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The Reaction of Bromobenzene with Copper(I) Chloride - Pyridine Complex in Nitrobenzene

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The Rosenmund - von Braun nitrile synthesis has been little studied from the viewpoint of its mechanism in spite of its usefulness as a synthetic procedure. Recently Bacon and Hill[1] investigated the substituent effect and the solvent effect in the reaction of aryl halide with copper(I) salts in polar solvents. However, the real reactive species were not elucidated. Ito and Watanabe[2] studied the kinetics of this reaction in nitrobenzene and pointed out an important role of the complexes of copper(I) salt and pyridine bases in the reaction. It was found that pyridine bases and copper(I) salt produced a 1 : 1 complex, and that the structure of pyridine bases affected the rate of the reaction. These results suggest that the Rosenmund - von Braun reaction and its related reactions must be reexamined in view of the reaction between organic halide and metal complex. Thus, the reaction of bromobenzene with copper(I) chloride - pyridine complex in nitrobenzene was investigated from this point of view.

Results and Discussion

It has already been reported that the reaction of bromobenzene with copper(I) cyanide - pyridine complex is second-order, that is, first-order in each of bromobenzene and copper(I) cyanide - pyridine complex.[2] Therefore, we determined the activation parameter of this reaction in order to obtain further information concerning this reaction. The second-order rate constants in the reaction of bromobenzene with copper(I) chloride - pyridine complex[*1] were measured in nitrobenzene at several temperatures. The results are summarized in Table 1. The activation enthalpy ($\Delta H^{\neq}$) of the reaction was calculated from the data in the table to be 8.6 kcal/mol, and the activation entropy ($\Delta S^{\neq}$), to be -38.4 e.u. (at 160°C). The activation enthalpy obtained in this study is not an unusual value in comparison with those of other reactions

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[1] R. G. R. Bacon and H. A. O. Hill, *J. Chem. Soc.*, **1964**, 1097.

[2] T. Ito and K. Watanabe, This Bulletin, **41**, 419 (1968).

[*1] This complex is insoluble in hydrocarbons and alcohols, but soluble in nitrobenzene, nitromethane, acetonitrile, pyridines, and dimethyl sulfoxide. The halogen-exchange reaction could not take place in nitromethane and acetonitrile at temperatures below their boiling points.

Table 1. The rate constants at various temperatures[a]

Temperature (°C)	k (l/mol·sec)
155.0	2.29
160.0	3.11
165.0	4.08
170.0	5.45
175.0	7.31

a) Bromobenzene, 1.0 ml; pyridine, 1.0 ml; copper(I) chloride, 0.94 g; nitrobenzene, 40 ml.

between organic halides and metal complexes. For example, the activation enthaply of the reaction of benzyl chloride with chromium(II) salt[3] is 14.0 kcal/mol, and that of the reduction of chloropentaamminechromium(III) complex with chromium(II) salt[4] is 11.1 kcal/mol. The transition these reaction is suggested to be a halogen-bridged state of activated complex (**1**) or (**2**):

$$[\mathrm{ArCH_2}\cdots\mathrm{Cl}\cdots\mathrm{Cr_{aq}}]^{2+} \qquad [(\mathrm{NH_3})_5\mathrm{Cr}\cdots\mathrm{Cl}\cdots\mathrm{Cr_{aq}}]^{2+}$$

(**1**) (**2**)

The activation entropy of the reaction described above is -14.3 e.u. in the former[3] and -23 e.u. in the latter.[4] The larger negative activation entropy obtained in the present study supports the hypothetical four-center type (or double-bridge) transition state previously proposed.[2]

A similar halogen-exchange was observed in the reactions of bromoferrocene with copper(I) halide - pyridine complex.[5] The reactions took place in nitrobenzene, as well as in nitromethane and acetonitrile, at much lower temperatures than those at which the halogen-exchange reactions of bromobenzene could be observed.[6] In the reactions of bromoferrocene, an astonishing solvent effect was observed that can be explained not by the solvation but only in terms of the difference in the coordination-ability of the solvent toward the copper(I) ion.[6]

