CHEMISTRY LETTERS, pp. 575-576, 1977. Published by the Chemical Society of Japan

A CONVENIENT METHOD FOR THE PREPARATION OF CARBODIIMIDES USING 2-CHLOROPYRIDINIUM SALT

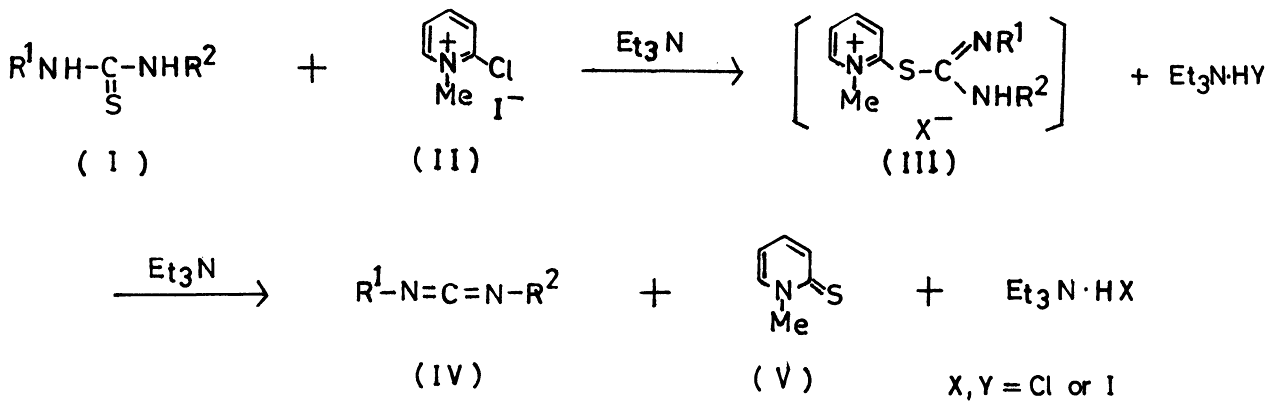
Tadao SHIBANUMA, Manzo SHIONO, and Teruaki MUKAIYAMA
Department of Chemistry, Faculty of Science,
The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113

Aromatic and aliphatic carbodiimides are prepared in good yields by treating N,N'-disubstituted thioureas with 2-chloro-1-methylpyridinium salt in the presence of triethylamine.

In the course of our investigation[1)] on the synthetic utilization of 2-halopyridinium salts, it was found that N,N'-disubstituted thioureas reacted with 2-chloropyridinium salts in the presence of triethylamine to afford the corresponding carbodiimides in good yields.

A typical procedure is described for the preparation of N-cyclohexyl-N'-isopropylcarbodiimide as follows.

A solution of triethylamine (242 mg, 2.4 mmol) in acetonitrile (5 ml) was added at room temperature under an argon atmosphere to a mixture of N-cyclohexyl-N'-isopropylthiourea (200 mg, 1 mmol) and 2-chloro-1-methylpyridinium iodide (306 mg, 1.2 mmol) and then reaction mixture was refluxed for 2 hr. After removal of the solvent under reduced pressure, dichloromethane (20 ml) was added to the reaction mixture and the resulting solution was washed with water (5 ml), dried over sodium sulfate. After evaporation of the solvent, N-cyclohexyl-N'-isopropylcarbodiimide was isolated by a short-path distillation (129 mg, 78% yield). In a similar manner, various carbodiimides were prepared in good yields as summarized in the Table.



As described in the equation, N,N'-disubstituted thiourea initially reacts with 2-chloropyridinium salt (II) to give a key intermediate (III), which is in turn converted to the corresponding carbodiimide (IV) and 1-methyl-2-pyridinethione (V) by the action of triethylamine.

Concerning the preparation of carbodiimides, which are particularly important coupling reagents in the synthesis of peptides and nucleotides, there have numerous publications2),3) appeared, which involve, for example, catalytic conversion of isocyanates, dehydration of N,N'-disubstituted ureas, desulfurization of thioureas with metal oxides and other metallic compounds, and desulfurization of thioureas with alkaline hypochlorite.

It is noted that the present method is of quite general utility; aromatic and aliphatic carbodiimides are obtained from the corresponding N,N'-disubstituted thioureas in good yields by a simple procedure using readily available 2-chloropyridinium salts.

Table. The Preparation of Carbodiimides4)

R^1-N=C=N-R^2		Reaction Temp.	Reaction Time (hr)	Isolated Yield 4) (%)
R^1	R^2			
C_6H_5-	C_6H_5-	r.t.	5	85a)
p-CH_3-C_6H_4-	p-CH_3-C_6H_4-	r.t.	5	97a)
C_6H_5-	C_6H_{11}-	r.t.	5	98a)
C_6H_{11}-	C_2H_5-	reflux	2	79
C_6H_{11}-	$(CH_3)_2CH$-	reflux	2	78
C_6H_{11}-	C_6H_{11}-	reflux	2	77b)

a) Aromatic carbodiimides were purified by t.l.c. on silica gel.
b) 1-Benzyl-2-chloropyridinium bromide was used as 2-chloropyridinium salt.

References and Note

1) K. Hojo and T. Mukaiyama, Chem. Lett., 619 (1976), and the other references cited therein.
2) H. G. Khorana, Chem, Rev., 53, 145 (1953).
3) F. Jurzer and K. Duraghi-Zadeh, Chem. Rev., 67, 107 (1967).
4) IR and NMR spectra of all the compounds were well agreed with the assigned structures.

(Received March 24, 1977)