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Synthetic Reactions by Complex Catalysts. XIII. Carbonylation of Amines by Group IB and IIB Metal Compound Catalysts[*1]

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The present investigation was undertaken in order to examine the catalytic activities of Group IB and IIB metal compounds in the carbonylation of aliphatic and aromatic amines with carbon monoxide, and in order to compare the catalyst activities with those of other metal compounds. It was found that: i) copper compounds are excellent catalysts for the carbonylation of aliphatic amines to produce the corresponding formamides; ii) the catalytic activities of copper compounds are enhanced by the addition of water; and iii) chloroauric acid catalyzes the carbonylation of aromatic amine, whereas copper compounds do not. The temperature effects on the carbonylation of morpholine were also examined.

We have preliminarily reported the copper-catalyzed carbonylation of amines; in this process primary and secondary amines are smoothly converted by carbon monoxide into the corresponding

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formamides.[1] Now, we wish to report more detailed and more comprehensive studies of the catalytic activities of Group IB and IIB metal compounds in the carbonylation of amines.

Various catalysts have hitherto been reported for the amine-carbon monoxide reaction. Transition metals of Groups IV to VIII,[2,3] their salts,[3–6] their metal carbonyls,[7–9] and the corresponding organometallic compounds[10] catalyze this reaction to produce a mixture of formamide, urea, isocyanate, and oxamide. The alkali metal alcoholate catalyzes the carbonylation of amine to produce the corresponding formamide.[11] In addition, one patent has claimed the production of *N*-methylformamide and *N,N*-dimethylformamide from methylamine and dimethylamine respectively by a catalyst selected from the group consisting of cuprous and cupric chlorides, ammonium chloride, potassium acetate, and boron fluoride.[12]

The purpose of the present investigation is to examine the catalytic activities of Group IB and IIB metal compounds in the carbonylation of aliphatic and aromatic amines with carbon monoxide. We have found that: i) copper compounds are excellent catalysts for the carbonylation of aliphatic amines to produce the corresponding formamides; ii) the catalytic activities of copper compounds are enhanced by the addition of water, and iii) chloroauric acid catalyzes the carbonylation of aromatic amine, but copper compounds do not.

Experimental[*2]

Materials. All the amines were distilled before use. The copper compounds and other metal salts were commercial reagents which were used as received. The carbon monoxide was reagent-grade.

Reaction Procedures. Method A. An amine and a catalyst were placed in a 200 m*l* stainless-steel autoclave equipped with a magnetic stirrer; the autoclave was then charged with carbon monoxide up to a pressure of 60—80 kg/cm^2 at room temperature. The autoclave was closed and heated at a given temperature for a given time. Then, any catalyst precipitated was separated by filtration, and the reaction mixture was distilled or analyzed directly by glpc.

Method B. The reaction was carried out in a 50 m*l* stainless-steel pressure tube without stirring. The after-treatment of the reaction mixture was carried out by the same procedure as in Method A.

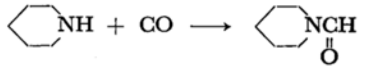
Identification and Analyses of the Products. The reaction products were identified by comparing their NMR and infrared spectra and the glpc retention times with those of the respective authentic samples. The columns of glpc were PEG 6000 and Silicone DC 550. The yields of the products were determined by glpc analyses and, in some cases, by fractional distillation.

Preparations of Authentic Samples. The authentic formamide derivatives were prepared by treating the respective amines with ethyl formate. The boiling points of these authentic samples were as follows: *N*-formylpiperidine: 90—92°C/9 mmHg; *N,N*-diethylformamide: 177—178°C; *N*-formylpyrrolidine: 97—98°C/15 mmHg; *N*-2-hydroxyethylformamide: 134—136°C/0.4 mmHg; *N*-*n*-butylformamide: 142—144°C/45 mmHg; *N*-allylformamide: 120—122°C/48 mmHg; *N*-ethylformamide: 109°C/30 mmHg; *N*-formylmorpholine: 121—124°C/15 mmHg; formanilide: 90—91°C/12 mmHg, (mp 47°C), and *N*-methylformanilide: 131—133°C/25 mmHg.

