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Reactions of Haloferrocenes. II.[1] Kinetic Studies of the Reaction of Haloferrocene with Copper(I) Chloride - Pyridine Complex

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The reaction of bromoferrocene with copper(I) chloride - pyridine complex was found to be second-order, that is, first-order in each of bromoferrocene and copper(I) chloride-pyridine complex. The results obtained from the competitive reactions between bromoferrocene and bromobenzene indicated that bromoferrocene was 10^3 times more reactive than bromobenzene in the halogen-exchange reaction. The effects of the pyridine bases on the halogen-exchange reaction of bromoferrocene were examined, and the trend of the results was found to be different from that of bromobenzene. The reason for this was discussed on the basis of the reaction mechanism.

In a previous paper,[1] we reported that, when haloferrocene was treated with copper(I) salt in boiling pyridine, a halogen-exchange reaction easily occurred. According to this procedure, chloro-, bromo-, and cyanoferrocene were prepared in high yields by treating iodoferrocene with copper(I) chloride, bromide, and cyanide respectively. Since the reaction of *p*-substituted halobenzene with copper(I) salt is facilitated by an electron-withdrawing group,[2,3] this reaction is generally regarded as a nucleophilic substitution.[4] In contrast with halobenzene, the reaction of haloferrocene with copper(I) salt was markedly retarded by a heteroannularly-substituted electron-withdrawing group. This interesting observation, along with the unusually high reactivity of haloferrocene in this reaction, prompted us to a kinetic study of this reaction in the hope of getting some information concerning the reaction mechanism.

Results

As was reported in an earlier paper,[2] the heterogeneous reaction mixture of bromobenzene and copper(I) cyanide in nitrobenzene was turned into a homogeneous solution by the addition of an organic base such as pyridine at 120°C, and the halogen-exchange reaction then took place at 160—180°C. When pyridine was added to the copper(I) chloride in chlorobenzene, a homogeneous solution similarly obtained at 100°C. The subsequent addition of bromoferrocene to the homogeneous solution gave rise to a considerably rapid halogen-

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

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

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

[4] J. F. Bunnett and R. E. Zahler, *Chem. Rev.*, **49**, 273 (1951).

exchange reaction of the bromoferrocene. During this procedure, chlorobenzene used as a solvent did not react with copper(I) bromide which arose from the reaction of bromoferrocene with copper(I) chloride. Hence, this procedure was employed for the kinetic study of the exchange reaction of haloferrocene. The effect of the base/Cu-salt ratio on the reaction rate was investigated by Ito and Watanabe.[2] It was found that, in comparison with the reaction rate when equimolar amounts of the base and the Cu-salt were used, the reaction rate stayed unchanged even if the base/Cu-salt ratio exceeded 1. However, when the base/Cu-salt ratio was less than 1, the reaction rate diminished in proportion to the base/Cu-salt ratio. Therefore, a little excess of pyridine over the copper(I) salt was used in the present experiment. When an excess of copper(I) chloride over bromoferrocene was used, a linear relationship was observed between the yield of chloroferrocene and the reaction time. When the initial concentration of bromoferrocene was kept constant and that of copper(I) chloride was varied, a linear relationship was generally found between the initial rate and the initial concentration of copper(I) chloride, although some deviations were observed. These observations clearly indicate that this reaction is second-order, that is, first-order in each of bromoferrocene and copper(I) chloride. Copper(I) salt and pyridine have been supposed to form a 1 : 1 complex in the reaction mixture.[2] Accordingly, the reaction rate may be represented as follows:

