Tetrahedron Letters No.6, pp. 521-524, 1967. Pergamon Press Ltd. Printed in Great Britain.

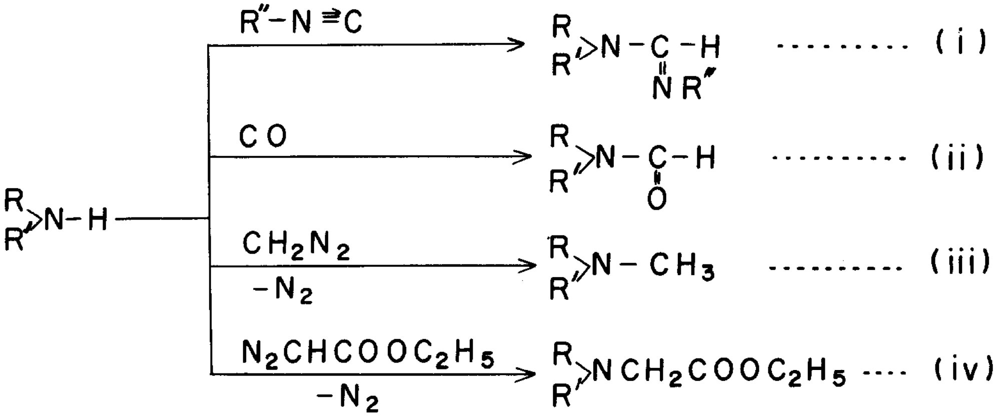
SYNTHETIC REACTION BY COMPLEX CATALYST IV.
COPPER CATALYZED REACTION OF ALCOHOL WITH ISOCYANIDE

Takeo Saegusa, Yoshihiko Ito, Shiro Kobayashi
and Kiwami Hirota

Department of Synthetic Chemistry, Faculty of Engineering,
Kyoto University, Kyoto, Japan

(Received 28 November 1966)

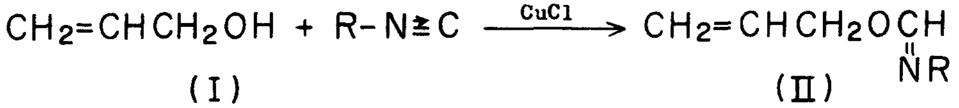
Recently we have explored a series of copper catalyzed reactions of amine with isocyanide[1)] (eq. (i)), carbon monoxide[2)] (eq. (ii)), diazomethane[3)] (eq. (iii)), and ethyl diazoacetate[3)] (eq. (iv)).



These reactions are characterized by a common feature that carbon atoms of isocyanide, carbon monoxide, and carbenes from diazocompounds, each of which bears lone pair electrons, are inserted between nitrogen and hydrogen of amine.

As an extension of the insertion reaction of carbon having lone pair electrons, we examined the reaction of alcohol with isocyanide. Based upon the fact that allyl alcohol forms a complex with cuprous chloride[4,5)], the reaction of allyl alcohol with isocyanide by cuprous chloride catalyst was first investigated.

It has now been found that in the presence of cuprous chloride allyl alcohol (I) reacts with isocyanide to produce allyl formimidate (II).



$$\underset{(I)}{CH_2{=}CHCH_2OH} + R{-}N{\equiv}C \xrightarrow{CuCl} \underset{(II)}{CH_2{=}CHCH_2O\overset{}{\underset{\underset{NR}{\|}}{C}}H} \quad \text{----(v)}$$

This constitutes a new insertion reaction of isocyanide between oxygen and hydrogen of alcohol.

In 4.1 g (0.070 mol) of allyl alcohol, 0.79 g (0.008 mol) of cuprous chloride was dissolved. To this solution, 4.4 g (0.040 mol) of cyclohexyl isocyanide was added, and the mixture was heated at 120°C for 5 hours. The reaction mixture was subjected to distillation under reduced pressure, and 4.5 g (67 %) of allyl N-cyclohexylformimidate was obtained, b.p. 105°C/32 mm Hg. As a by product, 1.3 g (25 %) of N-cyclohexylformamide was isolated, b.p. 100-103°C/3 mm Hg.

In the absence of cuprous chloride, both allyl alcohol and cyclohexyl isocyanide were recovered almost quantitatively from the heat-treated mixture. This observation is taken to demonstrate the catalysis activity of cuprous chloride.

