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# *N*-Cyanomethyl-β-chloroamines: a convenient source of aziridinium ions

François Couty,* Gwilherm Evano and Damien Prim

*SIRCOB, UMR CNRS 8086, Université de Versailles, 45, avenue des Etats-Unis, 78035 Versailles Cédex, France*

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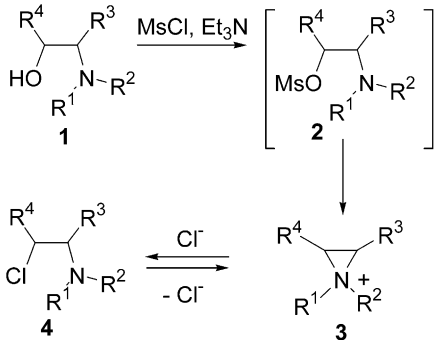
**Abstract**—*N*-Cyanomethyl-β-chloroamines smoothly react with a range of alcohols or amines to give regio- and stereoselectively 1,2-aminoethers or 1,2-diamines. The reaction proceeds through the formation of an intermediate aziridinium ion. The *N*-cyanomethyl group can then be cleaved easily.


Due to the discovery of efficient methods for the asymmetric synthesis of aziridines,[1] and systematic studies of their nucleophilic opening,[2] these compounds have emerged as useful electrophilic synthons within the past decades. In contrast, *N*,*N*-dialkyl aziridinium ions **3**, despite their stronger electrophilic character compared to neutral aziridines, have only scarcely been used as key intermediates in organic synthesis.[3] This can be explained by the lack of availability of a stable and easy to handle precursor to these highly electrophilic ammonium salts that would allow for a smooth and direct generation.

As a matter of fact, *N*,*N*-dialkyl aziridinium ions are most often produced by mesylation of the corresponding β-amino alcohol.[4] Beside the problem of regioselectivity in the course of the nucleophilic opening of the aziridinium, this activation affords various mixtures of aziridinium ion **3** and of β-chloro amine **4**, the sense of the equilibrium depicted in Scheme 1 depending of different factors such as the steric hindrance around the dialkyl amine and the electrophilic character (e.g., a benzylic position) of the chlorine bearing carbon.

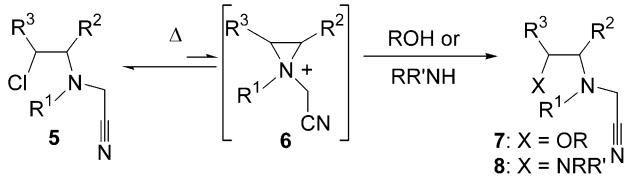
In addition to producing difficult to handle mixtures of neutral β-chloroamines and charged aziridinium ions, this method does not allow for the introduction of common and easy to cleave protecting groups ($R^1$ or $R^2$ in **1**) on the amine moiety of the starting β-amino alcohol. As




**Scheme 1.**

a matter of fact a carbamate would act as an internal nucleophile to produce oxazolidinones[5] and *N*-sulfonyl protecting groups, in addition to their difficult cleavage,[6] would deactivate the nucleophilic character of the nitrogen atom and prevent the formation of the aziridinium ion.

We wish to describe herein the use of *N*-cyanomethyl β-chloroamines **5** as stable precursors of aziridinium ions




**Scheme 2.**

*Keywords*: 1,2-Aminoethers; 1,2-Diamines.
* Corresponding author. Tel.: +33 1 39254455; fax: +33 1 39254452; e-mail: couty@chimie.uvsq.fr

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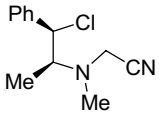
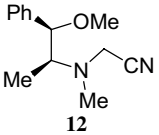
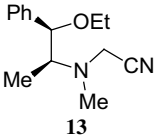
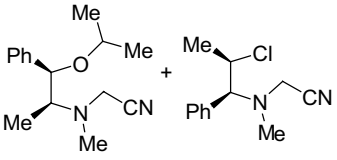
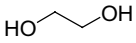
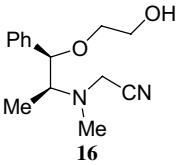
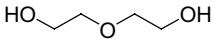
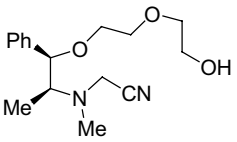
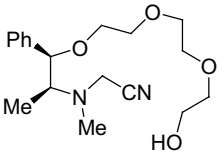
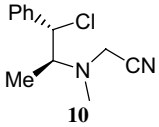
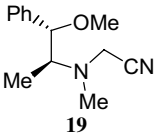
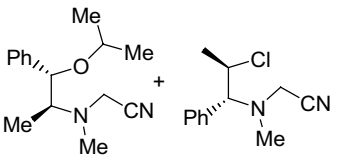
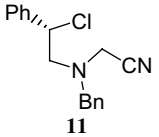
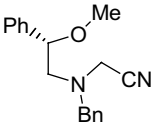
**6**, able to smoothly produce these electrophilic species and react further with alcohols or amines to give *N*-cyanomethyl protected β-aminoethers **7** or 1,2-diamines **8** (Scheme 2).

**Table 1.** Reaction of *N*-cyanomethyl β-chloroamines with alcohols

| Entry | Substrate | Nucleophile | Conditions | Product | Yield[a] (%) |
|---|---|---|---|---|---|
| 1 |  **9** | MeOH | Neat, 0.5 h, 70 °C |  **12** | 91 |
| 2 | **9** | EtOH | Neat, 0.5 h, 70 °C |  **13** | 71 |
| 3 | **9** | *i*-PrOH | Neat, 1 h, 100 °C |  **14** + **15** | 65 (for **14**)[b] **14**/**15**: 6.5/2.5 |
| 4 | **9** |  | Neat, 0.5 h, 80 °C |  **16** | 70 |
| 5 | **9** |  | Neat, 1 h, 80 °C |  **17** | 80 |
| 6 | **9** |  | Neat, 1 h, 80 °C |  **18** | 82 |
| 7 |  **10** | MeOH | Neat, reflux, 3 h |  **19** | 77 |
| 8 | **10** | *i*-PrOH | Neat, reflux, 4 h |  **20** + **21** | 16 (for **20**)[b] **20**/**21**: 1.6/4.4 |
| 9 |  **11** | MeOH | Neat, reflux, 24 h |  **22** | 90 |

[a] Yield of isolated products.
[b] Crude yield determined by NMR: see text.