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A CONVENIENT METHOD FOR THE PREPARATION OF ISOCYANIDES

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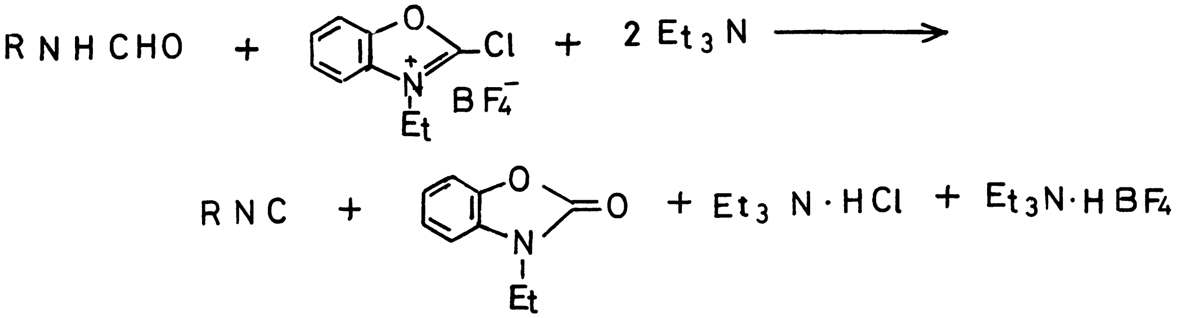
Treatment of formamides with 2-chloro-3-ethylbenzoxazolium tetrafluoroborate affords various isocyanides in good yields at room temperature in neutral media.

In the course of our synthetic investigation1) utilizing onium salts of azaaromatics, it was found that formamides were easily dehydrated to isocyanides in good yields on treatment with 2-chloro-3-ethylbenzoxazolium tetrafluoroborate in the presence of 2 molar amounts of triethylamine as shown in the following equation.



Some of the methods for the preparation of isocyanides,2),3) reported in the literature are (1) reaction of silver cyanide with alkyl halide,4) (2) reaction of primary amine with dichlorocarbene,5) (3) deoxygenation of isocyanate by trivalent phosphorus compound,6) and (4) dehydration of formamide with a dehydrating reagent such as phosgene,7) benzenesulfonyl chloride,8) phosphorus oxychloride,9) or triphenylphosphine-carbon tetrachloride.10)

Of these methods, the dehydration of formamides is most commonly employed for the preparation of isocyanide because formamides are readily available. These dehydrations, however, generally require prolonged refluxing in a solvent in the presence of an excess amount of triethylamine or potassium t-butoxide for the completion of reaction.

According to the present procedure using 2-chlorobenzoxazolium salt as a dehydrating reagent, formamide is smoothly converted to the corresponding isocyanide in good yield at room temperature in neutral media. The present isocyanide synthesis can be applied to both aliphatic and aromatic formamides. It is also applicable to the preparation of such secondary alkyl isocyanides as 1-methylheptyl isocyanide, which are not accessible by other methods mentioned above.11)

The following experiment provides a typical procedure for the preparation of benzyl isocyanide; to a mixture of N-benzylformamide (1.2 mmol, 162 mg) and 2-chloro-3-ethylbenzoxazolium tetrafluoroborate (1.5 mmol, 403 mg) was added triethylamine (3.0 mmol, 303 mg) in dry dichloromethane (5 ml) under an argon atmosphere and the mixture was stirred for two hours at room temperature to give a yellow clear solution. After evaporation of the solvent under reduced pressure, the residue was chromatographed on silica gel to give benzyl isocyanide (114 mg, 82% yield).

In a similar manner, various isocyanides were prepared in good yields as shown in Table.

Table. The Yield of Various Isocyanides from Formamides

Formamide	Isocyanide	Yield (%)
C_6H_5-NHCHO	C_6H_5-NC	81
2,6-$Cl_2C_6H_3$-NHCHO	2,6-$Cl_2C_6H_3$-NC	69
m-NO_2-C_6H_4-NHCHO	m-NO_2-C_6H_4-NC	86
C_6H_5-CH_2-NHCHO	C_6H_5-CH_2-NC	82
n-$C_{12}H_{25}$-NHCHO	n-$C_{12}H_{25}$-NC	71
CH_3-$(CH_2)_5$-$CH(CH_3)$-NHCHO	$CH_3(CH_2)_5CH(CH)_3$-NC	78

It should be noted that the present method is of quite general utility; various formamides are dehydrated to the corresponding isocyanides in good yields under mild conditions by a simple procedure using readily available 2-chloro-3-ethylbenzoxazolium tetrafluoroborate.

REFERENCES

1) For example, T. Mukaiyama, Y. Echigo, and M. Shiono, Chem. Lett., 179 (1977); K. Hojo and T. Mukaiyama, Chem. Lett., 619 (1976).
2) T. Saegusa, Y. Ito, S. Kobayashi, and K. Hirota, J. Am. Chem. Soc., 89, 2240 (1967).
3) I. Ugi and K. Offermann, Chem. Ber., 97, 2996 (1964).
4) E. G. Hartley, J. Chem. Soc., 109, 1296 (1916).
5) K. Pilgram and F. Korte, Tetrahedron Lett., 881 (1966).
6) T. Mukaiyama and Y. Yokota, Bull. Chem. Soc. Jpn., 38, 858 (1965).
7) I. Ugi and U. Fetzer, Chem. Ber., 95, 126 (1962).
8) I. Hagedorn and H. Tonjes, Pharmazie, 11, 409 (1956).
9) F. Lantenschlager and G. F. Wright, Can. J. Chem., 41, 863 (1963).
10) R. Appel, Angew. Chem., 83, 143 (1971).
11) I. Ugi, Ed., "Isonitrile Chemistry", Academic Press, New York, London (1971), p. 29.

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