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Lanthanoid(III) Alkoxides as Novel Catalysts for a Rapid Transhydrocyanation from Acetone Cyanohydrin to Aldehydes and Ketones

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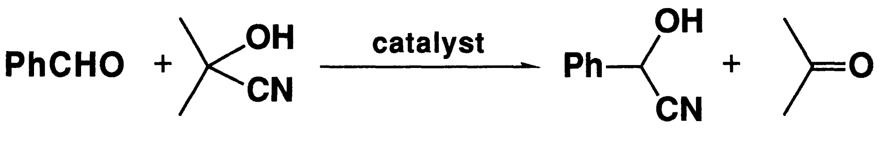
A rapid transhydrocyanation from acetone cyanohydrin to several aldehydes and ketones is promoted by a catalytic amount of lanthanoid(III) alkoxide to provide the corresponding cyanohydrins.

Since cyanohydrins are recognized as useful synthetic intermediates, development of an efficient cyanation reaction has attracted much attention in organic synthesis. Transhydrocyanation from acetone cyanohydrin to carbonyl compound has been considered as a practical cyanating method in laboratory level in the aspects of an alternative of hydrocyanation using volatile and highly toxic hydrogen cyanide. Transhydrocyanation is known to proceed in the presence of bases such as tertiary amines$^{1)}$ and potassium carbonate.$^{2)}$ We recently reported that the use of stoichiometric amount of titanium(IV) alkoxide promoted the transhydrocyanation,$^{3)}$ but the reactions using titanium(IV) alkoxide were still slow and a novel catalyst with higher reactivity has been required. On the other hand, recent studies on lanthanoid alkoxides toward organic synthesis$^{4, 5)}$ encouraged us to investigate the use of lanthanoid alkoxide as a catalyst for the transhydrocyanation. In this paper, a rapid transhydrocyanation from acetone cyanohydrin to several aldehydes and ketones promoted by a catalytic amount of lanthanoid alkoxide is described.



catalyst: La(O*i*-Pr)$_3$, Ce(O*i*-Pr)$_3$, Sm(O*i*-Pr)$_3$, Yb(O*i*-Pr)$_3$

Several lanthanoid reagents were examined as catalysts in the transhydrocyanation from acetone cyanohydrin to benzaldehyde. Reactions were carried out at room temperature using 1 equiv. of benzaldehyde and 1.2 equiv. of acetone cyanohydrin in the presence of a catalytic amount of lanthanoid reagents. Lanthanoid reagents were used as purchased or prepared by the reported procedures. La(O*i*-Pr)$_3$, Ce(O*i*-Pr)$_3$, Sm(O*i*-Pr)$_3$, and Yb(O*i*-Pr)$_3$ were prepared by the reaction of $LnCl_3$•3*i*-PrOH with 3 equiv. of BuLi by following Kagan's procedure$^{5a)}$ and used as a 0.3 M THF solution containing LiCl. Yb_2O_3 and $YbCl_3$•$6H_2O$ were purchased, and Yb(OTf)$_3$$^{6)}$ were synthesized, and they were used as powder. $Bu_3Yb$$^{7)}$ prepared by the reaction of $YbCl_3$ with 3 equiv. of BuLi was used as THF solution which contains LiCl, and MeLa(OTf)$_2$$^{8)}$ prepared by the reaction of La(OTf)$_3$ with 1 equiv. of MeLi was used as THF solution containing LiOTf. The results of the transhydrocyanation of benzaldehyde catalyzed by lanthanoid reagents are summarized in Table 1. In dramatic contrast with our previous results[3)] using $Ti(O\textit{i}-Pr)_4$ or $Al(O\textit{i}-Pr)_3$, the transhydrocyanation promoted by $Ln(O\textit{i}-Pr)_3$ proceeded even with a catalytic amount of the alkoxide (1 mol%) to give mandelonitrile in good yields. The reaction is rapid as exemplified by the transhydrocyanation catalyzed by 1 mol% of $Yb(O\textit{i}-Pr)_3$ which gave mandelonitrile in 18, 62, and 82% yield after 10 s, 1 min, and 3 min respectively. Bu_3Yb was also found to be as effective as $Ln(O\textit{i}-Pr)_3$. On the other hand, $MeLa(OTf)_2$ showed low activity, and the reaction did not proceed in the presence of Yb_2O_3, $Yb(OTf)_3$, and $YbCl_3 \cdot 6H_2O$.

Table 1. Transhydrocyanation from acetone cyanohydrin to benzaldehyde catalyzed by lanthanoid reagents