The Rosenmund - von Braun reaction takes place with ease in pyridine or quinoline,[7] and the halogen-exchange of aryl halide with copper(I) chloride proceeds easily in α-picoline.[8] 3-Halopyridine is converted more easily with copper(I) cyanide to 3-cyanopyridine than is halobenzene.[9] These facts led us to a detailed investigation of the role of the pyridine base as a ligand in the intermediate complex in the reaction between bromobenzene and copper(I) chloride - pyridine base complex in nitrobenzene. When an equimolar amount of 4-methyl-, 3-methyl-, 2-methyl-, 3-acetyl-, or 4-methoxycarbonylpyridine was added to a mixture of nitrobenzene and copper(I) chloride at 160°C, a clean homogeneous solution was obtained, while 4-cyano-, 3-cyano-, or 3-chloropyridine gave a complex insoluble in nitrobenzene. In the latter cases, the observed second-order rate constants for the halogen-exchange reaction showed considerably deviating results. This is probably due to the insolubility of the copper(I) chloride - pyridine base complex (**3**) caused by the enhanced ionic character of the complex, which is brought about by an N←Cu back donation when an electron-attracting group is introduced to the pyridine nucleus coordinated to the copper atom in the complex. The results of the kinetic measurements using various pyridine bases are shown in Table 2.

Table 2. The effect of substituents on pyridine bases[a]

Substituent	k (l/mol·min)[b]	k (l/mol·min)[c]
4-CH_3	5.2×10^{-2}	
3-CH_3		6.3×10^{-2}
H	4.3×10^{-2}	6.6×10^{-2}
4-$COOCH_3$	3.5×10^{-2}	
3-$COCH_3$		5.4×10^{-2}

a) Bromobenzene, 1.0 ml; nitrobenzene, 40 ml; copper(I) chloride, 0.94 g; pyridine bases, equimolar amount to copper(I) chloride.

b) Temperature, 160.2°C.

c) Temperature, 166.0°C.

The results are quite consistent with the observation by Ito and Watanabe.[2] The relative rate constants are in an almost linear relation to the pK_a's of the bases except for the case of 3-methylpyridine. This suggests that the reaction is accelerated by the strong coordination of pyridine bases to the metal in the complex (**3**).

Contrary to the favorable behavior of 4-methylpyridine, 2-methylpyridine was found to suppress the halogen-exchange reaction of bromobenzene; this fact has been explained in terms of steric hindrance of the methyl group at the 2-position toward the coordination of the pyridine base to copper(I) chloride.[2] A large size of a copper atom will cause a F-strain, proposed by Brown,[10] to the methyl group of 2-methylpyridine. Thus, the nitrogen atom of the pyridine base can be expected to coordinate more weakly to the copper

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[3] J. H. Kochi and D. D. Davis, *J. Amer. Chem. Soc.*, **86**, 5264 (1964).

[4] H. Taube and A. Ogard, *ibid.*, **80**, 1084 (1958).

[5] M. Sato, T. Ito, I. Motoyama, K. Watanabe and K. Hata, This Bulletin, **42**, 1976 (1969).

[6] M. Sato, I. Motoyama and K. Hata, *ibid.*, **43**, 1860 (1970).

[7] N. Akanuma, H. Amemiya, T. Hayashi, K. Watanabe, and K. Hata, *Nippon Kagaku Zasshi*, **81**, 333 (1960).

[8] W. B. Hardy and R. B. Fortenbaugh, *J. Amer. Chem. Soc.*, **80**, 1716 (1958).

