

A Novel Synthesis of α -Cyanoaziridines

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A new route to α -cyanoaziridines has been developed by reaction of α -chloroketimines with potassium cyanide in methanol, which involves nucleophilic addition and subsequent intramolecular nucleophilic substitution.

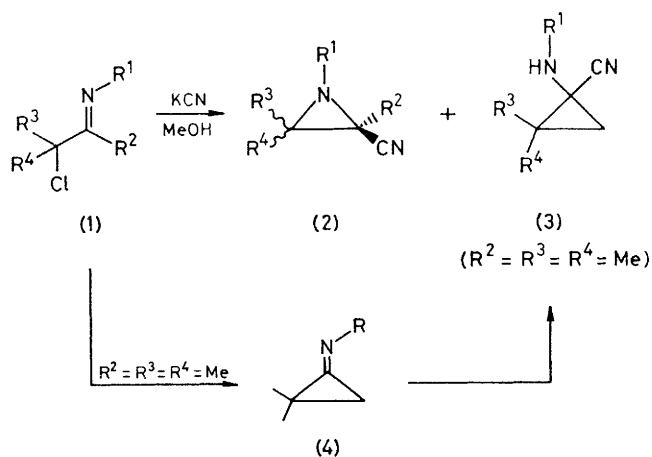
α -Cyanoaziridines are a class of functionalized aziridines which have received considerable attention in view of their ability to undergo 1,3-cycloadditions to, for instance, olefins or alkynes *via* azomethine ylides.^{1,2} The title compounds have already been prepared by reaction of α,β -unsaturated nitriles with nitrenes,³ *N*-unsubstituted oxaziridines⁴ and organic azides,⁵ the reaction of α -halogeno- α,β -unsaturated nitriles with amines,⁶ the addition of diazoacetonitrile to certain benzylideneanilines,⁷ or substitution by cyanide of α -chloroaziridines.⁸

We report a novel and simple synthesis of α -cyanoaziridines (2) by reaction of the readily available α -chloroketimines (1)^{9a} with potassium cyanide in methanol (Table 1, Scheme 1). All α -cyanoaziridines reported in this paper are new compounds. In two cases they are obtained as mixtures of *cis*- and *trans*-isomers (2; R³ = Me; R⁴ = H; R¹ = Prⁱ, cyclohexyl), which can easily be separated by gas chromatographic analysis [*cis/trans* ratio 85:15 (or *vice versa*; tentatively assigned); *cis* refers to the substituent at C-3 with respect to the nitrile function]. Alkyl-substituted α -cyanoaziridines (2)

Table 1. Synthesis of α -cyanoaziridines (2).^a

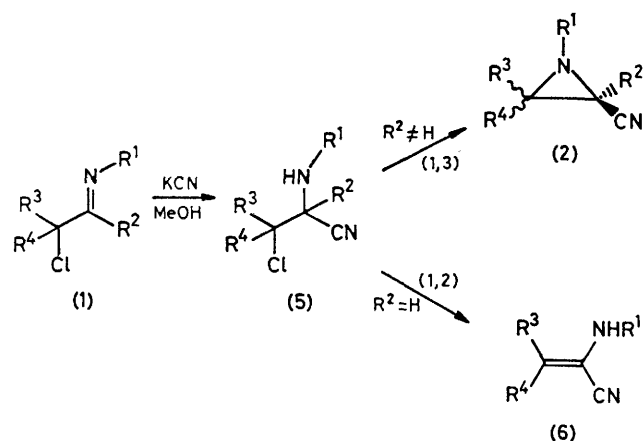
R ¹	R ²	R ³	R ⁴	% Yield ^b	B.p./°C (mmHg)
Pr ⁱ	Me	Me	H	88	58—66 (13) ^c
Bu ^t	Me	Me	H	74	70—75 (11) ^d
Cyclohexyl	Me	Me	H	73	123—130 (18) ^e
Pr ⁱ	Me	Me	Me	73	69—73 (19)
Cyclohexyl	Me	Me	Me	70	119—122 (14)
Pr ⁱ	Me	Ph	H	82 ^e	— ^f

^a Reaction conditions: 1.5—2 equiv. of KCN in methanol (reflux 1—2 h); all compounds gave spectral data (¹H and ¹³C n.m.r., i.r., m.s.) in agreement with the structure and gave satisfactory analytical data. ^b Isolated yield after distillation. ^c Mixture of *cis/trans* isomers (85:15). ^d One isomer (tentatively assigned as *trans*). ^e *cis*-Aziridines exclusively. ^f Isolated by preparative column chromatography (Sigel; CCl₄:diethyl ether 4:1).



Scheme 1

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Scheme 2

do not undergo interconversion of *cis*- and *trans*-isomers on heating, but the aryl-substituted derivative *cis*-2-cyano-1-isopropyl-2-methyl-3-phenylaziridine (2) (obtained as the sole product after reaction with KCN; Ph at C-3 *cis* with respect to the nitrile group) was completely isomerized to the *trans*-isomer by gas chromatographic analysis. This isomerism can best be explained in terms of conrotatory opening of the *cis*-isomer and isomerism of the azomethine thus formed.¹ The formation of α -cyanoaziridines can be interpreted as originating from a nucleophilic addition of cyanide anion to the imino-function, followed by intramolecular nucleophilic substitution (1,3-dehydrochlorination), whereas in the case of α -chloroaldimines (1; $R^2 = H$) a 1,2-dehydrochlorination of the resulting cyanohydrin, leading to α -cyanoenamines (6), was observed^{9b} (Scheme 2). In this respect, α -chloro ketimines parallel, in their reactive behaviour, α -halogeno ketones which yield α -cyanoepoxides on treatment with cyanide.¹⁰ Tertiary α -chloro ketimines (2; $R^3, R^4 \neq H$), with potassium cyanide in methanol, gave rise to a side reaction, namely the formation of cyclopropane derivatives (3). The isolation of these compounds in ca. 10% yield indicates the occurrence of a competitive Favorskii-type reaction, leading to intermediate cyclopropylideneamines (4), which are trapped as the cyanohydrin adducts (3). Formal 1,3-dehydrohalogenations to afford isolable or intermediate cyclopropylideneamines have recently been described.^{11,12} The trapping of cyclopropylideneamines by hydrogen cyanide reported in this paper provides more proof for the intermediacy of the nitrogen analogues of the

well known cyclopropanones during Favorskii-type reactions. On the other hand, the high yield synthesis of the title compounds provides new possibilities in the medicinal field because it was recently found that α -cyanoaziridines possess cancerostatic and immunostimulating properties.¹³

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