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Reaction of Ethyl Diazoacetate with Cupric Chloride

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The reaction of ethyl diazoacetate (**1**) with $CuCl_2$ was investigated. Ethyl chloroacetate (**2**), ethyl dichloroacetate (**3**) and a mixture of ethyl dichloromaleate (**4**) and ethyl dichlorofumarate (**5**) were produced. These products were explained by assuming 1-chloro-1-ehtoxycarbonylmethyl-copper complexes, (**10**) and (**11**). The reactions of **1** with $HgCl_2$ and $CoCl_2$ were examined in detail as reference reactions from the mechanistic view point.

The reaction of diazo compounds, especially diazomethane, with metal halides has been extensively studied, which provides a convenient method for the preparation of halomethylmetal compound.[1] Studies on the interaction between diazo compound and copper salts are restricted to the copper catalyzed decomposition of diazo compounds.[2]

This paper describes the reaction of ethyl diazoacetate (**1**) with $CuCl_2$. It has been found that $CuCl_2$ is distinguished from other copper salts. In equimolar reactions of **1** with cupric salts having negative groups of CN, SO_4 and NO_3 as well as cuprous chloride, only a mixture of ethyl maleate and fumarate was produced. On the other hand, the reaction of **1** with $CuCl_2$ produced ethyl chloroacetate (**2**), ethyl dichloroacetate (**3**), and a mixture of ethyl dichloromaleate (**4**) and ethyl dichlorofumarate (**5**). These products were explained by assuming ethoxycarbonyl-substituted chloromethyl-copper complexes, exemplified by **10** and **11**, as unstable intermediates. The reactions of **1** with $HgCl_2$ and $CoCl_2$ are described in more detail as reference reactions from the mechanistric view point. The reaction of diphenyldiazomethane with cupric chloride was also examined to complement mechanistic consideration.

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[1] D. Seyferth, *Chem. Rev.* **55**, 1155 (1955).

[2] a) W. Kirmse, "Carbene Chemistry," Academic Press Inc., New York, N. Y. (1964). b) T. Saegusa, Y. Ito, S. Kobayashi, K. Hirota and T. Shimizu, *J. Org. Chem.*, **33**, 544 (1968).

TABLE 1. REACTION OF DIAZOACETATE WITH COPPER CHLORIDES[a)]

Ethyl diazoacetate (mmol)	Copper chloride (mmol)		Products (%)[b)]				
			2	**3**	**4/5**	**9**	maleate/fumarate
18	CuCl	18	0	0	0	—	97
16.4	$CuCl_2$	16.4	16	40	3	—	30
10	$CuCl_2$	20	8	82	6	trace	0

[2]; $ClCH_2CO_2C_2H_5$ **[3]**; $Cl_2CHCO_2C_2H_5$

[4]/**[5]**; *cis* and *trans* $C_2H_5O_2CClC{=}CClCO_2C_2H_5$ **[9]**; $Cl_3CCO_2C_2H_5$

a) Reaction was carried out in 10 m*l* of acetonitrile at 15°C for 30 min.

b) Yields are calculated on the basis of the amount of ethyl diazoacetate.

Results and Discussion

Reactions of 1 with Copper Compounds. An equimolar reaction of **1** with CuCl took place smoothly at room temperature. A mixture of ethyl maleate and ethyl fumarate was produced in a quantitative yield (Table 1). Similarly, cupric salts having negative groups of CN, SO_4 and NO_3 gave a maleate-fumarate mixture. Its formation is explained by assuming the formation of ethoxycarbonylcarbene.[2)]

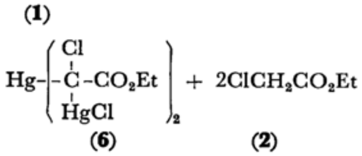
The reaction of **1** with $CuCl_2$ is quite different from that with other copper compounds. The products of an equimolar reaction at 15°C in acetonitrile were **2** (yield 16%), **3** (40%), a mixture of **4** and **5** (3%) and the maleate-fumarate mixture (30%). The maleate-fumarate mixture is probably produced also by the carbene reaction of **1**. It was not produced in the **1**-$CuCl_2$ reaction of 1 : 2 molar ratio. Here, $CuCl_2$ was reduced completely to CuCl. These findings can be rationalized by the assumption that the reaction of **1** with $CuCl_2$ is much faster than the carbene reaction of **1** induced by CuCl. In other words, the maleate-fumarate mixture is produced only after all $CuCl_2$ has been reduced to CuCl.