The authentic samples of 1,1′-carbonyldipiperidine and 4,4′-carbonyldimorpholine were prepared by the reaction of piperidine and morpholine with phosgene; the melting points were 42°C (lit.,[13] mp 42—43°C) and and 141—142°C (lit.,[13] mp 143°C) respectively.

Results and Discussion

Carbonylation of Piperidine. The Group IB and IIB metal compounds were examined for catalyst activity in the carbonylation of piperidine. Their catalytic activities were also compared with those of other metal compounds. The Group IB and IIB metal compounds, especially copper compounds, are quite active. The typical transition metal salts of the Group VIII elements, *e. g.*, Fe, Co, Ni and Pd, are less active than copper catalysts. Aluminum chloride, a strong Lewis acid, is a poor catalyst.



The catalytic behavior of the copper compounds in the amine-carbon monoxide reaction is distinguished from that of typical transition metal catalysts by the highly selective production of formamide. In the copper-catalyzed reaction, a small amount (usually only a few percent) of a *N,N′*-dialkyl derivative of urea was formed as the sole by-product.[1]

The amount of the by-product is much smaller than that in the reaction with palladium[6] and

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1) T. Saegusa, S. Kobayashi, K. Hirota and Y. Ito, *Tetrahedron Letters*, **1966**, 6125.

2) W. Hieber and N. Kahler, *Chem. Ber.*, **91**, 2223 (1958).

3) W. Reppe and H. Kröper, *Ann.*, **582**, 38 (1953).

4) H. Krizikalla and E. Woldan, Ger. Pat. 863800, Jan. 19 (1953).

5) E. W. Stern and M. L. Spector, *J. Org. Chem.*, **31**, 596 (1966).

6) J. Tsuji and N. Iwamoto, *Chem. Commun.*, **1966**, 380.

7) W. Reppe, *Ann.*, **582**, 1 (1953).

8) H. Sternberg, J. Wender, R. A. Friedel and M. Orchin, *J. Am. Chem. Soc.*, **75**, 3148 (1953).

9) F. Calderazzo, *Inorg. Chem.*, **4**, 293 (1965).

10) H. J. Cragg, U. S. Pat. 3099689, July 30 (1963).

11) H. Winteller, A. Bieler and A. Guyer, *Helv. Chim. Acta*, **37**, 2370 (1954).

12) U. S. Pat. 2677706 (1954).

[*2] All the temperature readings are uncorrected.

13) W. Brackman, Ger. Pat. 1105866, May 4 (1961).

TABLE 1. CARBONYLATION OF PIPERIDINE IN THE PRESENCE OF VARIOUS METAL COMPOUNDS[a)] (METHOD B)[b)]

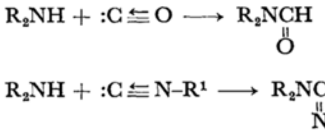
Exp. No.	Catalyst	Reaction conditions Temp. °C	Time hr	Yield of *N*-formylpiperidine (%)[c)]
1	CuCl	140	15	93
2	$Cu(CN)_2$	110	15	72
3[d)]	$CuCl_2$	120	14	17
4	CuCl-1.5-COD complex[e)]	130	14	96
5	AgCl	140	14	25
6	$HAuCl_4 \cdot 4H_2O$	130	14	15
7	$ZnCl_2$	135	16	18
8	$Cd(OAc)_2$	140	14	15
9	$Hg(OAc)_2$	130	14	60
10	$AlCl_3$	120	15	5
11	$Fe(AA)_3$	130	14	40
12	$CoCl_2$	110	15	20
13	$NiCl_2$	110	15	7
14	$PdCl_2$	120	14	5

a) 10 m*l* piperidine and 1.0 g of a catalyst were used.
b) See Experimental Section.
c) Based on the initially charged piperidine.
d) Ethanol (10 m*l*) was used as solvent.
e) The cuprous chloride-1.5-cyclooctadiene complex was prepared according to the reference.[14)]

manganese[9)] catalysts. The piperidine-carbon monoxide reaction with catalysts of Ag, Au, Zn, Cd, and Hg salts also produces a trace amount of 1,1′-carbonyldipiperidine (only a few percent) as a by-product.

