BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 44, 808—812 (1971)

Reactions of Haloferrocenes. IV.[1] The Condensation of Haloferrocenes with Various Carboxylic Acids in the Presence of Copper(I) Oxide

Masaru SATO, Yau Ping LAM, Izumi MOTOYAMA, and Kazuo HATA
Department of Chemistry, Faculty of Science, Tokyo Metropolitan University, Setagaya-ku, Tokyo

(Received August 21, 1970)

The condensation reaction of haloferrocenes with various carboxylic acids in the presence of copper(I) oxide was studied extensively. The reaction generally afforded the corresponding ferrocenyl carboxylates, along with a comparable amount of ferrocene. The change in the distribution of the reaction products was examined under various conditions in the reaction of bromoferrence with benzoic acid. From the discussion of the reaction mechanism, it was concluded that the ferrocenyl ester and ferrocene are produced through different active species. The reaction under proper conditions was found to be useful for the preparation of ferrocenyl esters.

The copper-catalyzed condensation reaction of halides with phenols or amines is well-known as a synthetic method of aryl ethers or arylamines.[2] However, a similar reaction of aryl halides with carboxylic acids to give aryl carboxylate has been little studied.[3] In a previous paper,[1] we reported that the reaction of haloferrocenes with copper(I) acetate in boiling pyridine gave ferrocenyl acetate; this result was different from that of aryl halides with copper(I) acetate. In this paper, the condensation reaction of haloferrocenes with various carboxylic acids in the presence of copper(I) oxide will be reported as an extension of the preceding study.

Results and Discussion

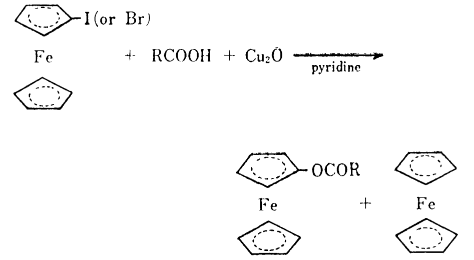
When iodoferrocene or bromoferrocene was refluxed with various carboxylic acids in the presence of copper(I) oxide in pyridine, the corresponding ferrocenyl carboxylates were obtained, together with a comparable amount of ferrocene. For example, when iodoferrocene was refluxed for half an hour with two equivalents of benzoic acid and one equivalent of copper(I) oxide in pyridine, ferrocenyl benzoate and ferrocene

---

[1] Part III: M. Sato, I. Motoyama, and K. Hata, This Bulletin, **43**, 2213 (1970).

[2] F. Ullmann, *Ber.*, **36**, 2383 (1903); F. Ullmann and P. Sponagel, *Ann.*, **350**, 83 (1906); F. Ullmann, *ibid.*, **355**, 312 (1907); F. Ullmann and C. Wagner, *ibid.*, **355**, 359 (1907).

[3] J. Forrest, *J. Chem. Soc.*, **1960**, 581.



(1)

were obtained in 54% and 36% yields respectively. All the results of the reaction of iodoferrocene with the various carboxylic acids examined are summarized in Table 1. Biferrocenyl, which was obtained as a coupling product in the reaction of iodoferrocene with copper(I) acetate and benzoate, together with ferrocenyl carboxylate and ferrocene, was hardly detected at all. Especially, it was never found in the similar reaction of bromoferrocene.

Table 1. The condensation of iodoferrocene with various carboxylic acids in the presence of copper(I) oxide in pyridine

Molar ratio: iodoferrocene : carboxylic acid : copper(I) oxide = 1 : 2 : 1.
Reaction temp.: 116°C, Reaction time: 0.5 hr