$$d[\mathrm{FcCl}]/dt = k[\mathrm{FcBr}][\text{CuCl-Pyridine Complex}]$$

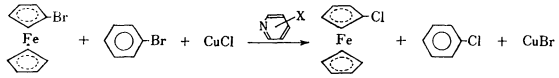
When a pyridine base was added to a heterogeneous mixture of copper(I) chloride and bromobenzene, a homogeneous solution was obtained at 102°C, and the reaction of bromobenzene with copper(I) chloride was observed to occur at this temperature. When bromoferrocene was added to this reaction system, together with bromobenzene, a competitive halogen-exchange reaction between bromoferrocene and bromobenzene was observed. The ratio of the reaction rates of the two halides was determined in such a competitive reaction using α-picoline, γ-picoline, methyl isonicotinate, or pyridine as the pyridine base. On the other hand, when the reactions of bromobenzene with copper(I) chloride in the presence of the cited pyridine bases were carried out using bromobenzene as the solvent and under conditions similar to those used in the competitive reaction, the pseudo first-order rate constants of the reaction were determined. The results of these kinetic studies are shown in Table 1, where k^{2}_{FcBr} and k^{2}_{PhBr} represent the second-order rate constants of bromoferrocene and bromobenzene respectively in the competitive reaction, and where k^{1}_{PhBr} stands for the pseudo first-order rate constant of the reaction of bromobenzene with copper(I) chloride in bromobenzene.

It is clear from Table 1 that bromoferrocene reacts 10^3 times or more faster than does bromobenzene in the reaction using any of these pyridine bases. This observations is qualitatively consistent with the results reported in a previous paper.[1]

In order to see the effect of the pyridine base on the halogen-exchange reaction of bromoferrocene, the k^{2}_{FcBr} values were calculated on the assumption that the coexistence of bromoferrocene will not affect the reaction rate of bromobenzene.[*1] The ratios of the rate constants, k^{2}_{FcBr}, thus obtained for pyridine, α-picoline, γ-picoline, and methyl isonicotinate are 1.00, 1.47, 1.22, and 1.57 respectively.

The solvent effect on the halogen-exchange reactions was examined using three kinds of aprotic polar solvents, that is, nitrobenzene, nitromethane, and acetonitrile. These solvents gave a homogeneous solution with copper(I) chloride, even at a lower temperature (30—50°C), in the presence of an equimolar amount of pyridine. However, in the observation of the kinetics on the reaction of bromoferrocene with copper(I) chloride in these solvents,

Tbale 1. Rate constants of the reactions between bromoferrocene or bromobenzene and copper(I) chloride in the presence of various pyridine bases



Exp. No.	Pyridine base	$k^{2}_{\mathrm{FcBr}}/k^{2}_{\mathrm{PhBr}}$	k^{1}_{PhBr} (min^{-1})	k^{2}_{FcBr}* (l/mol·min)
1	γ-Picoline	1.02×10^{3}	8.10×10^{-3}	8.3
2	α-Picoline	9.4×10^{3}	1.06×10^{-3}	10.0
3	Pyridine	1.15×10^{3}	5.87×10^{-3}	6.8
4	Methyl isonicotinate	3.10×10^{3}	3.45×10^{-3}	10.7

* Calculated from the values of $k^{2}_{\mathrm{FcBr}}/k^{2}_{\mathrm{PhBr}}$ and k^{1}_{PhBr}.

[*1] No appreciable change in the reaction rate was observed on the addition of ferrocene instead of bromoferrocene to the reaction mixture.

Table 2. Solvent effect on the reaction between bromoferrocene and copper(I) chloride-pyridine complex at 50.0°C

Solvent	Dielectric constants[a] (20°C)	Initial rate (mol/l·min)
Nitrobenzene	35.7	5.1×10^{-2}
Nitromethane	37.5	5.7×10^{-2}
Acetonitrile	37.5	6×10^{-4}

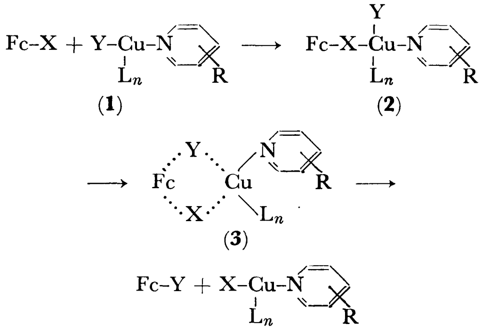
a) J. Hine, "Physical Organic Chemistry," 2nd Ed., McGraw-Hill, Inc., New York (1960), p. 39.

the plots of the rate constant gradually deviated from the second-order relation, unlike as in the reaction using bromobenzene or chlorobenzene as a solvent. Hence, the solvent effects were compared with each other by the initial reaction rates observed in these three solvents, as is shown in Table 2. These results clearly indicate that a remarkable solvent effect is present in the halogen-exchange reaction of bromoferrocene, but no significant correlation was observed between the relative rates and the dielectric constants of these solvents.

