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Ring Opening of Epoxides with Acetone Cyanohydrin Catalyzed by Lanthanoid(III) Alkoxides

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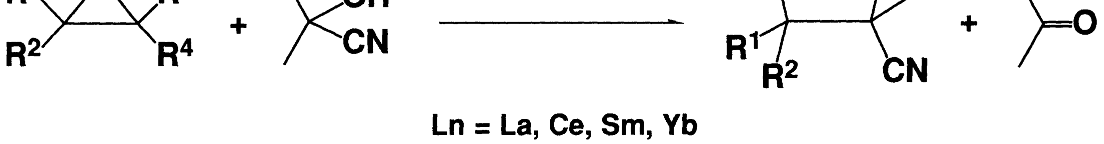
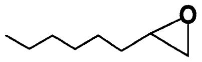
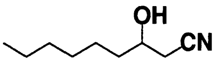
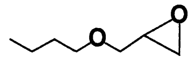
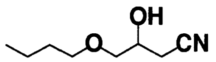
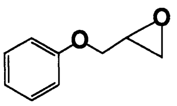
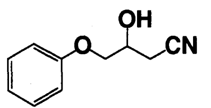
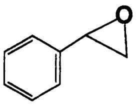
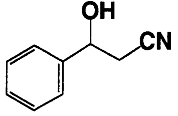
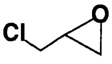
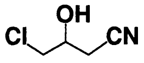
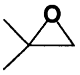
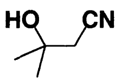
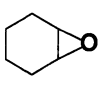
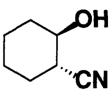
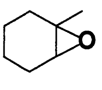
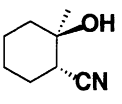
Ring opening of epoxide and aziridine with acetone cyanohydrin is promoted by a catalytic amount of lanthanoid(III) alkoxide to provide β-hydroxy nitrile and β-amino nitrile, respectively.

Recently, we demonstrated the utility of lanthanoid(III) alkoxides as catalysts for a rapid transhydrocyanation from acetone cyanohydrin to several aldehydes and ketones to give the corresponding cyanohydrins.(1) This result encouraged us to investigate the ring opening of epoxides with acetone cyanohydrin in the presence of lanthanoid(III) alkoxide to give β-hydroxy nitriles. Since β-hydroxy nitriles are recognized as versatile intermediates in organic chemistry, an efficient and practical route to obtain the compounds has been important. It is reported that lanthanoid compounds catalyze the ring opening of epoxides with Me_3SiCN to form β-hydroxy nitriles.(2, 3) In addition, the reaction using HCN(4) and LiCN(5) have also been developed for the ring opening of epoxides. But few attempts have been made using acetone cyanohydrin as cyanating reagents. Acetone cyanohydrin is inexpensive and easy to handle compared with volatile and highly toxic HCN, therefore the successful ring opening of epoxide with acetone cyanohydrin is considered to be significant in the synthesis of β-hydroxy nitriles. Mitchell and Koenig recently reported the use of triethylamine as a promoter for the ring opening of epoxides with acetone cyanohydrin,(6) but the reaction required a stoichiometric amount of Et_3N and a high reaction temperature. In this paper, we describe that the ring opening of epoxides with acetone cyanohydrin *proceeded by a catalytic amount of lanthanoid(III) alkoxide* to give β-hydroxy nitriles.



Ln = La, Ce, Sm, Yb

Table 1. Ring opening of several epoxides with acetone cyanohydrin in the presence of a catalytic amount of lanthanoid(III) alkoxide[a)]

Cat.	Substrate	Temp / °C	Time / h	Product[b)]	Yield[c)] / %
La(O*i*-Pr)$_3$		r.t.	7		59
		50	1		80
Ce(O*i*-Pr)$_3$		50	1		73
Sm(O*i*-Pr)$_3$		50	1		63
Yb(O*i*-Pr)$_3$		50	1		70
Et$_3$N		50	1		2
La(O*i*-Pr)$_3$		r.t.	5		72
		50	1		94
		50	2		70
		50	1		72
		50	1		65
		50	4		60
		50	24		35

a) Reactions were carried out using 1.0 equiv. of epoxide, 1.2 equiv. of acetone cyanohydrin, and 5 mol% of catalyst in 0.3 M THF solution.

b) Products were identified by ^{1}H NMR and IR.

c) Isolated yield.