Carboxylic acid	Iodoferrocene recovered (%)	Ferrocenyl ester (%)	Ferrocene (%)	Chloroferrocene (%)
p-$CH_3C_6H_4COOH$	5	47.2	35.9	
p-$CH_3OC_6H_4COOH$	29.6	30.9	34.2	
C_6H_5COOH	8.2	53.6	35.6	
p-ClC_6H_4COOH	8.5	51	27.5	
o-ClC_6H_4COOH	41.7	13.4	2.2	32.6
p-$CH_3COC_6H_4COOH$	28.8	38.1	35	
p-$NO_2C_6H_4COOH$	9.3	52.4	31.7	
o-$NO_2C_6H_4COOH$	14.9	52.0	25.1	
CH_3COOH	Trace	58.6	36.8	
CH_3CH_2COOH	1.3	54.8	34.8	
$ClCH_2COOH$	27.6	2.2[a]	31.1	38
Cl_3CCOOH	32.9	—	Trace	55.8
C_6H_5CH=$CHCOOH$	13.0	23.3	33.6	
CH_3CH=$CHCOOH$	—	41.6	44.6	

a) Ferrocenyl acetate was obtained instead of the expected chloroacetate.

As is shown in Table 1, ferrocenyl ester is a main product in most of the cases under the conditions employed. On the other hand, the corresponding reaction of 1-bromonaphthalene with acetic acid in boiling pyridine for 3 hr was reported to afford exclusively the dehalogenated product, *i.e.*, naphthalene, in a moderate yield.[4] Similarly, when o-nitrohalobenzene was boiled with benzoic acid in the presence of metallic copper, it was dehalogenated to give nitrobenzene.[5] The only example of the copper-catalyzed condensation, which afforded aryl carboxylate as a product, was reported as a side-reaction in the Ullmann coupling of substituted iodobenzene, using benzoic acid as the diluent.[3] The maximum yield of the aryl benzoate was reported to be 27%. The present results, shown in Table 1, are very different from those reported in the benzene series. This tendency is consistent with the fact that haloferrocene reacts easily with copper(I) acetate to give ferrocenyl acetate in a good yield,[1] while aryl halides react with the copper(I) salt to give only dehalogenated products.[4,6]

Variation in the carboxylic acid component seems to have no significant effect on the reaction and on the product distribution. The effect of the *para*-substituent of benzoic acid on the reaction is also not clear, and there is no appreciable difference in the reactivities between aromatic and aliphatic acids. These facts indicate that the reaction is not influenced by the dissociation constant of carboxylic acid. A double bond conjugated to the carboxyl group also appears to have no effect on this reaction. Although o-nitrobenzoic acid has been reported to be decarboxylated in the presence of copper(I) oxide at a high temperature,[7] no such decarboxylation product was found in the present reaction.

It was found, however, that the reaction was affected significantly by an α-halogen substituent of aliphatic acid or by an *ortho*-halogen substituent of benzoic acid. For instance, when iodoferrocene was refluxed with chloroacetic acid or trichloroacetic acid in the presence of copper(I) oxide in pyridine, the main product was not a corresponding ferrocenyl ester, but chloroferrocene. Similarly, the reaction of iodoferrocene with o-chlorobenzoic acid gave chloroferrocene as the main product, while the reaction with the p-isomer gave ferrocenyl p-chlorobenzoate and no chloroferrocene. A similar effect of the halogen substituent adjacent to the carboxyl group has been reported by Bacon and Hill[4] in the reaction of aryl halides with o-chlorobenzoic anhydride or chloroacetic anhydride.

It is quite interesting that the reaction of haloferrocene with any of carboxylic acids in the presence of copper(I) oxide produced a condensation product (ferrocenyl ester) together with a comparative amount of a dehalogenation product (ferrocene), whereas only dehalogenated products were obtained in the reaction of aryl halides under similar conditions. These facts inspired us to consider the mechanism of this condensation reaction. The reaction of haloferrocene with carboxylic acid in the presence of copper(I) oxide was considered to be suitable for examining the reaction mechanism, because it proceeds easily and gives good yields of the products. In the first place, the reaction between bromoferrocene and benzoic acid was investigated under various conditions. Whereas bromoferrocene reacted with benzoic acid when they were refluxed in the presence of copper(I) oxide in pyridine, no reaction occurred when bromoferrocene was treated either with copper(I) oxide or with benzoic acid alone in boiling pyridine. Therefore, it is reasonable to assume that benzoic acid initially reacts with copper(I) oxide to form a certain active species, which subse-

---

[4] R. G. R. Bacon and H. A. O. Hill, *ibid.*, **1964**, 1112.

[5] W. T. Smith, Jr., *J. Amer. Chem. Soc.*, **71**, 2855 (1949); W T. Smith, Jr., and L. Campanaro, *ibid.*, **75**, 3602 (1953).

