Utilization of heterobimetallic complexes as Lewis acids

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Abstract

The lithium-containing multifunctional heterobimetallic catalysts such as LaLi$_3$tris((R)-6,6′-dibromobinaphthoxide) showed moderate Lewis acidity in non-polar solvents. Asymmetric Diels–Alder reactions proceeded efficiently in the presence of the heterobimetallic catalyst. This is the first application of heterobimetallic asymmetric catalysts solely as Lewis acids. © 1998 Elsevier Science Ltd. All rights reserved.

1. Introduction

We have developed heterobimetallic asymmetric catalysts which function as both Brønsted bases and Lewis acids at the same time.[1] For example, LaLi$_3$tris(binaphthoxide) complex (LLB; L=lanthanum, L=lithium, and B=binaphthoxide, respectively) is quite effective in catalytic asymmetric nitroaldol and direct aldol reactions,[1b,2c–e] and AlLibis(binaphthoxide) complex[3] (ALB; A=aluminum, and L=lithium, respectively) shows high enantioselectivity in either catalytic asymmetric Michael reactions or catalytic asymmetric tandem Michael–aldol reactions. Both of these catalysts are also complementarily effective towards enantioselective addition of dimethyl phosphite to various types of aldehydes.[1,2a] Recently we have also revealed that the regio- and enantioselective addition of Horner–Wadsworth–Emmons reagents to enones[2f] and the catalytic asymmetric ring-opening of meso-epoxides[2b] efficiently proceed by activated ALB[4] and GaLibis(binaphthoxide) complex (GaLB),[2b] respectively. The structures of most of these heterobimetallic asymmetric catalysts have been unequivocally determined by spectroscopic analyses and X-ray crystallography, as shown in Fig. 1.[1–4]

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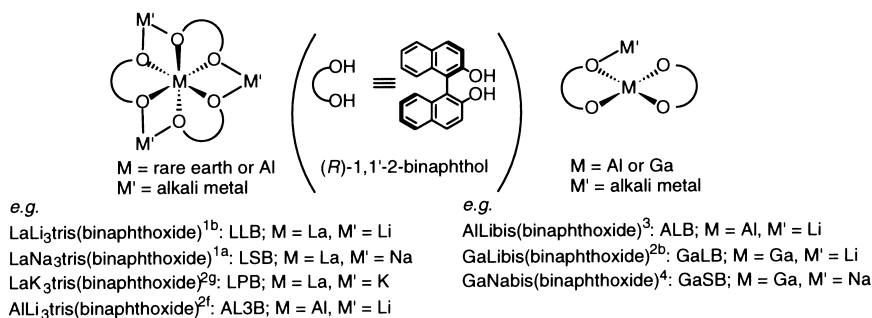
Fig. 1. Structures and abbreviations of representative heterobimetallic complexes

M = rare earth or Al
M' = alkali metal

(*R*)-1,1'-2-binaphthol

M = Al or Ga
M' = alkali metal

e.g.
LaLi$_3$tris(binaphthoxide)[1b]: LLB; M = La, M' = Li
LaNa$_3$tris(binaphthoxide)[1a]: LSB; M = La, M' = Na
LaK$_3$tris(binaphthoxide)[2g]: LPB; M = La, M' = K
AlLi$_3$tris(binaphthoxide)[2f]: AL3B; M = Al, M' = Li

e.g.
AlLibis(binaphthoxide)[3]: ALB; M = Al, M' = Li
GaLibis(binaphthoxide)[2b]: GaLB; M = Ga, M' = Li
GaNabis(binaphthoxide)[4]: GaSB; M = Ga, M' = Na

2. Results and discussion

We have already reported several pieces of evidence which indicate that the central metals in heterobimetallic catalysts are the origin of Lewis acidity and the role of alkali metal binaphthoxide moieties is as Brønsted bases. In order to promote efficient enantioselective reactions by heterobimetallic complexes, the balance of the synergistic cooperation of Brønsted basicity and Lewis acidity would be important. If the basicity (or acidity) of these asymmetric catalysts is too strong compared to the other function, the reactions would be governed by only one function of the catalyst which would give lower enantioselectivities. Though the basicity of the catalysts can be estimated by a proton abstraction from various types of substrates, the assessment of the magnitude of Lewis acidity is rather difficult. Thus, we made attempts to investigate the Lewis acidity of the heterobimetallic asymmetric catalysts by the asymmetric Diels–Alder reaction of cyclopentadiene (**1**) with α,β-unsaturated N-acyloxazolidinones (e.g., **2**), which could be carried out with a number of different optically active Lewis acids.[5] We report here the first application of the optically active heterobimetallic complexes solely as asymmetric Lewis acids.

