

SYNTHETIC REACTION BY COMPLEX CATALYST. I.
COPPER CATALYZED REACTION OF AMINE WITH ISOCYANIDE

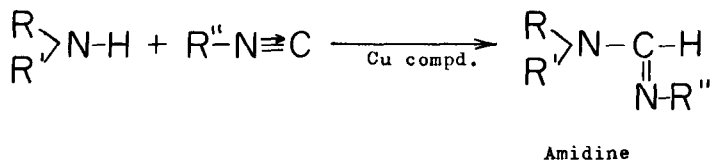
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Various synthetic reactions with copper compound catalysts have long been known. Catalysis by copper compound in the reactions of nitrogen-containing compounds, e.g., amines, amino acids, acid amides, nitriles, and diazo compounds, constitutes one of catalysis features of copper, which may be due to a strong tendency of copper to form coordination complexes with nitrogen compounds.

In the present study, we tried the reaction of amine with isocyanide based upon the fact that isocyanide also forms a coordination complex with copper cyanide (1).

It has now been found that copper compound catalyzes the reactions of primary and secondary amines with isocyanide to



give amidines in almost quantitative yields. The reaction is the insertion of $\begin{array}{c} \text{---C---} \\ | \\ \text{H} \\ | \\ \text{NR}^n \end{array}$ group between nitrogen and hydrogen in amine. The above reaction was once performed by using zinc chloride catalyst (2). However, a quite low yield of the product amidine was reported in the zinc chloride catalyzed reaction.

A ternary mixture of 3.27 g(0.03 mole) of cyclohexylisocyanide, 8.50 g(0.10 mole) of piperidine, and 0.02 g(0.2m mole) of cuprous chloride was stirred at 110°-120°C for 1 hr. The infra-red spectrum of the 1 hr's reaction mixture did not show the absorption band of isocyanide at 2140 cm^{-1} ($\nu_{\text{N=C}}$) (3). In addition, a very disagreeable odor of isocyanide was no longer perceivable. The reaction mixture was distilled to yield 5.6 g (96 %) of N,N-pentamethylene-N'-cyclohexyl-formamidine, b.p. 155-156°(28 mm Hg). Anal. Calcd. for $\text{C}_{10}\text{H}_{20}\text{N}_2$:C, 74.17; H, 11.41; N, 14.42. Found: C, 74.40; H, 11.71; N, 14.53.

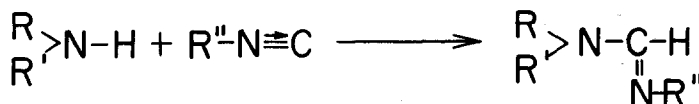
The results of the reactions of some amines with isocyanides are shown in Table 1. The products amidines were identified by infra-red and n.m.r. spectra and by elemental analysis.












By the disappearance rate of the characteristic band of isocyanide in the infra-red spectrum of the reaction mixture, it has been qualitatively disclosed that aliphatic amine reacts with cyclohexylisocyanide much faster than aromatic amine does.

The catalytic effect of copper compound in the present reaction has been manifested by the reference run in which without copper catalyst no reaction was observed.

Coordination of isocyanide as well as that of amine to

TABLE I

Reaction of Amine with Isocyanide by Copper Compound Catalyst^{a)}

Amine	Isocyanide	Catalyst (m Mol)	Reaction time (hr)	Product ^{b)} amidine ^{c)}	Yield (%)
 NH	 -N≡C	none	18	no reaction ^{d)}	
n-C ₄ H ₉ NH	n-C ₄ H ₉ -N≡C	CuCl (1.0)	1	I	88
 NH	n-C ₄ H ₉ -N≡C	CuCl (1.0)	10 ^{e)}	II	87
 NH	 -N≡C	CuCl (0.2)	1	III	96
 NH	 -N≡C	CuCl (1.0)	1	III	94
 NH	 -N≡C	Cu(CN) ₂ (1.0)	1	III	94
 NH ₂	 -N≡C	CuCl (5.0)	24	IV	85

a) A mixture of 0.03 mole of isocyanide, 0.10 mole of amine and a copper compound catalyst was stirred at the indicated temperature.

b) Reaction temperature was 110-120°C.

c) Product amidine.

I: n-C₄H₉-N=CH-NH-C₄H₉-n (b.p. 142-144°C/25 mm Hg)

II: n-C₄H₉-N=CH-N (b.p. 118-120°C/27 mm Hg)

III: -N=CH-N (b.p. 155-156°C/28 mm Hg)

IV: -N=CH-NH- (m.p. 87-89°C)

d) The two reagents, amine and isocyanide, were recovered almost quantitatively.

e) Reaction temperature was 20°C.

copper seem to play an important role in the catalysis.

Coordination of isocyanide to the compounds of transition metals of Groups from VI to VIII of the Periodic Table has also been known (4,5). In relation to the present studies, nickel and cobalt salts were found to catalyze the reaction of amine with isocyanide. However, the reaction product with nickel and cobalt catalysts was different from that with copper catalyst.

Detailed studies upon the amine-isocyanide reaction with copper catalyst as well as that with nickel and cobalt catalysts will be reported in the near future.

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