[6] W. G. H. Edwards and R. G. Stewart, *Chem. Ind.* (London), **1952**. 472.

[7] M. Nilsson, *Acta Chem. Scand.*, **20**, 423 (1966).

TABLE 2. THE INFLUENCE OF THE MOLAR RATIO OF THE REACTION COMPONENTS

Reaction temp.: 116°C, Reaction time: 0.5 hr
Bromoferrocene: 0.005 mol, Pyridine: 20 m*l*

Molar ratio of components			Distribution of products (%)		
FcBr	C_6H_5COOH	Cu_2O	FcBr	C_6H_5COOFc	FcH
1	1	0.5	54.9	23.5	20.4
1	2	1	23.0	34.6	40.9
1	3	1.5	3.0	36.6	56.0
1	4	2	—	35.3	62.4
1	1	0.5[a)]	44.4	32.7	21.5
1	2	0.5[a)]	46.6	27.4	24.7
1	4	0.5[a)]	56.3	13.7	18.3

a) Reaction time: 1.0 hr

quently reacts with bromoferrocene to give both the dehalogenation and the condensation products. This assumption is strongly supported by the results of the experiments listed in Table 2, in which the effect of the change in the molar ratio of the reaction components on the distribution of the products is summarized. The following facts are clearly shown in this table: (i) When the molar ratio of benzoic acid to copper(I) oxide is kept constant ($C_6H_5COOH/Cu_2O=2$) and when the molar ratio of the mixture to bromoferrocene is increased, the yields of both ferrocenyl benzoate and ferrocene increase; there is a particularly striking increase in the formation of ferrocene. (ii) When only the ratio of benzoic acid to the other components is increased, the yields of both products rather decrease. The latter fact seems to strongly support the assumption presented above.

TABLE 3. THE REACTION OF VARIOUS HALOFERROCENES WITH BENZOIC ACID IN THE PRESENCE OF COPPER(I) OXIDE IN PYRIDINE

Haloferrocene: 0.005 mol, Benzoic acid: 0.01 mol
Copper(I) oxide: 0.005 mol, Pyridine: 20 m*l*
Reaction temp.: 116°C, Reaction time: 0.5 hr

Haloferrocene	Haloferrocene recovered (%)	Ferrocenyl benzoate (%)	Ferrocene (%)
Iodoferrocene	8.2	53.6	35.6
Bromoferrocene	23.0	34.6	40.9
Chloroferrocene	92.5	2.6	2.4

The influence of the kind of halogen in haloferrocenes on the reaction was also studied; the results are shown in Table 3. It is clear from Table 3 that the reactivity of haloferrocene is in the order: FcI> FcBr>FcCl, an order which is similar to that in the reaction of haloferrocene with various copper(I) salts,[1,8)] and that the product distribution is also influenced by the kind of the halogen. Iodoferrocene produced predominantly ferrocenyl benzoate over ferrocene. The reaction of bromoferrocene seems to be somewhat favorable to the formation of ferrocene. As for chloroferrocene, comparable yields of both products were obtained, but the comparison of the yields seems to be of little significance because of the low reactivity of chloroferrocene.

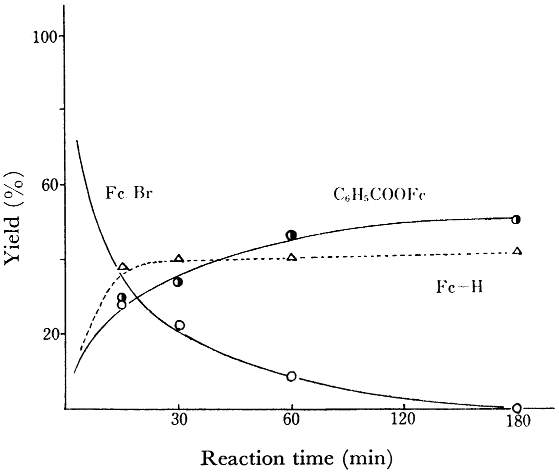


Fig. 1. The plot of the product distribution against reaction time.

