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A CONVENIENT METHOD FOR THE PREPARATION OF α-CHLORONITRILES

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2-Chloro-3-ethylbenzoxazolium tetrafluoroborate reacts smoothly with various cyanohydrins in the presence of tetraethylammonium chloride to afford α-chloronitriles in good yields.

α-Chloronitriles are conventionally synthesized by 1) dehydration of α-chloroamides,[1)] 2) chlorination of nitriles,[1)2)] or 3) chlorination of cyanohydrins.[3)] These procedures, however, are not always satisfactory as a preparative method. That is, the methods 1) and 2) require vigorous reaction conditions (high reaction temperature or the use of a strong base). The method 3) is rather satisfactory, but it was only applied in the case of mandelonitrile.

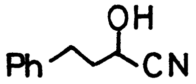
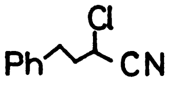
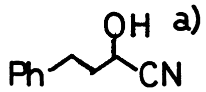
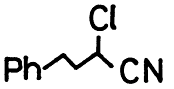
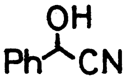
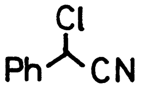
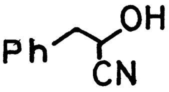
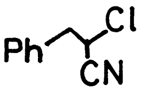
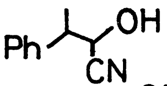
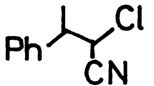
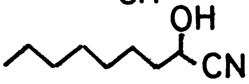
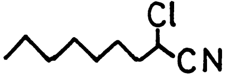
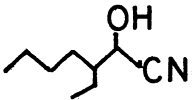
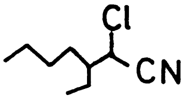
During the course of our synthetic investigations using onium salts of azaaromatics, we found that 2-chloro-3-ethylbenzoxazolium tetrafluoroborate is a very strong dehydrating reagent[4)] and alcohols are easily transformed to alkyl chlorides at room temperature in the presence of tetraethylammonium chloride and triethyl amine.[4a)] In this communication we wish to report a convenient method for the transformation of cyanohydrins to α-chloronitriles, by the reaction with 2-chloro-3-ethylbenzoxazolium tetrafluoroborate in the presence of tetraethylammonium chloride and triethylamine.

The following is a typical procedure for the preparation of α-chloronitriles by the present method.

To a stirred suspension of 2-chloro-3-ethylbenzoxazolium tetrafluoroborate (538 mg, 2 mmol) and tetraethylammonium chloride (497 mg, 3 mmol) in dichloromethane (1.4 ml) cooled to 0°C was added dropwise 2-hydroxy-3-ethylheptanenitrile (155 mg, 1 mmol) in dichloromethane (2 ml) under an argon atmosphere. To the mixture was added dropwise triethylamine (131 mg, 1.3 mmol) in dichloromethane (1 ml) over a period of 15 minutes and the resulting mixture was stirred at the same temperature for an additional 30 minutes. After the reaction mixture was stirred overnight at room temperature, the reaction was quenched with water. The products was extracted with dichloromethane and separated by column-chromatography to give 2-chloro-3-ethylheptanenitrile in 91% yield. (The structure was identified by NMR.)

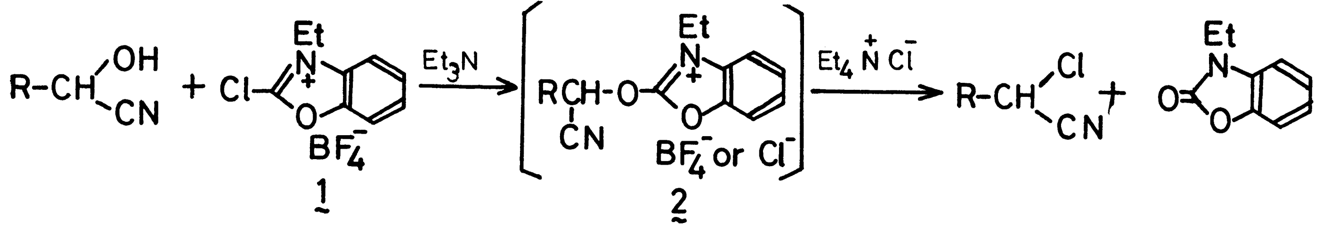
As shown in Table, various cyanohydrins were converted to the corresponding α-chloronitriles in good yields.

Table The Preparation of α-chloronitriles

cyanohydrin	conditions temp.	 time	α-chloronitrile	yield(%)
	0°C then rt	2days		94
 a)	-78°C then rt	overnight		77
	0°C then rt	2days		69
	0°C then rt	overnight		80
	0°C then rt	overnight		70
	0°C then rt	overnight		78
	0°C then rt	overnight		91

a) In this case 2-fluoro-3-ethylbenzothiazolium tetrafluoroborate was used according to the method reported in ref. 5).

The initial step of this reaction is the rapid formation of the intermediate 2 under the mild condition from cyanohydrins and 2-chloro-3-ethylbenzoxazolium tetrafluoroborate. This prevents the dissociation of the cyanohydrins into the component compounds. Thus, the further reaction of the chloride ion with the intermediate 2 affords the corresponding α-chloronitriles in good yields.



As mentioned above, it is noted that various α-chloronitriles were prepared in good yields from the cyanohydrins by the use of 2-chloro-3-ethylbenzoxazolium tetrafluoroborate under the mild reaction condition.

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5) K. Hojo and T. Mukaiyama, Chem. Lett., 1977, 619.

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