

Preparation and Utility of Novel Water-Tolerant Higher-Order Lanthanoid Alkoxide Complexes as a Base Catalyst

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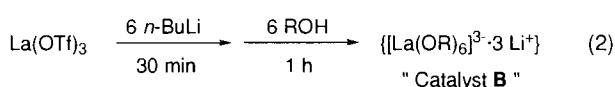
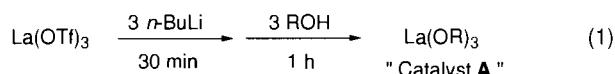
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A series of higher-order lanthanoid-lithium mixed-alkoxide complexes have been prepared as a novel water-tolerant base catalyst which effectively promotes the Robinson-type reaction in the presence of water.

Lanthanoid salts of strong acids such as triflates and perlates have recently been used as a useful water-tolerant Lewis acid catalyst in organic synthesis.¹ On the other hand, lanthanoid alkoxides,² which in turn work as a base catalyst,³ are quite sensitive to water. They are easily hydrolyzed with a small amount of water and tend to produce polymeric hydroxide complexes which are insoluble in most organic solvents thus loosing their catalytic activity as a base. In order to circumvent this situation, Okano et al. successfully used Molecular Sieves 4A in the lanthanum(III) tri-isopropoxide-catalyzed Robinson-type annelation reaction.^{3g} As an alternative way, we planned to use a thermodynamically stable higher-order ate-type complex which may potentially have a self-healing⁴ nature in the presence of water by virtue of the high coordination number of the lanthanoid ions in combination with polydentate ligands.

Based on this idea, the following two types of lanthanum alkoxide complexes (types **A** and **B**) were prepared from $\text{La}(\text{OTf})_3$ by treating them with 3 eq or 6 eq of *n*-BuLi and various mono- or polyols according to equations 1 and 2.



Their relative catalytic activities were compared in the Robinson-type reaction of chalcone with 2-butanone (Eq 3). Some selected results are summarized in Table 1. As expected, the higher-order ate-complexes (type **B**) catalyzed the reaction more effectively than the type **A** complexes.^{5,6} The observed low catalytic activity of the lanthanum tri-methoxyethoxyethoxide compared to the corresponding tri-isopropoxide may be imputable to the lower basicity of the former due to the smaller pK_a value of methoxyethoxyethanol ($pK_a \approx 14$) than that of 2-propanol ($pK_a \approx 18$). It should also be noted that the type **B** catalysts showed generally higher activity than the corresponding dilithium alkoxides (see footnote b in Table 1: runs 8, 10, 11, and 12).

Among the alcohols tested, polyethylene glycol (PEG) with an average molecular weight of ca. 200, the major part of which must be tetraethylene glycol, was found to be the best. Therefore, the effect of the central metal ions of a series of Ln -PEG-Li

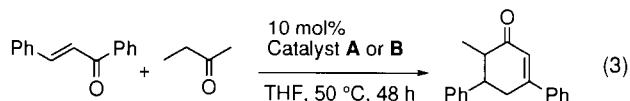


Table 1. Effect of alcoholic ligands used for the preparation of the catalysts (**A** or **B**) on the yield of the product (Eq. 3)^a

Run	ROH (eq)	Catalyst/type	Yield/% ^b
1	—	$\text{La}(\text{O-}i\text{-Pr})_3^c$	71
2		(3) A	33
3 ^d		(3) A	16 ^e
4 ^d		(3) A	48 ^c
5		(3) A	59 ^c
6		(3) A	52 ^f
7		(3) B	67
8		(3) B	78 (69)
9		(3) B	73
10		(3) B	87 (60)
	M. W. ca. 200		
11	M. W. ca. 300	(3) B	87 (51)
12	M. W. ca. 400	(3) B	73 (62)

^aCatalysts were prepared according to Eq. 1 or 2. ^bIsolated yield of the product. In parentheses are shown the yields obtained by using the corresponding dilithium alkoxides. ^cPurchased from Kojundo Chemical Co., Ltd., Japan. ^d20 mol% of the catalyst was used. ^eReaction time: 24 h. ^fReaction time: 72 h.