Discussion

When iodoferrocene and copper(I) iodide were refluxed in pyridine, iodoferrocene was recovered quantitatively; neither ferrocene nor biferrocenyl, both of which had been expected as the dehalogenation or coupling products, could be detected in the reaction mixture. This is consistent with the observation by Bacon and Hill,[3] who investigated the reaction of chlorobenzene with copper(I) chloride carried out by refluxing in pyridine using an isotopic chloride. The Ullmann coupling reaction of chlorobenzene was also reported not to occur at the boiling temperature of pyridine.[5] On the other hand, when iodoferrocene was treated with activated copper in boiling pyridine, both the coupling product (biferrocenyl) and the dehalogenated product (ferrocene) were isolated.[6] In view of the above facts, the most reasonable conclusion is that neither the ferrocenyl radical nor ferrocenylcopper,[7] which would give biferrocenyl and ferrocene, may be involved as the intermediate in the reaction between haloferrocene and copper(I) salts.

The reaction of bromoferrocene with copper(I) chloride-pyridine complex in chlorobenzene was confirmed to be a second-order reaction, in just the same manner as the reaction of aryl halides with copper(I) salts.[2,3] This fact strongly suggests that the reaction of haloferrocene with copper(I) chloride-pyridine complex proceeds through a process similar to that previously proposed in the benzene series.[2,3] Probably, the halogen atom in haloferrocene coordinates to the copper(I) chloride-pyridine complex (**1**) to form a metastable, reactive intermediate (**2**), which then provides a final product *via* the four-center-type transition state (**3**).



L = Pyridine base or solvent

The above reaction mechanism was strongly supported by a remarkable solvent effect found in this reaction. As is shown in Table 2, the reaction proceeds quickly in nitrobenzene and nitromethane, but slowly in acetonitrile. The observed difference seems to arise from their coordinating ability to produce a copper complex, because there is no significant correlation between the reaction rates and the dielectric constants of the solvents used. The slow reaction rate in acetonitrile may be interpreted as follows: the vacant coordination site of copper(I) chloride will be almost entirely occupied by acetonitrile because of its large affinity for copper(I) ion;[8] thus, the coordination of haloferrocene to copper(I) atom suffers a considerable hindrance, which brings about the fall in the reaction rate. An example of such a solvent effect in the reaction of a metal complex was found in the reaction between *trans*-dichlorobis(pyridine)platinum and the isotopic chloride ion in various solvents.[9] It has been shown that this halogen-exchange reaction proceeds more rapidly in nitromethane as a solvent than in acetonitrile, much as with the present result shown in Table 2.

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5) P. E. Fanta, *Chem. Rev.*, **38**, 139 (1946).

6) M. Sato, I. Motoyama and K. Hata, to be published in the subsequent paper.

7) A. H. Lewin and T. Cohen, *Tetrahedron Lett.*, **1965**, 4531.

8) I. M. Kolthoff and J. F. Coetzee, *J. Amer. Chem. Soc.*, **79**, 1852 (1957).

9) R. G. Pearson, H. B. Gray and F. Basolo, *ibid.*, **82**, 787 (1960).

Recently it was suggested[2)] that the structure of the pyridine base coordinated in the copper(I) complex exerted a definite influence on the reaction of halobenzene with copper(I) salt. The reexamination of this reaction led to the conclusion that the more strongly the nitrogen atom of the pyridine base is coordinated to the copper atom, the more the reaction is accelerated.[10)] The acceleration of the reaction of bromobenzene with copper(I) chloride by γ-picoline, and the retardation of the reaction by methyl isonicotinate, each in comparison with pyridine, were explained by means of studying the electronic effect of the substituent upon the electron density on the nitrogen atom of the base, which might affect the coordination of the base to copper(I) chloride. On the other hand, the retardation by α-picoline was attributed to the steric hindrance to the coordination of the base to copper(I) chloride. A similar trend was also observed in the substituent effect expressed by k^1_{PhBr} in Table 1.

