# Heterobimetallic asymmetric catalysts. Developments and applications
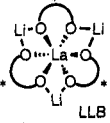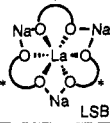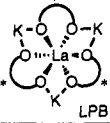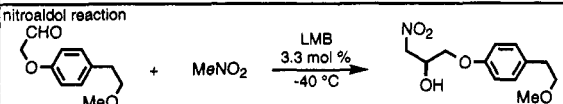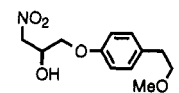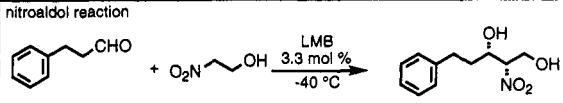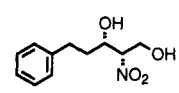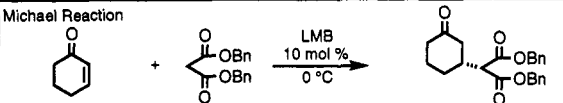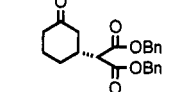
Masakatsu Shibasaki,* Hiroaki Sasai, Takayoshi Arai, and Takehiko Iida

*Graduate School of Pharmaceutical Sciences, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113, Japan*

*Abstract*: Further development of a variety of catalytic asymmetric reactions promoted by heterobimetallic asymmetric complexes such as a tandem inter-intramolecular catalytic asymmetric nitroaldol reaction, a direct catalytic asymmetric reaction of aldehydes and unmodified ketones, an enantioselective ring opening of epoxides with thiols, and a catalytic asymmetric epoxidation of $\alpha,\beta$-unsaturated ketones are described.

Rare earth-alkali metal-BINOL complexes such as $LnM_3tris$(binaphthoxide) complexes (LnMB, Ln = rare earth, M = alkali metal, B = BINOL or its derivatives) are readily prepared from the corresponding rare earth trichlorides and/or rare earth isopropoxides. Moreover, group 13 element-alkali metal-BINOL complexes (ALB, GaLB, and GaSB, A = aluminium, L = lithium, B = BINOL, Ga = gallium, S = sodium) are also readily prepared from $LiAlH_4$ and/or $GaCl_3$. The X-ray structures of these heterobimetallic complexes are shown in Fig. 1. The heterobimetallic asymmetric complexes function as both a Brønsted base and as a Lewis acid, just as enzymes do, making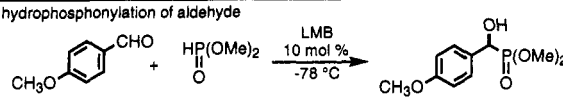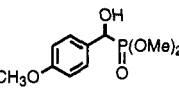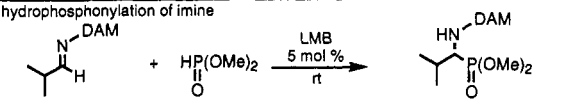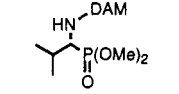 possible a variety of efficient catalytic asymmetric reactions. The already reported examples are summarized in Table 1 and Scheme 1.(1)