It will be useful, in examining the reaction mechanism, to follow the change in the product distribution of this reaction with the lapse of the reaction time. Thus, the product distribution in the reaction of bromoferrocene with benzoic acid in the presence of copper(I) oxide in boiling pyridine was plotted against the reaction time (Fig. 1). As is shown in Fig. 1, (i) ferrocene and ferrocenyl benzoate are formed competitively in the initial stage; (ii) the formation of ferrocene is faster than that of ferrocenyl benzoate in the beginning of the reaction, but it ceases after about 30 min; (iii) the formation of the benzoate gradually increases as the reaction proceeds. The facts described above suggest unequivocally that ferrocene and ferrocenyl benzoate are produced independently through the reaction of bromoferrocene with different active species, not through an step-by-step mechanism in which one of the products is formed initially and then reacts with an active species to give the other. The more likely mechanism that the formation of ferrocene precedes that of ferrocenyl benzoate is also excluded by the fact that ferrocenyl benzoate was never obtained when ferrocene refluxed with benzoic acid and copper(I) oxide in pyridine. It is plausible, from an examination of Table 2, to conclude that the active species which affords ferrocenyl benzoate is probably copper(I) benzoate-pyridine complex, because copper(I) benzoate can be formed through the reaction of benzoic acid with copper(I) oxide in the reaction mixture.

$$2C_6H_5COOH + Cu_2O \longrightarrow 2C_6H_5COOCu + H_2O \quad (2)$$

$$C_6H_5COOCu \xrightarrow[\text{pyridine}]{} C_6H_5COOCu\text{-}Py_n$$

Since the formation of a coupling product (biferrocenyl) was never observed in this reaction, the formation of ferrocenyl benzoate seems unlikely to be through a radical mechanism. Furthermore, the radical mechanism may be excluded by the fact that, as is shown in Table 2, the formation of ferrocene does not increase even when the molar ratio of ben-

---

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

Table 4. Effect of the additional material
Bromoferrocene: 0.005 mol, Copper(I) benzoate: 0.01 mol, Annex: 0.01 mol, Pyridine: 20 m*l*
Reaction temp.: 116°C, Reaction time: 0.5 hr

Reaction	Annex	Product (%)		
		FcBr	C_6H_5COOFc	FcH
$FcBr+C_6H_5COOH+Cu_2O$[a)]		23.0	34.6	40.9
$FcBr+C_6H_5COOCu$		11.3	62.8	2.5
$FcBr+C_6H_5COOCu$	H_2O	7.5	49.7	39.8
$FcBr+C_6H_5COOCu$	CH_3OH	—	49.7	34.4

a) Benzoic acid: 0.01 mol, Cu_2O: 0.005 mol

zoic acid as a hydrogen donor increase. Therefore, the formation of ferrocenyl benzoate is probably due to a mechanism similar to that of the reaction of haloferrocene with copper(I) benzoate in pyridine, which was reported in the preceding paper.[1)]

On the other hand, the explanation of the formation of ferrocene is not yet clear, although the following considerations are possible on the basis of the results of the experiments shown in Table 4. Benzoic acid must be responsible for the formation of ferrocene, because the latter could be scarcely found at all in the reaction product when copper(I) benzoate was used instead of benzoic acid and copper(I) oxide. However, it was found that, when water or methanol was added as a hydrogen donor to the reaction of bromoferrocene with copper(I) benzoate in pyridine, the formation of ferrocene was comparable to that in the reaction using benzoic acid and copper(I) oxide. These observations support the assumption that the source of hydrogen for the formation of ferrocene in this reaction is the acidic hydrogen of benzoic acid. The acid probably reacts with copper(I) oxide to produce water through Eq. (2), and the water would react with haloferrocene through some participation in the formation of an active species such as a copper(I) complex.