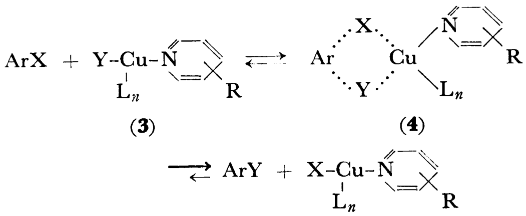
[9] L. C. Craig, *ibid.*, **56**, 231 (1934).

[10] H. C. Brown, *J. Chem. Soc.*, **1956**, 1248.

atom in the copper(I) salts - pyridine complex. In any case, it can be concluded that the weak coordination by steric and/or electronic factors brings about a retardation of the reaction of bromobenzene with copper(I) chloride - pyridine complex.

On the other hand, the effect of the substituents in pyridine bases upon the rates of halogen-exchange reactions between bromoferrocene and copper(I) chloride - pyridine complexes was found to be the opposite of that in the reactions of bromobenzene.[6]

The correlation of rate constants with the coordination abilities of pyridine bases may be explicable in terms of the four-center (double-bridge) mechanism which has been proposed in the preceding paper.[2] In the first stage, aryl halide will coordinate to the copper(I) chloride - pyridine complex (**3**) to form a metastable intermediate $(\mathrm{ArX}\rightarrow\mathrm{CuY}\langle^{\mathrm{Py}}_{\mathrm{L}_n})$. Such coordination is reasonable, because the complex, in which aryl halide coordinates to a certain transition metal, has been isolated.[11] The intermediate will turn into the final product through a four-center-type transition state (**4**). In the transition state (**4**), the increase in electron density on the copper atom will facilitate the attack of the halogen atom Y on the carbon atom in the aromatic nucleus (Y→C attack). Thus, an electron-releasing substituent on the pyridine base will accelerate the halogen-exchange reaction. The importance of the Y→C attack is also suggested by the fact that the substituent effect in the reaction of the substituted aryl halide with the copper(I) complex was found to be somewhat nucleophilic.[1,5] On the contrary, the increase in electron density on the copper atom of the complex (**3**) will retard the attack of the halogen atom X on the copper atom in the complex (**3**) (X→Cu attack). Thus, the rate of the halogen-exchange reaction may be regulated by two counteracting factors, that is, the promotion of the Y→C attack and the retardation of the X→Cu attack. The contradiction between these two factors results in the facts that the effect of the substituent on both the aryl halide and pyridine bases upon the reaction rate is not so remarkable as in the ordinary substitution reactions. There would be a certain balance between the Y→C attack and the X→Cu attack. The reactions between bromobenzene and copper(I) chloride - pyridine base complex in nitrobenzene seem to be governed by the ease of the Y→C attack rather than by the X→Cu attack.



L = Pyridine base and/or solvent

Experimental

Materials. Copper(I) chloride was prepared from commercial copper(II) chloride according to the literature.[12] Pyridine bases and nitrobenzene were purified by distillation under reduced pressure.

Kinetic Measurements. A typical procedure was as follows. In a 100-m*l*, three-necked, round-bottomed flask fitted with a sealed stirrer, a thermometer, a nitrogen-inlet tube, and a reflux condenser, were placed 40 m*l* of nitrobenzene, 0.94 g of copper(I) chloride, and 1.0 m*l* of pyridine. The contents were heated to 160°C on an oil bath. When the temperature was regulated to be constant (160±0.1°C), 1 m*l* of bromobenzene was added to the mixture. A small quantity of the reaction mixture was taken out every 5 min and analyzed by gas chromatography. From these measurements, the rate constant was calculated by the usual way.

Gas Chromatography. Apparatus: Ohkura Model 1100; column, 10% Carbowax 1500 on Celite; length, 3.5 m; temperature, 140°C; flow rate, 4 m*l*/min; carrier gas, H_2.

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[11] W. Reppe and W. J. Schweckendiek, *Ann. Chem.*, **560**, 110 (1948).

[12] H. S. Booth, "Inorg. Syntheses," Vol. II, p. 1 (1946).