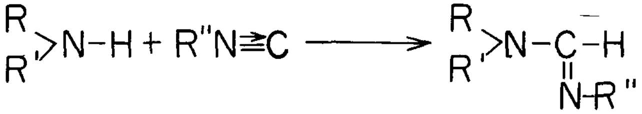
Tetrahedron Letters No.49, pp. 6125-6129, 1966. Pergamon Press Ltd.
Printed in Great Britain.

SYNTHETIC REACTION BY COMPLEX CATALYST. II
COPPER CATALYZED CARBONYLATION OF AMINE

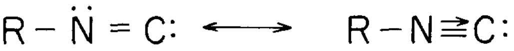
Takeo Saegusa, Shiro Kobayashi, Kiwami Hirota
and Yoshihiko Ito
Department of Synthetic Chemistry, Faculty of Engineering,
Kyoto University, Kyoto, Japan

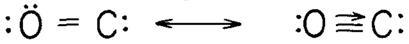
(Received 16 September 1966)

In the preceding communication (1), we have reported that primary and secondary amines react with isocyanide in the presence of copper compound as the catalyst to produce amidines in almost quantitative yields.

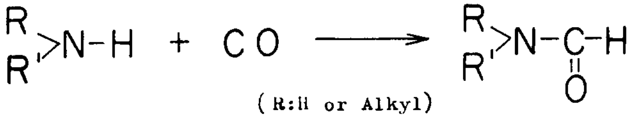

(i)

In view of the fact that carbon monoxide is isoelectronic with isocyanide (2), the above finding prompted us to explore the possibility of the reaction of amine with carbon monoxide by copper catalyst.


Isocyanide


Carbon monoxide

Now we have found that copper compounds as well as metallic copper catalyze the reaction of primary and secondary amines with carbon monoxide producing the corresponding N-alkylformamides. It seems quite interesting to note that these



$$\begin{matrix}R\\R'\end{matrix}\!>\!N\text{-}H \;+\; CO \;\xrightarrow[\text{(R:H or Alkyl)}]{}\; \begin{matrix}R\\R'\end{matrix}\!>\!N\text{-}\overset{}{\underset{\underset{O}{\|}}{C}}\text{-}H \qquad \text{(ii)}$$

two reactions of amine by copper catalyst are characterized by a common feature, i.e., the carbon atoms bearing a lone pair of electrons, the carbon atoms of isocyanide(eq.(i)) and of carbon monoxide(eq.(ii)), are inserted between nitrogen and hydrogen of amine.

Reaction of amine with carbon monoxide has hitherto been studied by many groups of workers. Transition metal compounds, e.g., metal carbonyls, metal halides and organometallic compounds, of Groups IVa, Va, VIa, VIIa, and VIII of the Periodic Table have been employed as the catalyst (3-9), and the products are the compounds having nitrogen-carbonyl linkage, i.e., isocyanates and N-alkylformamides, ureas and oxamides. Copper is located outside the typical transition metals of Groups from IV to VIII in the Periodic Table, and the copper catalysis in the amine-carbon monoxide reaction is distinguished from other catalysts by the highly selective production of N-alkylformamide. As a by-product, N-alkyl derivative of urea was sometimes formed, however, its yield is quite low(below a few percent), much lower than that in the carbonylations with nickel (3) and palladium catalysts (9). The urea formation with copper catalyst may be ascribed to the presence of a small amount of oxygen probably arising from incomplete removal of air from the reaction system.

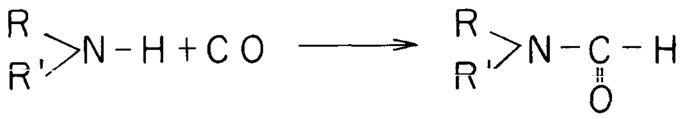
The copper catalyzed reaction of amine with a gaseous mixture of carbon monoxide and oxygen has been described in a patent (10), in which N-alkyl derivatives of ureas instead of N-alkylformamides are formed.

Some results of the copper catalyzed reaction of amine with carbon monoxide are given in Table 1.