The production of considerable amounts of **3** is taken to differentiate $CuCl_2$ from other metal chlorides.

Reactions of 1 with $HgCl_2$ and $CoCl_2$. Nesmeyanov[3)] reported the reaction of **1** with $HgCl_2$ which produced **2** and organomercury compound (**6**).

$$4N_2CHCO_2Et + 3HgCl_2 \rightarrow$$

(1)



$$Hg\left(\begin{array}{c} Cl \\ | \\ -C-CO_2Et \\ | \\ HgCl \end{array}\right)_2 + 2ClCH_2CO_2Et \qquad (1)$$

(6) **(2)**

In order to characterize the **1**-$CuCl_2$ reaction and to elucidate its reaction mechanism, the reactions of **1** with $HgCl_2$ and $CoCl_2$ were examined as reference reactions. At room temperature, these metallic chlorides reacted with **1** only very slowly. At refluxing temperature (about 80°C), the reactions proceeded at considerable rates. In the **1**-$CoCl_2$ reaction, the heat-treated reaction mixture was separated into liquid and solid parts. From the liquid part, **2** was isolated by distillation. By glpc analysis, a trace of the **4/5** mixture and **9** was detected in the liquid part. The solid part did not dissolve in common solvents, and further purification without decomposition was impossible. However, the solid part showed an IR spectrum which was almost the same as that of the organomercury complex (**6**) prepared according to Nesmeyanov's procedure. Consequently, an organocobalt complex (**7**) corresponding to **6** can be assumed to be the essential constituent of the solid part of the **1**-$CoCl_2$ reaction mixture.

In the reaction of **1** with $HgCl_2$, a trace of the **4/5** mixture and **9** was detected in addition to the two products indicated in Eq. (1). These results are summarized in Table 2.

TABLE 2. REACTION OF **1** WITH $HgCl_2$ AND $CoCl_2$[a)]

Metal chloride	Products (%)[b)]			
	2	**4/5**	**9**	Organometal complex
$HgCl_2$	41	trace	trace	40[c)]
$CoCl_2$	31	trace	trace	35[d)]

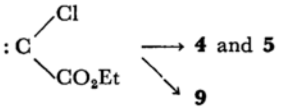
a) A mixture of 10.0 mmol of **1**, 20.0 mmol of metal chloride and 20 m*l* of acetonitrile was refluxed for 4 hr.

b) Yields are calculated on the basis of **1**.

c) Organomercury compound (**6**).

d) The yield is calculated on the assumption that the essential constituent is an organocobalt complex (**7**) corresponding to the organomercury complex (**6**).

Formation of the **4/5** mixture and **9** in these reactions, although their yield is not high, suggests the transient production of ethoxycarbonylcarbene complex (**8**).



(complexed)

(8)

[3)] A. N. Nesmeyanov and G. S. Powich, *Ber.*, **67**, B, 971 (1934).

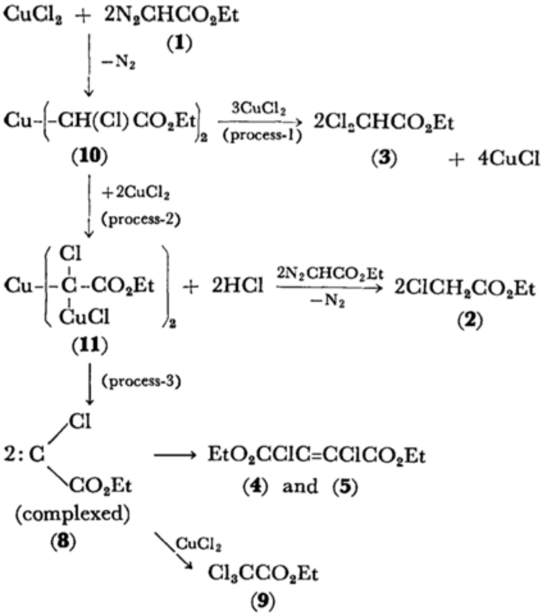
It is interesting that **6** is comparatively inert towards $HgCl_2$ and $CoCl_2$ but easily decomposed by $CuCl_2$ to produce the **4**/**5** mixture and **9**. This finding has an important bearing upon the mechanism of the **1**-$CuCl_2$ reaction, especially the production of the **4**/**5** mixture.