Although various heterobimetallic catalysts promote asymmetric reactions enantioselectively in THF,[1–4] all the heterobimetallic catalysts examined (LLB, LSB, LPB, ALB, and AL3B[2f]) gave an almost racemic adduct **3**. However in non-polar and non-coordinative solvents such as toluene or CH$_2$Cl$_2$, moderate enantioselectivities were observed using LLB. The enantiomeric excesses of *endo*-**3** were increased when the reactions were carried out at lower temperature. Representative results are shown in Table 1.

It is interesting to note that AL3B, which has a saturated coordination number with respect to the aluminum atom, gave 16% ee of *endo*-**3** (Table 1, entry 8). This result suggests that the lithium atoms in the heterobimetallic complexes act as Lewis acids in non-polar solvents.[6] Even though the dienophile **2** is activated by the center metal of a heterobimetallic catalyst such as LLB, the approach of **1** to **2** would be difficult due to the steric repulsion. Although the first purpose of assessing the Lewis acidity of the heterobimetallic complexes was invalidated, we continued to optimize the asymmetric catalysis since good enantioselectivities were obtained using LLB-type catalysts.

The introduction of 6,6′-substituents to binaphthol is effective in preparing efficient LLB-type catalysts for catalytic asymmetric nitroaldol reactions.[7] The 6,6′-substituted binaphthol-derived LLB-type catalyst also showed high enantioselectivities in the Diels–Alder reaction. As shown in Table 2, the LaLi$_3$tris(6,6′-ethynylbinaphthoxide) complex gave a 93% yield of *endo*-**3** in 78% ee (*endo*:*exo*=19:1). Moreover, the LaLi$_3$tris(6,6′-dibromobinaphthoxide) complex gave a quantitative yield of **3** in 86% ee with a high *endo* selectivity (*endo*:*exo*=36:1). The bromo substituents appeared to increase the Lewis acidity of the LLB-type catalyst. The nature of the center metal in LLB-type catalysts also affects the enantioselectivity in

Table 1

Catalytic asymmetric Diels–Alder reaction promoted by the heterobimetallic complexes
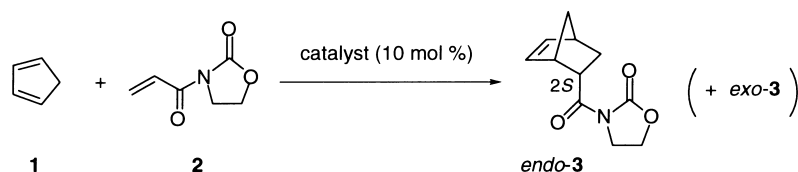
entry	catalyst[a]	solvent	temp (°C)	time (h)	yield (%)	*endo : exo*[b]	ee of *endo*-3 (%)[b,c]
1	LLB	THF	0	16	66	14 : 1	1
2	LLB	CH$_2$Cl$_2$	0	16	57	20 : 1	33
3	LLB	toluene	0	16	62	16 : 1	35
4	LLB	toluene	-20	48	82	15 : 1	63
5	LSB	toluene	0	16	78	9 : 1	4
6	LPB	toluene	0	40	63	8 : 1	1
7	ALB	CH$_2$Cl$_2$	-20	96	67	9 : 1	2
8	AL3B	CH$_2$Cl$_2$	-20	48	65	16 : 1	16
9	none	CH$_2$Cl$_2$	-20	48	72	14 : 1	0

a) Prepared from (*R*)-1,1′-2-binaphthol.   b) Determined by HPLC analysis.   c) Absolute configurations were determined to be *S*. See reference 5.

nitroaldol reactions.[1b,2e] In this case (Table 2, entries 3–8), the La-derived catalyst gave the highest enantiomeric excess (Pr=79% ee, Sm=70% ee, Gd=68% ee, Dy=70% ee, Yb=58% ee). It is also noteworthy that LLB-type catalysts can be utilized in Diels–Alder reactions without any special care regarding oxygen and moisture.