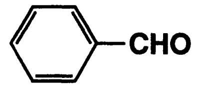
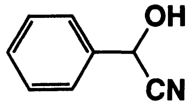
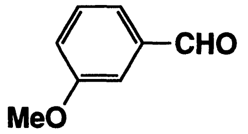
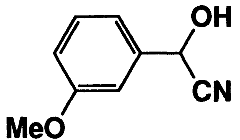
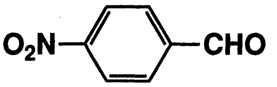
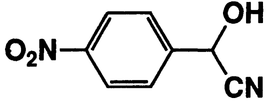
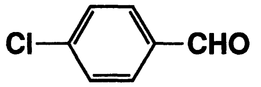
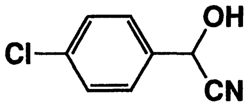
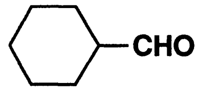
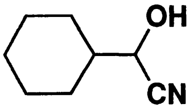
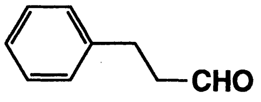
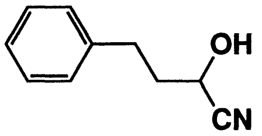
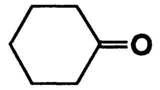
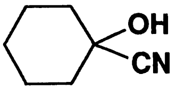
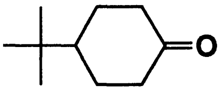
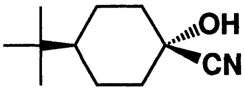
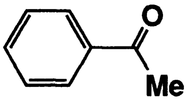
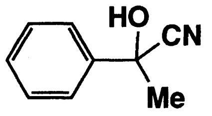
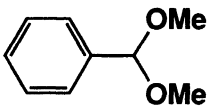
Catalyst	mol%	Time / h	Yield[b)] / %
$La(O\textit{i}-Pr)_3$	1	0.5	86
$Ce(O\textit{i}-Pr)_3$	1	0.5	88
$Sm(O\textit{i}-Pr)_3$	1	0.5	86
$Yb(O\textit{i}-Pr)_3$	1	0.5	91
	1	10 s	18
	1	1 min	62
	1	3 min	82
Bu_3Yb	1	0.5	82
$MeLa(OTf)_2$	1	24	47
Yb_2O_3	1	24	trace
$Yb(OTf)_3$	1	24	0
$YbCl_3 \cdot 6H_2O$	1	24	0
$Ti(O\textit{i}-Pr)_4$[a)]	100	19	quant
	5	48	0
$Al(O\textit{i}-Pr)_3$	5	0.5	12

a) Data of our previous study.[3)]
b) Determined by ^1H NMR of crude product as a mixture of mandelonitrile and unreacted benzaldehyde.

Table 2 summarizes the transhydrocyanations from acetone cyanohydrin to several aldehydes and ketones to give the corresponding cyanohydrins in the presence of a catalytic amount (1 mol%) of $Yb(O\textit{i}-Pr)_3$ which showed a high catalytic activity toward benzaldehyde. Aromatic aldehydes containing electron donating or withdrawing group were also converted to the corresponding cyanohydrins in good yields. In addition, the reaction proceeded smoothly with aliphatic aldehydes and ketones. In the case of acetophenone as a substrate, however, only 5% yield of the corresponding cyanohydrin was obtained. Benzaldehyde dimethyl acetal did not react with acetone cyanohydrin.

The rapid transhydrocyanation is considered due to the strong basicity of $Ln(O\textit{i}-Pr)_3$, although the detail mechanism of the reaction catalyzed by $Ln(O\textit{i}-Pr)_3$ is yet to be clarified.

Table 2. Transhydrocyanation from acetone cyanohydrin to several aldehydes and ketones in the presence of a catalytic amount (1 mol%) of $\mathrm{Yb(O}i\mathrm{\text{-}Pr)_3}$[a)]

Substrate	Product	Yield / %
		91[b)]
		83[b)]
		50[b)]
		83[b)]
		86[c)]
		97[c)]
		94[c)]
		93[c, d)]
		5[c)]
	no reaction[e)]	

a) Reactions were carried out using 1.0 equiv. of aldehyde or ketone, 1.2 equiv. of acetone cyanohydrin and 1 mol% of $\mathrm{Yb(O}i\mathrm{\text{-}Pr)_3}$ in 0.3 M THF solution at rt for 30 min.

b) Determined by ^{1}H NMR of a mixture of cyanohydrin and unreacted aldehyde.

c) Isolated yield.

d) The isomer ratio was 73:27.

e) Reaction time was 1 h.

Typical procedure for the transhydrocyanation from acetone cyanohydrin to benzaldehyde by the use of Yb(O*i*-Pr)$_3$ as a catalyst is as follows: To a mixture of benzaldehyde (2.5 mmol) and acetone cyanohydrin (3.0 mmol) was added Yb(O*i*-Pr)$_3$ (0.025 mmol, 0.083 ml of 0.3 M THF solution) under argon, and the mixture was stirred for 3 min at room temperature. The reaction was quenched with 2 M HCl, and the organic materials were extracted with ether. The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated in vacuo to leave a mixture of mandelonitrile and unreacted benzaldehyde as a colorless liquid (conversion 82% by ^{1}H NMR). The crude product was purified by chromatography on silica gel (hexane : ethyl acetate = 10 : 1), after removal of the solvent, to afford 0.27 g (80%) of mandelonitrile.

In conclusion, lanthanoid alkoxides such as La(O*i*-Pr)$_3$, Ce(O*i*-Pr)$_3$, Sm(O*i*-Pr)$_3$, and Yb(O*i*-Pr)$_3$ were found to be efficient catalysts for the transhydrocyanation from acetone cyanohydrin to several aldehydes and ketones.

References

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