TABLE 3. REACTION OF **6** WITH $CuCl_2$[a)]

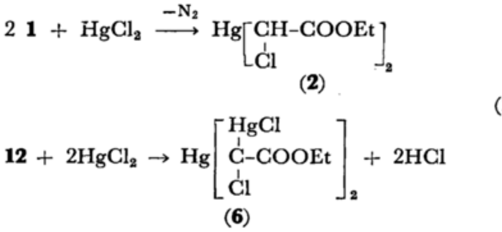
6 (mmol)	$CuCl_2$ (mmol)	Products (%)[b)]	
		4/5	**9**
5	15	60	27

a) Reaction was carried out in 10 m*l* of acetonitrile at 80°C for 1 hr.
b) Yields are calculated on the basis of **6**.

Mechanism of Reaction of 1 with $CuCl_2$. The following scheme of reaction may explain the production of **3**, the **4**/**5** mixture and **9**. As the first unstable intermediate, 1-chloro-1-ethoxycarbonylmethylcopper complex (**10**) is postulated, whose reaction with $CuCl_2$ (process-1) will produce **3** and CuCl. Process-1 is the process of the chlorine ligand transfer from $CuCl_2$ to 1-chloro-1-ethoxycarbonylmethyl moiety, which seems to resemble the so-called ligand transfer[4)] between organic free radical and the ligand of metal salt. As to the production of **2**, the origin of the second α-hydrogen atom is an essential problem.



In the **1**-$HgCl_2$ reaction, Nesmeyanov[3)] proposed that **2** is produced from **1** and hydrogen chloride which is liberated by the mercuration of the acidic α-hydrogen of an organomercury compound (**12**).



$$2\,\mathbf{1} + HgCl_2 \xrightarrow{-N_2} Hg\begin{bmatrix} CH\text{-}COOEt \\ Cl \end{bmatrix}_2 \quad (\mathbf{2})$$

$$\mathbf{12} + 2HgCl_2 \rightarrow Hg\begin{bmatrix} HgCl \\ C\text{-}COOEt \\ Cl \end{bmatrix}_2 + 2HCl \quad (\mathbf{6}) \qquad (2)$$

In the **1**-$CuCl_2$ reaction of the present study, an experiment using α-deuterio-diazoacetate (**1**-*d*) was carried out. It has been established that the second hydrogen atom of **2** originates in another molecule of **1**. **1**-*d* of a degree of deuteration over 98% was prepared from **1** and deuterium oxide in the presence of triethylamine catalyst. The products **2** and **3** in the reaction of **1**-*d* with $CuCl_2$ under the regular reaction conditions were of the same degree of deuteration over 98% as that of **1**-*d*. Consequently it is clear that the α-hydrogen atom of **2** does not originate from acetonitrile or from water which might be present as an impurity.

This conclusion is supported by the reaction of diphenyldiazomethane (**13**) having no α-hydrogen with $CuCl_2$. The products of the reaction of **13** with excess $CuCl_2$ (molar ratio 1 : 2) were dichlorodiphenylmethane (yield 48%), benzophenone azine (34%) and tetraphenylethylene (9%). Diphenylchloromethane which corresponds to **2** in the reaction of **1** was not detected among the products.

In relation to Nesmeyanov's mechanism for the reaction of $HgCl_2$, the conversion of **10** by $CuCl_2$ to **11** (process-2) liberating hydrogen chloride may be cited as one possible mechanism of the elimination of hydrogen from **1**. In the reaction of **1** with $HgCl_2$, the species corresponding to **11** was actually isolated. In the **1**-$CuCl_2$ reaction, **11** was not isolated. This may be ascribed to the fact that **11** is much less stable due to the weakness of copper-carbon bond and that **11** is readily decomposed with $CuCl_2$. In addition, **11** is assumed to be a key intermediate in the course of reaction leading to the **4**/**5** mixture and **9**. The reaction of **11** with $CuCl_2$ producing the **4**/**5** mixture and **9** has been supported by reference experiments in which the mercury species corresponding to **11** was reacted with $CuCl_2$ to give the **4**/**5** mixture and **9**. Probably, the **4**/**5** mixture and **9** would be derived from the common precursor **8**. The process of the formation of **9** seems to correspond to that of **3** in the **1**-$CuCl_2$ reaction.