($\text{Ln}=\text{Sc, Y, and La-Lu}$) complexes (**1**) on the product yield were then investigated. As shown in Table 2, almost all complexes were found to be as effective as the lanthanum catalyst.

Taking the best catalyst (Tb-PEG-Li), we then examined the influence of water on the activity of the catalyst. The results

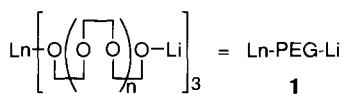


Table 2. Effect of Ln of the catalyst (Ln-PEG-Li) on the yield of the product (Eq. 3)

Ln	Yield/% ^a	Ln	Yield/% ^a
Sc	87	Gd	87
Y	77	Tb	94
La	87	Dy	75
Ce	73	Ho	89
Pr	83	Er	79
Nd	85	Tm	78
Sm	90	Yb	86
Eu	85	Lu	91

^aIsolated yield.

Table 3. The catalytic Robinson-type annelation in the presence of water^a

Substrates (mmol)	Catalyst ^b	Product	Yield/% ^c
	Tb-PEG-Li		68 (80) ^d
	Li-PEG-Li		12
	La(O-i-Pr) ₃		nr
	Li(O-i-Pr)		16
	Tb-PEG-Li		62
	La(O-i-Pr) ₃		trace
	Tb-PEG-Li		70
	La(O-i-Pr) ₃		10
	Tb-PEG-Li		46 ^c
	La(O-i-Pr) ₃		nr ^c
	Tb-PEG-Li		33 ^{f, g}
	La(O-i-Pr) ₃		1 ^{f, h}

^a300-600 mol% of H₂O was added. Unless otherwise noted, the reactions were performed at 50 °C for 48 h. ^b10 mol%. ^cIsolated yield. nr = no reaction. ^dReaction time: 138 h. ^eReaction time: 96 h. ^fGC yield. ^gUncyclized product (16%) was also produced. ^hUncyclized product (6%).

shown in Table 3 clearly indicate the superiority of the Tb-PEG-Li complex over the others.⁷ Although the precise structure of the complex is not known at present, it must have some self-healing character in order to maintain its catalytic activity.

In summary, we prepared a novel ate-type lanthanoid alkoxide complex which can work as an effective base catalyst in the presence of water. Further efforts toward the development of lanthanoid-involved solid base catalysts are being made along this line.

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References and Notes

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- Recently, 1,1'-binaphthol-derived ate-type chiral lanthanoid complexes bearing Li⁺, Na⁺, or K⁺ ions as co-cations have been prepared and successfully used in a variety of asymmetric syntheses: a) M. Shibasaki, H. Sasai, and T. Arai, *Angew. Chem., Int. Ed. Engl.*, **36**, 1236 (1997) and references cited therein. b) Y. M. A. Yamada, N. Yoshikawa, H. Sasai, and M. Shibasaki, *Angew. Chem., Int. Ed. Engl.*, **36**, 1871 (1997). However, the catalysts were found not to be effective to the Robinson-type annelation reaction.^{3g}
- Presented at the 74th Meeting of the Chemical Society of Japan, Kyoto, March, 1998.
- A typical experimental procedure follows. To a solution of Tb(OTf)₃ (12.1 mg, 0.02 mmol) in THF (1 ml) was added a hexane solution of *n*-BuLi (1.58 M, 76 μ l, 0.12 mmol). After stirring for 30 min at room temperature, a THF solution of polyethylene glycol (mol. wt. ca. 200, 10.7 μ l, 0.06 mmol) was added and the mixture was stirred further for 1 h. To this mixture was added a solution of chalcone (41.6 mg, 0.2 mmol) and 2-butanone (180 ml, 2.0 mmol) in THF (1 ml) and the whole mixture was stirred for 48 h at 50 °C. The reaction mixture was passed through a short column of silica gel. After evaporation of the solvent, the crude product was purified by preparative TLC (hexane/CH₂Cl₂=10/1, two times development) to give 3,5-diphenyl-6-methyl-2-cyclohexen-1-one (49.3 mg, 94%) as a diastereomeric mixture (81:19).