Similarly, other β,γ-unsaturated alcohols such as methally alcohol and cinnamyl alcohol were reacted with cyclohexyl isocyanide in the presence of cuprous chloride catalyst to give the corresponding esters of N-cyclohexylformimidic acid. The results are given in Table 1. The formimidates were identified by elemental analysis and IR and NMR spectra analyses.

TABLE I

Reaction of β,γ-Unsaturated Alcohol with Cyclohexyl Isocyanide*

β,γ-Unsaturated alcohol	Products (Yield %)	
$CH_2{=}CHCH_2OH$	$CH_2{=}CHCH_2OCH{=}N$-⟨H⟩ [a] (67),	⟨H⟩-NHCHO (25)
$CH_2{=}C(CH_3)CH_2OH$	$CH_2{=}C(CH_3)CH_2OCH{=}N$-⟨H⟩ [b] (50),	⟨H⟩-NHCHO (32)
⌬-$CH{=}CHCH_2OH$	⌬-$CH{=}CHCH_2OCH{=}N$-⟨H⟩ [c] (45),	⟨H⟩-NHCHO (20)

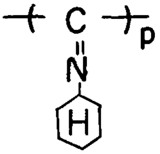
a) b.p. 105°C/32 mm Hg, b) b.p. 116°C/27 mm Hg, c) b.p. 130°C/3 mm Hg

* Cyclohexyl isocyanide contains a small quantity (about 0.5 % to 1 %) of pyridine as impurities.

The formation of N-cyclohexylformamide as a by-product is usually observed, for which a few possible reaction routes may be assumed. Elucidation of the mechanism of the N-cyclohexylformamide formation is being made now.

The specific nature of β,γ-unsaturated alcohol in the insertion reaction of isocyanide between oxygen and hydrogen of alcohol by cuprous chloride catalyst was illustrated on finding that saturated alcohols such as ethanol, isopropanol, and tert-butanol did not react with isocyanide in the presence of cuprous chloride catalyst. The specificity of β,γ-unsaturated alcohol in the reaction with isocyanide may be due to its nature of complex formation with cuprous chloride. In fact, we[6)] have observed in a separate experiment that the IR olefinic band at 1640 cm^{-1} of allyl alcohol shifts to 1550 cm^{-1} when allyl alcohol is mixed with cuprous chloride. It seems likely that the cuprous chloride-allyl alcohol complex by means of hydroxyl group as well as olefinic group plays an important role in the present reaction.

Catalysis behavior of cupric chloride differs from that of cuprous chloride. When a mixture of allyl alcohol, cyclohexyl isocyanide and a small amount of cupric chloride was heated at 120°C for 10 hours, no formimidate was formed, but light brown powder of isocyanide polymer was produced. The IR spectrum of polymer of cyclohexyl isocyanide by cupric chloride was quite similar to that prepared by Hagihara and coworkers[7)] using nikel and cobalt carbonyls as the polymerization catalyst, for which the following structure was presented.



In the reaction of saturated alcohol with cyclohexyl isocyanide by cupric chloride catalyst, N-cyclohexylcarbamate of the corresponding alcohol and N-cyclohexylformamide were formed in low yields.

Chlorides of nikel (II), cabalt (II) and palladium (II) do not catalyze the allyl alcohol-isocyanide reaction. The polymer of cyclohexyl isocyanide was formed when a mixture of cyclohexyl isocyanide and allyl alcohol was treated with these metal halides.

The reaction of mercaptan with isocyanide has also been examined. The insertion of isocyanide between sulfur and hydrogen of mercaptan occurs without copper catalyst.

Detailed studies upon the reactions of alcohol and mercaptan with isocyanide will be reported in the near future.

REFERENCES

1) T. Saegusa, Y. Ito, S. Kobayashi, K. Hirota and H. Yoshioka, Tetrahedron Letters, 1966 No.49.
2) T. Saegusa, S. Kobayashi, K. Hirota, and Y. Ito, Tetrahedron Letters, 1966, No.49.
3) T. Saegusa, Y. Ito, S. Kobayashi, K. Hirota, and T. Shimizu, Tetrahedron Letters, 1966, No.49.
4) R. E. Kepner and L. J. Andrews, J. Org. Chem., 13, 208 (1948).
5) R. M. Keefer and L. J. Andrews, J. Am. Chem. Soc., 71, 1723 (1949).
6) T. Saegusa and N. Takeda, unpublished work.
7) Presented at 14th Annual Meeting of Society of Polymer Science, Japan, 1965.