Recently, bis(diazoethoxycarbonylmethyl) mercury $Hg[C(N_2)CO_2Et]_2$ (**14**)[5)] attracts much

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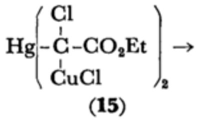
[4)] a) J. K. Kochi and D. D. Davis, *J. Am. Chem. Soc.*, **86**, 5264 (1964). b) J. K. Kochi, *Science*, **155**, 415 (1967).

[5)] a) E. Buchner, *Ber.*, **28**, 215 (1895). b) T. DoMinch, H. E. Gunning and O. P. Strausz, *J. Am. Chem. Soc.*, **89**, 6785 (1967). c) O. P. Strausz, T. DoMinch and J. Font, *ibid.*, **90**, 1930 (1968). d) U. Schöllkopf and N. Rieber, *Angew. Chem.*, **79**, 906 (1967). e) F. Gerhart, U. Schöllkopf and H. Schumacher, *ibid.*, **79**, 50 (1967).

attention as the source of carbyne species. We found that **4**/**5** mixture and **9** were produced in the **14**-$CuCl_2$ reaction. Also in this case, an intermediate (**15**) corresponding to **11** would be involved.

$$\text{Hg[C(N}_2\text{)CO}_2\text{Et]}_2 + 2\text{CuCl}_2 \rightarrow$$

(**14**)



$$\text{Hg}\left(-\underset{\text{CuCl}}{\overset{\text{Cl}}{\text{C}}}-\text{CO}_2\text{Et}\right)_2 \rightarrow \textbf{4/5}\text{ and }\textbf{9} \qquad (3)$$

(**15**)

TABLE 4. REACTION OF **14** WITH $CuCl_2$[a)]

14 (mmol)	$CuCl_2$ (mmol)	Products (%)[b)]	
		4/5	**9**
5	15	33	10

a) Reaction was carried out at 0°C for 1 hr.
b) Yields are calculated on the basis of **14**.

Experimetnal

Reaction of Ethyl Diazoacetate (1) with CuCl. To a stirred mixture of CuCl (18.0 mmol) and acetonitrile, **1** (18.0 mmol) was added dropwise at 15°C. The reaction proceeded smoothly, evolving N_2 gas, and ceased in 30 min. The reaction mixture was filtered to remove an insoluble copper salt, and was subjected to distillation. A mixture of ethyl maleate and fumarate (80—85°C/30 mmHg) was obtained in 97% yield.

Reaction of Ethyl Diazoacetate (1) with $CuCl_2$. To a stirred mixture of $CuCl_2$ (16.4 mmol) and acetonitrile (10 m*l*), **1** (16.4 mmol) was added dropwise at 15°C. The N_2 gas evolution ceased in 30 min and the mixture turned to red-brown. The reaction mixture was filtered to remove the insoluble salt and subjected to distillation. The distillate of bp 60—100°C/20 mmHg was analyzed by glpc. The products were ethyl chloroacetate (**2**) (16%), ethyl dichloroacetate (**3**) (40%), a mixture of ethyl dichloromaleate (**4**) and ethyl dichlorofumarate (**5**) (3%) and a mixture of ethyl maleate and fumarate (30%). The products **2**, **3**, **4**, **5**, ethyl maleate and ethyl fumarate were identified by comparison of the glpc retention time and the IR spectrum with those of the corresponding authentic samples. The insoluble part was analyzed by IR and redox titration. The IR spectrum of the insoluble part showed no absorption band in the region of ordinary organic compounds. Thus, the salt did not contain any organic moiety. The valence of copper was measured by redox titration. $CuCl_2$ was completely reduced to CuCl after the reaction.