Table 5. Solvent effect
Bromoferrocene: 0.005 mol, Benzoic acid: 0.01 mol
Copper(I) oxide: 0.005 mol, Solvent: 20 m*l*
Reaction time: 1.0 hr

Solvent	Reaction temp. (°C)	FcBr recovered (%)	Product	
			C_6H_5COOFc	FcH
Pyridine	116	9.0	47.0	40.9
Acetonitrile	82	—	89.4	8.2
Nitromethane	101	9.1	86.0	3.2
Toluene	110	28.8	42.0	26.9

Pyridine was supposed to act not only as a solvent but also as a ligand coordinating to the copper(I) salt which is formed by the reaction of benzoic acid with copper(I) oxide. Accordingly, in order to examine the role of pyridine in this reaction, the reaction was studied in other solvents; the results are summarized in Table 5. As is shown in Table 5, when the reaction was carried out in acetonitrile or nitromethane the condensation product (ferrocenyl ester) was formed in an extraordinarily high yield in place of a low yield of the dehalogenation product (ferrocene). This trend is more striking in the latter solvent. Thus, the condensation reaction in these solvents is suitable for the preparation of ferrocenyl esters. The participation of pyridine in the formation of ferrocene is obvious in Table 5. The special behavior of pyridine in this reaction is probably due to the basicity and the coordination ability of pyridine. The formation of ferrocene may be effected by the reaction of haloferrocene with a certain active species formed by the addition of water (or methanol) to the copper(I) benzoate-pyridine complex, which is expected to exist in the reaction mixture.

On the other hand, ferrocene is also obtained in a considerable amount by the reaction using toluene as a solvent. However, it seems reasonable to consider that the reaction in toluene may proceed through a different mechanism, since the product distribution is considerably different from that by the reaction using pyridine; in the previously-reported reaction between bromoferrocene and copper(I) benzoate,[1)] the product distribution by the reaction using toluene as a solvent was also quite different from that by the reaction using pyridine.

Experimental

The Procedure for the Preparation of Ferrocenyl Carboxylates. Ferrocenyl Benzoate: Iodoferrocene (1.56 g, 0.005 mol), benzoic acid (1.22 g, 0.01 mol) copper(I) oxide (0.72 g, 0.005 mol), and 20 m*l* of pyridine were placed in a 100-m*l*, three-necked, round-bottomed flask fitted with a mechanical stirrer, a reflux condenser, and a gas-inlet tube. The mixture in the flask was refluxed on an oil bath maintained at 120—125°C for 0.5 hr under an atmosphere of nitrogen. After the reaction had been completed, 80 m*l* of ether was added to the cooled reaction mixture. The dark blue precipitate was separated by filtration and washed with a small portion of ether. The combined ether solution was washed successively with water, dilute hydrochloric acid, and water, and then dried over anhydrous magnesium sulfate. After the removal of the solvent under reduced pressure, the orange residue was chromatographed on silica gel, using *n*-hexane - benzene (1 : 1) as the eluent. The first fraction gave orange crystals (0.46 g), which were found to be a mixture of ferrocene (0.33 g, 35.6%) and iodoferrocene (0.13 g, 8.2%) by a gas-chromatographic analysis.[9)] From the second fraction of the chromatography, ferrocenyl benzoate (0.82 g, 53.6%) was obtained; it was recrystallized from *n*-hexane - benzene (1 : 1), mp 108.5—109.5°C (lit,[11)] 108.5—109.5°C).

The other ferrocenyl esters, listed in Table 1, were similarly prepared by the reaction of iodoferrocene with various carboxylic acids in the presence of copper(I) oxide in boiling pyridine. The analytical data of the ferrocenyl esters thus obtained are as follows:

Ferrocenyl *p*-methoxybenzoate, mp 107.2—107.8°C. Found: C, 64.47; H, 4.91%. Calcd for $C_{18}H_{16}O_3Fe$: C, 64.30; H, 4.81%.

Ferrocenyl *p*-methylbenzoate, mp 94.5—95.5°C. Found:

---

9) The analytical conditions for the gas-chromatographic analysis were the same as those reported in a previous paper.[10)]

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

11) A. N. Nesmeyanov, V. A. Sazonova, and V. N. Drozd, *Chem. Ber.*, **93**, 2717 (1960).

C, 67.97; H, 5.02%. Calcd for $C_{18}H_{16}O_2Fe$: C, 67.51; H, 5.05%.

Ferrocenyl *p*-chlorobenzoate, mp 109—110.5°C. Found: C, 60.09; H, 3.95%. Calcd for $C_{17}H_{13}O_2ClFe$: C, 59.94; H, 3.85%.