TABLE 1. Catalytic Asymmetric Reactions Using LnMB

| asymmetric reaction / LnMB | LLB | LSB | LPB |
|---|---|---|---|
| **nitroaldol reaction** (CHO + MeNO₂, LMB 3.3 mol %, −40 °C) | y. 90% 94% ee | y. 92% 2% ee | not examined |
| **nitroaldol reaction** (CHO + O₂N–OH, LMB 3.3 mol %, −40 °C) | y. 96% (*syn / anti* = 92 / 8) 95% ee | not examined | not examined |
| **Michael Reaction** (+ OBn/OBn, LMB 10 mol %, 0 °C) | y. 78% 2% ee | y. 91% 92% ee | y. 99% 48% ee |
| **hydrophosphonylation of aldehyde** (CHO + HP(OMe)₂, LMB 10 mol %, −78 °C) | y. 87% 93% ee | not examined | not examined |
| **hydrophosphonylation of imine** (N-DAM + HP(OMe)₂, LMB 5 mol %, rt) | y. 46% 38% ee | y. 38% 49% ee | y. 70% 96% ee |
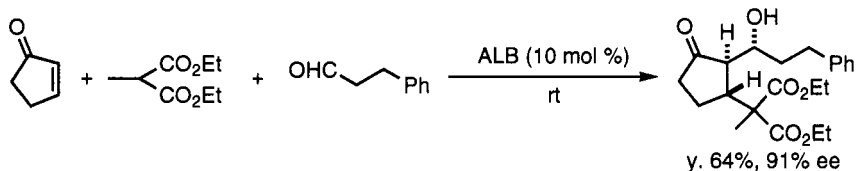
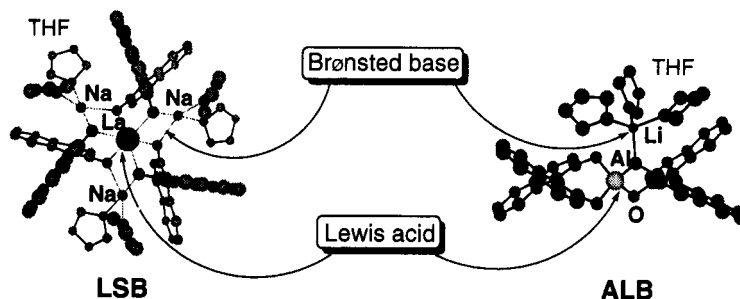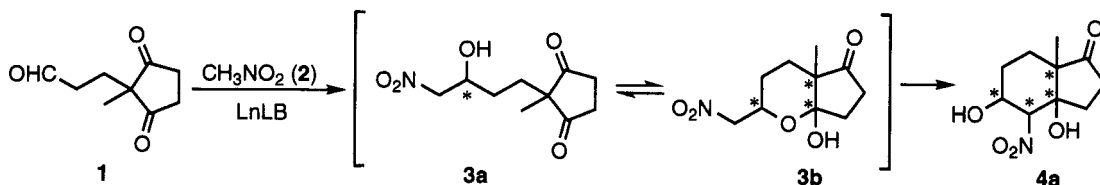Scheme 1.   Catalytic Asymmetric Reactions Using ALB



Fig. 1. X-ray Structure of Multifunctional Heterobimetallic Complexes

Herein we wish to report further development using heterobimetallic asymmetric catalysts.

1.    A   Tandem   Inter-intramolecular   Catalytic   Asymmetric   Nitroaldol   Reaction   Using   a
LnLi₃tris(binaphthoxide) Complex

Recently, tandem reactions have been of interest in organic synthesis due to their efficient structural construction.    Tandem catalytic asymmetric syntheses are especially useful because optically active compounds with several chiral centers can be constructed from simple achiral compounds in one vessel using a small amount of an asymmetric catalyst.    The development of such methods has been recognized as one of the greatest challenges in organic synthesis.    It was expected that a tandem inter-intramolecular catalytic asymmetric nitroaldol reaction could be achieved using **1** and nitromethane (**2**) in the presence of a catalytic amount of LnLB (Scheme 2).



Scheme 2.   A Plan for the Tandem Inter-intramolecular Catalytic Asymmetric Nitroaldol Reaction

After many experiments, It was found that treatment of **1** with 30 equiv of **2** in the presence of PrLB (5 mol %) in THF at -40 ℃ for 112 h and at room temperature for 24 h gave **4c** with 65% ee. Although the purification of **4c** by silica gel column chromatography was quite difficult, direct crystallization of the crude mixture from $CH_2Cl_2$ afforded a white powder of **4c** with 79% ee in 41% yield.    The optical purity of **4c** was increased to 96% ee (57% yield) after recrystallization from AcOEt-hexane (3/1) in the presence of a small amount of $CH_3OH$.    Table 2 shows only the modest to good results using LnLB in THF. This is the first example of a tandem inter-intramolecular catalytic asymmetric nitroaldol reaction.    The mechanistic studies revealed the following.    The nitroaldol products **3a** and **3b** together with one diastereomer of **4c** (**4b**) were formed at -40 ℃, and then these compounds were gradually converted to **4c** at room temperature, clearly indicating that **4c** is a thermodynamically controlled product.    Moreover, it was found that, in an intramolecular reaction, there was no kinetic resolution, because the reaction of a mixture of **3a** and **3b**, prepared with PrLB at -40 ℃, in the presence of NaO-*t*-Bu instead of PrLB, generated **4c** with 66% ee.    That is, it was confirmed that the optical purity of **4c** depend only on the enantioselection of the intermolecular nitroaldol reaction.    Optically active **4c** would be a key intermediate for the synthesis of natural products and/or bioactive compounds.(2)