Reaction of Ethyl Diazoacetate (1) with $HgCl_2$. To a mixture of $HgCl_2$ (20 mmol) and acetonitrile (10 m*l*), **1** (10 mmol) was added slowly at 15°C and then the reaction mixture was heated at refluxing temperature (80°C) for 4 hr. The reaction mixture was filtered to remove the insoluble solid. The filtrate was distilled to give ethyl chloroacetate (41%). The organomercury compound (**6**) was isolated from the insoluble part according to Nesmeyanov's[3)] procedure (yield 40%). IR of **6** (Nujol): $\nu_{C=O}$ 1660 cm^{-1}, ν_{C-O} 1200 cm^{-1}, ν_{C-Cl} 775 cm^{-1}.

Reaction of Ethyl Diazoacetate (1) with $CoCl_2$. A mixture of $CoCl_2$ (20 mmol), ethyl diazoacetate (**1**) (10 mmol) and acetonitrile (10 m*l*) was heated at 80°C for 4 hr. The solid and liquid parts were separated. From the liquid part, **2** was isolated by distillation (yield 31%). The solid part did not dissolve in common solvents. Further purification without decomposition was impossible. The amount of solid part was 0.86 g (IR (Nujol): $\nu_{C=O}$ 1665 cm^{-1}, ν_{C-O} 1205 sm^{-1}, ν_{C-Cl} 770 cm^{-1}).

Reaction of Diphenyldiazomethane (13) with $CuCl_2$. To a mixture of $CuCl_2$ (20 mmol) and acetonitrile (10 m*l*), a solution of **13** (10 mmol) in acetonitrile (5 m*l*) was added slowly at 15°C. The reaction proceeded smoothly evolving N_2 gas and ceased in about 15 min. The reaction mixture was filtered to remove a white solid. The filtrate was dried up *in vacuo*, and the residue was analyzed by column chromatography (silica gel, benzene-petroleum ether) to obtain dichlorodiphenylmethane (48%), benzophenone azine (34%) and tetraphenylethylene (9%). These three products were identified by comparison of the IR spectra and/or the melting points with those of the corresponding authentic samples.

Preparation of Ethyl α-Deuterio-diazoacetate (1-*d*.).[6)] A heterogeneous mixture of **1** (4 m*l*), deuterium oxide (15 m*l*) and triethylamine (0.1 m*l*) was stirred for 1 hr. The layer of diazoacetate was separated and treated with deuterium oxide again. The diazoacetate layer was dried with anhydrous Na_2SO_4 and distilled to give ethyl α-deuterio-diazoacetate in 80% yield. The NMR spectrum analysis revealed that the α-position was deuterated to an extent over 98%.

Reaction of Ethyl α-Deuterio-diazoacetate (1-*d*) with $CuCl_2$. The reaction was carried out in the same way as that of the **1**-$CuCl_2$ reaction. The products of **2**, **3** and the **4**/**5** mixture were isolated by preparative glpc. By NMR spectrum, the extents of deuteration at α-hydrogen of **2** and **3** were found to be over 98%.

Reaction of Hg$\left[-\underset{\text{HgCl}}{\text{C(Cl)CO}_2\text{Et}}\right]_2$ (6) with $CuCl_2$. A mixture of **6** (5 mmol), $CuCl_2$ (15 mmol) and acetonitrile (10 m*l*) was heated at 80°C for 1 hr. The reaction mixture was filtered to remove the solid part. The filtrate was concentrated *in vacuo* and analyzed by glpc. The products were the **4**/**5** mixture (60%) and trichloroacetate (**9**) (27%).

Reaction of $Hg(N_2CCO_2Et)_2$[5a)] (14) with $CuCl_2$. A solution of **14** (5 mmol) in acetonitrile (5 m*l*) was added dropwise to a mixture of cupric chloride (15 mmol) and acetonitrile (10 m*l*) at 0°C. After 1 hr, the reaction mixture was filtered to remove the insoluble solid.

The filtrate was analyzed by glpc to obtain ethyl trichloroacetate (10%) and a mixture of ethyl dichloromaleate and ethyl dichlorofumarate (33%).

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6) G. W. Robinson and M. McCartrty, Jr., *J. Am. Chem. Soc.*, **82**, 1859 (1960).