On the contrary, no such trend of the substituent effect was observed in the reactions of bromoferrocene with copper(I) chloride-pyridinebase complexes. Those reactions were accelerated by any of the substituted pyridines examined. However, it is interesting that the trend is the opposite of that of the benzene series. As an exception, γ-picoline accelerates both the reaction of bromobenzene and that of bromoferrocene, but the acceleration in the latter is not so marked as by α-picoline or methyl isonicotinate. The equivocal behavior of the substituted pyridines might be explained by a very delicate and complicated balance among the following factors: (1) the stability of the intermediate (**2**); (2) the ease of the attack of the halogen atom in haloferrocene on the copper atom (X→Cu attack), and (3) the nucleophilicity of the halogen atom of the complex (**2**) toward the carbon atom in the ferrocene ring (Y→C attack). The results of the experiments (Table 1) suggest that the reaction of bromoferrocene with copper(I) chloride-pyridine base complex might be governed rather by the ease of the X→Cu attack in (2) than by the Y→C attack in (3), unlike the similar reaction of bromobenzene.[10)]

The discussion presented above is useful in explaining most of the facts observed in the reaction of bromoferrocene with the copper(I) chloride-pyridine complex, but some difficulties still remain in explaining the fact that bromoferrocene is 10^3 times or more reactive than bromobenzene in this reaction and that heteroannular substituents on bromoferrocene exert a marked electrophilic effect upon this reaction.[1)] It is necessary to consider additional factors specific to the ferrocene series in order to elucidate the mechanism of this reaction further.

Experimental

All of the reactions were operated under an atmosphere of nitrogen.

Procedure for a Competitive Reaction (Table 1, Exp. 3). In a 100-m*l*, three-necked flask fitted with a sealed stirrer, a thermometer, a gas-inlet tube, and a reflux condenser, were placed 1.20 g (4.5 mmol) of bromoferrocene, 0.50 m*l* (5.0 mmol) of pyridine, 30 m*l* of bromobenzene, 0.25 m*l* (2.0 mmol) of ethylbenzene, and 0.70 g (4.5 mmol) of biphenyl. The last two substances were added as the internal standard for gas chromatography, by which process the products were analyzed. The contents were then heated to 102°C on an oil bath. When the temperature was regulated to be constant (102.7±0.1°C), 0.45 g (4.5 mmol) of copper(I) chloride was quickly added to the solution. A small quantity of the reaction mixture was taken out every two minutes and quenched with dilute hydrochloric acid. The organic layer was analyzed by gas chromatography. From the results of these measurements, the ratio of the rate constants ($k^2_{\text{FcBr}}/k^2_{\text{PhBr}}$) was calculated by the following equation:

$$-\frac{d(\text{FcBr})}{d(\text{PhCl})} = \frac{k^2_{\text{FcBr}}}{k^2_{\text{PhBr}}} \times \frac{(\text{FcBr})}{a}$$

$$\text{or} \quad -\ln\frac{(\text{FcBr})}{(\text{FcBr})_0} = \frac{k^2_{\text{FcBr}}}{k^2_{\text{PhBr}} \times a} \times (\text{PhCl})$$

where a and $(\text{FcBr})_0$ are the initial concentrations of bromobenzene and bromoferrocene respectively.

Analytical Conditions for Gas Chromatography. Apparatus: OHKURA Model 1100. Column: a 2 m× 6 mm stainless-steel column packed with 5% Silicone Grease on Diachrom A (60—80 meshes). Temperature: 165°C. Carrier gas: H_2. Flow rate: 80 m*l*/min. Relative retention times: Ferrocene (0.88). Biphenyl (1.00), Chloroferrocene (1.39), Bromoferrocene (1.88), and Iodoferrocene (2.59).

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10) M. Sato, I. Motoyama and K. Hata, to be published in the subsequent paper.