In Method A, 60 ml. of 40 % aqueous solution of dimethylamine and a copper catalyst were placed in a magnetically-stirred 200 ml stainless steel autoclave, to which carbon monoxide was compressed up to 60 atm. at room temperature. The content of autoclave was then stirred and heated at a given temperature. In Method B, 10 ml of amine and a catalyst were placed in a 50 ml stainless steel pressure tube, to which carbon monoxide was compressed up to 60 atm. at room temperature. The content of tube was heated without stirring and shaking. After cooling, gas was vented and the contents of autoclave or pressure tube was subjected to distillation. N-alkylformamide was isolated by distillation, which was identified by boiling point, retention time of v.p.c., elemental analysis, infra-red spectrum, and n.m.r. spectrum. In Method B, neither stirring nor shaking was applied during reaction. Consequently, a much improved yield of product may be expected for the reaction with stirring.

The carbonylation of allylamine by copper catalyst yields N-allylformamide. This offers a sharp contrast with the allylamine carbonylation by cobalt carbonyl catalyst in which cyclization to 2-pyrrolidinone occurs (11). With copper compound catalyst, some amines, e.g., piperidine, are carbonylated even

TABLE I. Carbonylation of Amine by Copper



$$\begin{matrix}R\\R'\end{matrix}\!>\!N-H+CO \longrightarrow \begin{matrix}R\\R'\end{matrix}\!>\!N-\underset{\overset{\|}{O}}{C}-H$$

Amine	Cu catalyst	(g.)	Method	Reaction temp. (C)	Reaction Time (hr)	Yield of N-alkyl formamide (%)
$(CH_3)_2NH$ 40 % aq. soln.	None		A	100-110	5	8
	$Cu(CN)_2$	1.0	A	100-110	5	34
	None		A	145-150	2	18
	CuCN	1.0	A	145-150	2	57
	$Cu(CN)_2$	2.0	A	120-130	10	85
	Cu-metal[a)]	0.5	B	135	20	45
$(C_2H_5)_2NH$	$Cu(OCOCH_3)_2$	1.3	B	120	40	48
$\underline{n}$-$C_4H_9NH_2$	CuCl	1.0	B	115	16	20
Piperidine	CuCl	1.0	B	140	15	93
$CH_2{=}CHCH_2NH_2$	$CuCl_2$	0.5	B	120	15	15

a) Copper powder was prepared by the reduction of $CuSO_4$ by zinc powder according to the procedure given in Organic Syntheses, Coll. Vol. II, p.432 John Wiley and Sons, Inc., New York, (1941) at ordinary pressure of carbon monoxide at room temperature.

By the carbonylation of the present studies, ammonia(as 28 % ammonia water) is also carbonylated to formamide. On the other hand, the copper catalyzed carbonylation of aromatic amines including aniline, N-alkylanilines and pyrrole has not been observed yet.

Mechanistic studies and the extension of this reaction are being carried out, which will be published in the near future.

REFERENCES

1. T. Saegusa, Y. Ito, S. Kobayashi, K. Hirota and H. Yoshioka, the preceding paper.
2. J. D. Roberts and M. C. Caserio, Basic Principle of Organic Chemistry, p.684, W. A. Benjamin Inc., New York (1965).
3. H. Krizkalla and E. Woldan, Ger. Pat., 863,800 (Jan. 19. 1953).
4. W. Reppe, Ann., 582, 1 (1953).
5. Ya. Yu. Aliev, I. B. Romanova and L. Kh. Freidlin, Uzbekh. Khim. Zhur., 1960, 72, Chem. Abst., 55, 10444 (1961); Uzbekh. Khim. Zhur., 1961, 54, Chem. Abst., 57, 8413(1962).
6. F. Calderazzo, Inorg. Chem., 4, 293 (1965).
7. E. W. Stern and M. L. Spector, J. Org. Chem., 31, 596 (1966).
8. H. J. Cragg, U. S. Pat., 3,099,689 (July 30, 1963).
9. N. Iwamoto and J. Tsuji, 19th Annual Meeting of Japan Chem. Soc., April, 1966, Tokyo (Abstracts Vol. III, p.326).
10. W. Brackman, Ger. Pat., 1,105,866 (May 4, 1961).
11. J. Falbe and F. Korte, Ber. 98, 1928 (1965).