Ferrocenyl *o*-chlorobenzoate, orange liquid. Found: C, 61.49; H, 3.99%. Calcd for $C_{17}H_{13}O_2ClFe$: C, 59.94; H, 3.85%.

Ferrocenyl *p*-acetylbenzoate, mp 141—142°C. Found: C, 65.73; H, 4.60%. Calcd for $C_{19}H_{16}O_3Fe$: C, 65.53; H, 4.64%.

Ferrocenyl *p*-nitrobenzoate, mp 184—185°C. Found: C, 58.09; H, 3.89; N, 3.99%. Calcd for $C_{17}H_{13}O_4NFe$: C, 58.14; H, 3.74; N, 3.99%.

Ferrocenyl *o*-nitrobenzoate, mp 115—116°C. Found: C, 58.42; H, 3.89; N, 4.24%. Calcd for $C_{17}H_{13}O_4NFe$: C, 58.14; H, 3.74; N, 3.99%.

Ferrocenyl propionate, bp 108—110°C/0.05—0.06 mmHg. Found: C, 60.48; H, 5.71%. Calcd for $C_{13}H_{14}O_2Fe$: C, 60.48; H, 5.48%.

Ferrocenyl crotonate, mp 60—61.5°C. Found: C, 62.39; H, 5.21%. Calcd for $C_{14}H_{14}O_2Fe$: C, 62.24; H, 5.23%.

Ferrocenyl cinnamate, mp 88.5—90°C. Found: C, 68.81; H, 4.76%. Calcd for $C_{19}H_{16}O_2Fe$: C, 68.69; H, 4.86%.

The Reaction between Bromoferrocene and Benzoic Acid in the Presence of Copper(I) Oxide in Pyridine (Tables 2 and 3). A typical procedure was as follows. Bromoferrocene (1.33 g, 0.005 mol), benzoic acid (1.22 g, 0.01 mol), and copper(I) oxide (0.72 g, 0.005 mol) were mixed with 20 m*l* of pyridine, and then the mixture was refluxed on an oil bath for 0.5 hr under an atmosphere of nitrogen. After the reaction had been completed, the reaction mixture was treated in a manner similar to that described for the preparation of ferrocenyl benzoate. Finally, chromatographic separation afforded ferrocene, bromoferrocene, and ferrocenyl benzoate in 40.9% (0.38 g), 23.0% (0.31 g), and 34.6% (0.53 g) yields respectively.

The Reaction of Bromoferrocene with Copper(I) Benzoate in Pyridine in the Presence of Water (Table 4). Water (0.09 m*l*, 0.005 mol) was added to a mixture of bromoferrocene (1.33 g, 0.005 mol) and copper(I) benzoate (1.85 g, 0.01 mol) in 15 m*l* of pyridine; then the mixture was refluxed for 0.5 hr under an atmosphere of nitrogen. After the reaction had been completed, the reaction mixture was treated much as has been described for the preparation of ferrocenyl benzoate. The chromatography of the product gave ferrocene, bromoferrocene, and ferrocenyl benzoate in 39.8% (0.37 g), 7.5% (0.10 g), and 49.7% (0.76 g) yields respectively.

The Reaction between Bromoferrocene and Benzoic Acid in the Presence of Copper(I) Oxide in Nitromethane (Table 5). Bromoferrocene (0.67 g, 0.0025 mol), benzoic acid (0.61 g, 0.005 mol), and copper(I) oxide (0.36 g, 0.0025 mol) in 10 m*l* of nitromethane were refluxed for 1.0 hr under an atmosphere of nitrogen. After the reaction had been completed, the reaction mixture was cooled and filtered. The precipitate collected on the filter was washed with ether. The filtrate and the washings were combined, and then the combined solution was washed thoroughly with water and dried over anhydrous magnesium sulfate. After the removal of the solvent under reduced pressure, the orange residue was treated much as has been described for the preparation of ferrocenyl benzoate. Finally, ferrocene (0.015 g, 3.2% yield), bromoferrocene (0.061 g, 9.1% yield), and ferrocenyl benzoate (0.658 g, 86% yield) were obtained.

The reaction using acetonitrile or toluene as the solvent was carried out in the same manner.