nitro group in the exchange reaction.[3,4b,11] The retention of stereochemistry in vinyl systems[18] is also expected from this mechanism since oxidative addition of vinyl halides apparently occurs with complete retention.[24] In a subsequent publication we shall comment upon the applicability of this type of scheme to the Ullmann coupling of aryl and vinyl halides.[19] It is becoming increasingly evident that the great utility of copper reagents in organic chemistry is largely due to the availability of the copper(III) state and the bond formation which accompanies reductive elimination from this state.

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