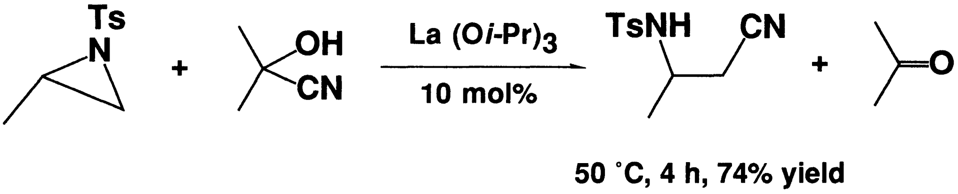
Table 1 summarizes the ring opening of several epoxides with acetone cyanohydrin in the presence of a catalytic amount of lanthanoid(III) alkoxide. Reactions were carried out using 1 equiv. of epoxide and 1.2 equiv. of acetone cyanohydrin in the presence of a catalytic amount (5 mol%) of lanthanoid alkoxides.[7, 8] The reaction of 1, 2-epoxyoctane was first examined using $La(Oi\text{-}Pr)_3$ at room temperature for 7 h to give the corresponding 1-cyano-2-hydroxyoctane in 59% yield. When the reaction was carried out at 50 °C for 1 h, the yield increased to 80%. Other lanthanoid(III) alkoxides such as $Ce(Oi\text{-}Pr)_3$, $Sm(Oi\text{-}Pr)_3$, and $Yb(Oi\text{-}Pr)_3$ similarly exhibited high catalytic activities. The reactions proceeded highly regioselectively by the attack of cyano group at the less substituted carbon on the epoxy ring to yield 1-cyano-2-hydroxyoctane as the sole product. A series of epoxides such as terminal, geminally and vicinally disubstituted, and trisubstituted ones also reacted with acetone cyanohydrin in the presence of a catalytic amount (5 mol%) of $La(Oi\text{-}Pr)_3$ to give the corresponding β-hydroxy nitriles in good yield. It should be pointed out that lanthanoid(III) alkoxides showed a higher reactivity than Et_3N in the ring opening of epoxides with acetone cyanohydrin.[6)] In fact, when the reaction of 1, 2-epoxyoctane was carried out using 5 mol% of Et_3N at 50 °C for 1 h, only 2% of the product was obtained. In addition, the ring opening of cyclohexene oxide, which was reported to be inert to acetone cyanohydrin even with a stoichiometric amount of Et_3N in refluxing THF, proceeded in the presence of a catalytic amount (5 mol%) of $La(Oi\text{-}Pr)_3$ at 50 °C for 4 h in 60% yield.

The reactive species of the catalytic system is considered to be a lanthanoid cyanide. When 2-octanone cyanohydrin was mixed with equimolar amount of $La(Oi\text{-}Pr)_3$ and the mixture was stirred at room temperature for 10 min, most of the cyanohydrin was converted to 2-octanone, which was confirmed by thin layer chromatography on silica gel (stained with phosphomolybdic acid). This result suggested the formation of a lanthanoid cyanide. The addition of 1, 2-epoxyoctane to the mixture afforded the corresponding β-hydroxy nitrile. But the reactive species in our catalytic system would not necessarily be lanthanoid tricyanide. When $Yb(CN)_3$[2b)] was used as catalyst, the reaction of 1, 2-epoxyoctane with acetone cyanohydrin under similar conditions to that using $Ln(Oi\text{-}Pr)_3$ as catalyst gave the corresponding β-hydroxy nitrile in 30% yield at 50 °C for 1 h.

A typical procedure for the reaction of epoxides with acetone cyanohydrin by the use of $La(Oi\text{-}Pr)_3$ as a catalyst is as follows: To a mixture of 1, 2-epoxyoctane (2.5 mmol) and acetone cyanohydrin (3.0 mmol) was added $La(Oi\text{-}Pr)_3$ (0.125 mmol, 0.42 mL of 0.3 M THF solution) under argon, and the mixture was stirred for 1 h at 50 °C. The reaction was quenched with 10 mL of H_2O, and the organic materials were extracted twice with 50 mL of ether. The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated in vacuo to leave a crude product, which was purified by chromatography on silica gel (hexane : ethyl acetate = 4

: 1), after removal of solvent, to afford 0.31 g (80%) of 1-cyano-2-hydroxyoctane as a colorless oil.

The ring opening reaction with acetone cyanohydrin catalyzed by lanthanoid(III) alkoxides was also effective for aziridine.9) As shown below, the ring opening of N-(4-toluenesulfonyl)-propyleneimine proceeded using 10 mol% of La(O*i*-Pr)$_3$ at 50 °C for 4 h to give the corresponding N-(4-toluenesulfonyl)-*β*-amino nitrile in 74% yield.



In conclusion, the ring opening of epoxide and aziridine with acetone cyanohydrin was shown to proceed smoothly catalyzed by lanthanoid(III) alkoxides such as La(O*i*-Pr)$_3$, Ce(O*i*-Pr)$_3$, Sm(O*i*-Pr)$_3$, and Yb(O*i*-Pr)$_3$. It is apparent that the titled catalytic reaction by lanthanoid(III) alkoxides is efficient in organic synthesis, since inexpensive and easy to handle acetone cyanohydrin is available as a cyanating reagent.

References

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8) When Ln(O*i*-Pr)$_3$ in the presence of LiCl was used as catalyst for the ring opening of 1, 2-epoxyoctane with acetone cyanohydrin, the corresponding chlorohydrin was obtained in 5-10% yield along with β-hydroxy nitrile as the major product (≈ca: 70% yield).

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