The coordination of carbon monoxide with cuprous salts in the presence of amine is well known.[15)] It is not unreasonable to assume that carbon monoxide coordination plays an important role in the catalysis. When cupric salts are used as catalysts, they may be reduced by carbon monoxide into cuprous species which are possibly the real active species of the catalyst.

Copper compounds also catalyze the α,α-addition of the nitrogen-hydrogen bond of aliphatic amine to isocyanide.[16)] It is interesting to note that the reaction with the aliphatic amine-isocyanide is similar to the reaction of the present studies, since isocyanide and carbon monoxide are isoelectronic. These two reactions caused by copper catalysts may be formulated in an analogous manner:



$$R_2NH + :C\equiv O \longrightarrow R_2N\underset{\underset{O}{\|}}{C}H$$

$$R_2NH + :C\equiv N\text{-}R^1 \longrightarrow R_2N\underset{\underset{N\text{-}R'}{\|}}{C}H$$

Carbonylation of Dimethylamine. Copper compounds also catalyze the dimethylamine (DMA)-carbon monoxide reaction to produce *N,N*-dimethylformamide (DMF) (Table 2). The by-product is *N,N,N′,N′*-tetramethylurea, produced only in small amounts. It is quite interesting to observe that the catalytic activity of the copper catalyst is enhanced by the addition of water. The accelerating effect of water may be closely related to the fact that CuCl-CO complexization

TABLE 2. CARBONYLATION OF DMA WITH COPPER CATALYSTS

Exp. No.	Catalyst	g	DMA m*l*	Method[a)]	Reaction conditions Temp. °C	Time hr	Initial rate[b)] mmol/min	Yield of DMF (%)[c)]
15	CuCl	1.0	10	B	100	13	—	73
16	$Cu(CN)_2$	1.0	10	B	100	13	—	52
17	CuCN	0.5	5	B	135	15	—	78
18	CuCl	2.0	30	A	180	28	—	96
19	None		60[d)]	A	145—150	2	—	18
20	CuCN	1.0	60[d)]	A	145—150	2	—	57
21	$Cu(CN)_2$	2.0	60[d)]	A	120—130	10	—	85
22	CuCN	1.0	30[e)]	A	175	3.0	1.2	20
23	CuCN	1.0	30[f)]	A	175	3.0	5.7	84

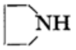
a) See Experimental Section.
b) The rates of gas consumption during the initial 30 min are taken as a measure of the initial rate.
c) Based on DMA.
d) 40% aqueous DMA solution (60 m*l*) was charged.
e) Anhydrous DMA dried with potassium carbonate, was employed.
f) DMA containing 10 mol% of water was employed.

[14)] H. L. Haight, J. R. Doyle, N. C. Baenziger and G. F. Richards, *Inorg. Chem.*, **2**, 1301 (1963).

[15)] "Gmelins Handbuch der Anorganischen Chemie," System Nummer 60, Verlag Chemie GMBH, Weinheim, p. 240.

[16)] T. Saegusa, Y. Ito, S. Kobayashi, K. Hirota and H. Yoshioka, *Tetrahedron Letters*, **1966**, 6121.

Table 3. Carbonylation of miscellaneous aliphatic amines with copper catalysts

Exp. No.	Amine	m*l*	Catalyst	g	Method[a)]	Reaction conditions Temp. °C	Time hr	Yield of formylated product (%)[b)]
24	$(C_2H_5)_2NH$	50	$Cu(OAc)_2$	2.5	A	170	20	46
25		10	$Cu(CN)_2$	0.5	B	120	13	65
26	$HOCH_2CH_2NH_2$	20	$CuCl_2$	1.0	B	105	20	23
27	*n*-$C_4H_9NH_2$	10	CuCl	1.0	B	115	16	20
28	$C_2H_5NH_2$	10	CuCN	1.0	B	165	20	25
29	$CH_2=CHCH_2NH_2$	10	$CuCl_2$	0.5	B	120	15	15