Since mono- and dilithium salts of 6,6′-dibromobinaphthol catalyzed Diels–Alder reactions which proceeded with low enantioselectivities, an asymmetric environment constructed by heterobimetallic catalysts would be essential for obtaining high enantiomeric excesses. In all cases, (*R*)-binaphthol- and/or (*R*)-6,6′-disubstituted binaphthol-derived catalysts gave a 2*S*-configuration of *endo*-3. The proposed mode of enantioselection of the Diels–Alder reaction catalyzed by LaLi$_3$tris((*R*)-6,6′-dibromobinaphthoxide) is depicted in Fig. 2.[8] When the dienophile 2 coordinates to the lithium, one side of the π-face of 2 would be concealed by the binaphthyl ring of the complex.

In conclusion, we have succeeded in applying the heterobimetallic catalyst, LnLi$_3$tris(6,6′-dibromobinaphthoxide) complex, to asymmetric Diels–Alder reactions in non-polar solvents. This is the first example of using a heterobimetallic asymmetric catalyst solely as a Lewis acid. Further examinations using heterobimetallic catalysts as Lewis acid catalysts are under study.[9]

3. Experimental section

The optimized procedure: After concentrating a THF solution of 0.025 M LaLi$_3$tris(6,6′-dibromobinaphthoxide) complex (0.8 mL, 0.02 mmol), which was prepared from La(O-*i*-Pr)$_3$,[10] 3 mol equiv. of (*R*)-6,6′-dibromobinaphthol and 3 mol equiv. of BuLi, the resulting powder was redissolved in toluene (2 mL) and cooled to −20°C. To this solution were added dienophile 2 (28.2 mg, 0.2 mmol) and cyclopentadiene 1 (0.2 mL, 2.4 mol). After stirring for 20 h at −20°C, the reaction

Table 2

Optimization of the catalytic asymmetric Diels–Alder reaction

$$1 + 2 \xrightarrow[\text{toluene, -20 °C}]{} 3$$
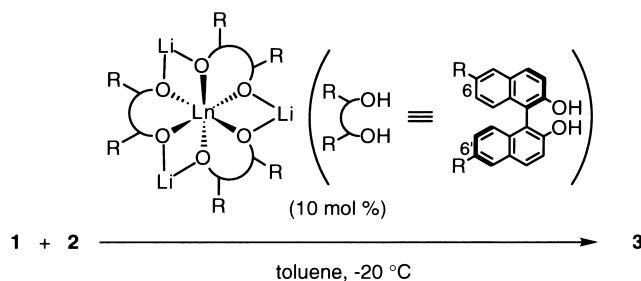
entry[a]	R	Ln	time (h)	yield (%)	*endo* : *exo*[b]	ee of *endo*-3 (%)[b,c]
1	H-≡-	La	24	93	19 : 1	78
2	Me$_3$Si-≡-	La	24	89	16 : 1	74
3	Br	La	20	100	36 : 1	86
4	Br	Pr	20	94	25 : 1	79
5	Br	Sm	48	92	18 : 1	70
6	Br	Gd	48	92	18 : 1	68
7	Br	Dy	48	97	22 : 1	70
8	Br	Yb	48	100	19 : 1	58