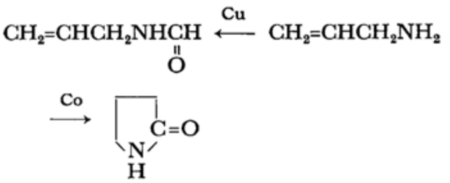
a) See Experimental Section.
b) Based upon the charged amine.

is favored by water.[15)]

The effect of a small amount of water is clearly demonstrated in the last two runs of Table 2, where the carbonylation by the CuCN catalyst was carried out both in the absence (Exp. No. 22) and in the presence of water (Exp. No. 23). The addition of 10 mol% of water increases the rate and the conversion four or five fold. Furthermore, DMA carbonylation is efficiently carried out in an aqueous system (Exp. No. 19 to No. 21, Table 2). There are two possible explanations of the effect of water. First, the water molecule is incorporated into the copper-DMA complex as a ligand, thus possibly modifying (increasing) the catalyst activity. Second, the water converts carbon monoxide to formic acid, which may then be responsible for the carbonylation reaction. In fact, it has been established that the addition of water to a reaction system without a metallic catalyst increases the rate of carbonylation, although the actual rate is quite low.[11)]

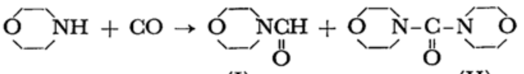
Carbonylations of Miscellaneous Amines. Other aliphatic amines can also be carbonylated by means of copper-compound catalysts (Table 3). The carbonylation of secondary amines appears to be easier than that of primary amines.

The carbonylation of allylamine differentiates the copper catalyst from the cobalt carbonyl catalyst. The copper-catalyzed carbonylation of allylamine yields only *N*-allylformamide, whereas the cobalt carbonyl-catalyzed reaction gives the cyclization product, 2-pyrrolidinone.



Temperature Effects on the Carbonylation of Morpholine. The rate of the carbonylation of morpholine is increased by raising the reaction temperature (Table 4). A small amount of 4,4′-carbonyldimorpholine by-product was formed at a higher reaction temperature (Exp. No. 33). The

Table 4. Carbonylation of morpholine with cuprous chloride catalyst at various temperatures



(I) (II)

Exp. No.	Temp. °C	Yield (%) I	II
30	80	3	—
31	115	14	trace
32	150	42	trace
33	180	76	2

Reaction conditions: morpholine 30 m*l*, CuCl 2.0 g as catalyst, initial CO pressure 80 kg/cm² at room temperature, with stirring for 6.5 hr.

Table 5. Formylation of aniline and *N*-methylaniline (method B)[a)]

Exp. No.	Amine	mmol	Catalyst	mmol	Reaction conditions Temp., °C	Time, hr	Yield of formanilide (%)
34	$C_6H_5NH_2$	100	$HAuCl_4 \cdot 4H_2O$	1.0	180	15	17
35	$C_6H_5NH_2$	100	CuCl	1.0	180	15	0
36	$C_6H_5NH_2$	100	AgCl	1.0	180	15	0
37	$C_6H_5NHCH_3$	100	$HAuCl_4 \cdot 4H_2O$	0.8	175	40	33

a) See Experimental Section.
b) Based on the charged amine.

urea may be produced by the copper-catalyzed oxidation of morpholine with oxygen,[13] which is possibly present as a contaminant in the reaction system.

Carbonylation of Aromatic Amines. Copper compounds are inactive in the reaction of aromatic amines with carbon monoxide. On the other hand, chloroauric acid is active (Table 5).

From the isoelectronic relationship between carbon monoxide and isocyanide, it is also of interest to note that copper compounds do not work as effectively in the aromatic amine-isocyanide reaction as does chloroauric acid.[17]

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[17] T. Saegusa, Y. Ito, S. Kobayashi, K. Hirota and H. Yoshioka, To be published.