a) All catalysts are prepared from (*R*)-6,6'-disubstituted binaphthol.   b) Determined by HPLC analysis.   c) Absolute configurations were determined to be *S*.   See reference 5.
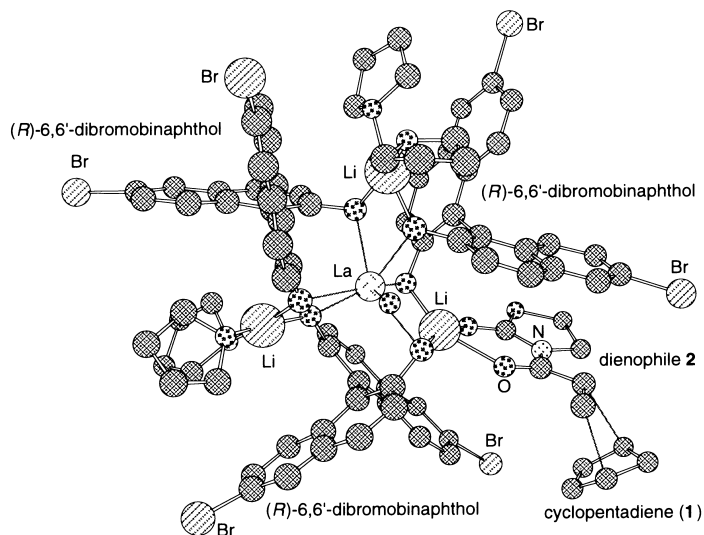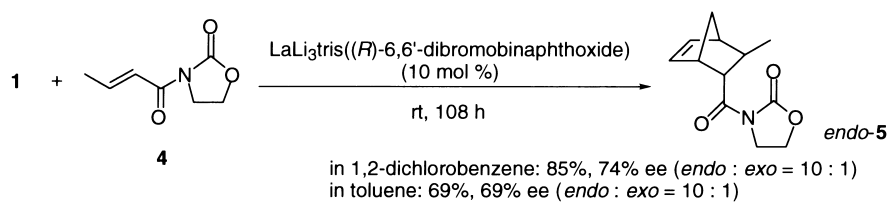
Fig. 2. Proposed mechanism for the mode of enantioselection

mixture was treated with 1 N HCl (2.0 mL) followed by extraction with EtOAc (3×10 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated to give a residue. Purification by flash chromatography (SiO_2, 10% acetone/hexane) gave the Diels–Alder product **3** (41 mg, 100%). The enantiomeric excess of *endo*-**3** was determined as 86% by HPLC (Daicel Chiralcel OD, hexane:*i*-PrOH=98:2).

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6. Addition of 12-crown-4 to AL3B and/or LLB catalyzed Diels–Alder reaction resulted in the formation of **3** with much lower enantiomeric excess (<5% ee). This result also appears to suggest that the lithium cation(s) play a key role in activation of the dienophile.

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8. Catalyst structure was based on the X-ray crystallography of LSB, and the sodium atoms were replaced with lithium atoms. Since a small amount of THF remained after drying LaLi₃tris(6,6′-dibromobinaphthoxide) in THF, the coordination of two of each of the THF molecule to lithium atoms other than active site would be reasonable. The forming C–C bond lengths in the *S-cis* transition state structure of **1** and methyl acrylate, calculated by Houk et al., were taken into account in the reaction of **1** with **2**. The geometry of the whole structure other than the forming C–C bond lengths was optimized by UFF calculation. For the transition state, see (a) Pascual-Teresa, B.; Gonzalez, J.; Asensio, A.; Houk, K. N. *J. Am. Chem. Soc*. **1995**, *117*, 4347–4356. For UFF calculation, see Ref. 1(a) and (b) Rappé, A. K.; Colwell, K. S.; Casewit, C. J. *Inorg. Chem*. **1993**, *32*, 3438–3450 and references therein.

9. We also examined the methyl-substituted dienophile **4**, which is less reactive than **2**. The LaLi₃tris(6,6′-dibromobinaphthoxide) complex was also an effective catalyst for the reaction between **1** and **4** in non-polar solvents.

LaLi₃tris((*R*)-6,6'-dibromobinaphthoxide)
(10 mol %)

rt, 108 h

in 1,2-dichlorobenzene: 85%, 74% ee (*endo* : *exo* = 10 : 1)
in toluene: 69%, 69% ee (*endo* : *exo* = 10 : 1)

10. Purchased from Kojundo Chemical Laboratory Co., Ltd, 5-1-28 Chiyoda, Sakado-shi, Saitama 350-0214, Japan. Fax: +81-492-84-1351.