TABLE 2. Tandem Inter-interamolecular Catalytic Asymmetric Nitroaldol Reaction
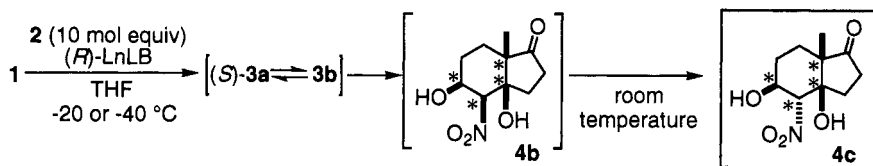


| entry | catalyst (mol %) | temp (°C) (time (h)) | ee of crude 4c | yield of 4c (%) (1st crop) | ee of 4c (%) (1st crop) |
|---|---|---|---|---|---|
| 1 | LLB (10) | -20 (115) to rt (24) | 39 | 59 | 41 |
| 2 | PrLB (10) | -20 (119) to rt (24) | 48 | 47 | 60 |
| 3 | SmLB (10) | -20 (119) to rt (24) | 28 | 43 | 51 |
| 4 | GdLB (10) | -20 (119) to rt (24) | 36 | 47 | 41 |
| 5 | DyLB (10) | -20 (119) to rt (24) | 34 | 34 | 43 |
| 6 | YbLB (10) | -20 (119) to rt (24) | 7 | 37 | 12 |
| 7 | PrLB (10) | -40 (115) to rt (24) | 58 | 42 | 71 |
| 8 | PrLB (5) | -40 (145) to rt (71) | 53 | 45 | 66 |
| 9[a] | PrLB (5) | -40 (112) to rt (24) | 65 | 41 | 79 |

a: 30 mol equiv of nitromethane were used.

## 2. Direct Catalytic Asymmetric Reactions of Aldehydes and Unmodified Ketones

The aldol reaction is generally regarded as one of the most powerful of carbon-carbon bond-forming reactions, and the development of a range of catalytic asymmetric aldol-type reactions has thus proven to be a valuable contribution to asymmetric synthesis.(3)   In all of these asymmetric aldol-type reactions, however, pre-conversion of the ketone moiety to a more reactive species such as an enol silyl ether, enol methyl ether, or ketene silyl acetal is an unavoidable necessity.   The development of a direct catalytic asymmetric aldol reaction, starting from aldehydes and unmodified ketones, would therefore be worthwhile (Scheme 3).
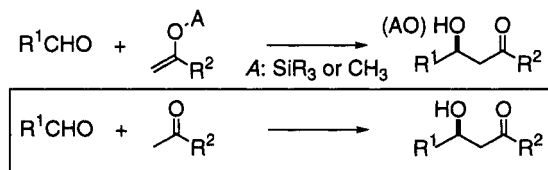


Scheme 3.   Various Types of Catalytic Asymmetric Aldol Reactions

The direct catalytic asymmetric aldol reaction of aldehydes and unmodified ketones has been carried out for the first time by using multifunctional heterobimetallic asymmetric catalysts, in particular LaLi$_3$tris(binaphthoxide) (LLB). Treatment of pivalaldehyde (5a) with 10 equiv of acetophenone (6a) in the presence of 20 mol % of LLB at -20 °C for 91 h was found to give the corresponding aldol product 7a with 91% ee in 81% yield, and the reaction of pivalaldehyde (5a) with acetone (6c) afforded the aldol adduct 7h with 73% ee in 53% yield.   Moreover, treatment of 2,2-dimethyl-4-phenylpropanal (5d) with 2-butanone (6d) gave the aldol 7i with 94% ee in 71% yield.   This direct catalytic asymmetric aldol reaction was found to proceed even in cases where aldehydes possessing α-hydrogens were used.   Thus, the reaction of isobutyraldehyde (5c) with acetophenone (6a) gave the desired aldol adduct 7c with 54% ee in 59% yield, and treatment of cyclohexanecarboxaldehyde (5b) with acetophenone (6a) afforded the aldol product 7b with 44% ee in 72% yield.   In addition, the reaction of hydrocinnamaldehyde (5e) with acetophenone (6a) gave the corresponding aldol 7f with 52% ee, but this time in rather low yield (28%).   The results are summarized in Table 3.

Mechanistic studies using NMR spectroscopy revealed that the La atom functions as a Lewis acid while a lithium naphthoxide moiety acts as a Brφnsted base in these reactions, thereby allowing the

production of a variety of aldol adducts with moderate to high enantiomeric excesses. (4)

Although the reaction is still rather slow, requires a rather large excess of ketones and 20 mol % of LLB catalyst, and provides only moderate to good enantioselectivities, the results reported here may provide a solid foundation for further work.

TABLE 3.    Catalytic Asymmetric Aldol Reactions Promoted by ($R$)-LLB (20 mol %)

$$R^1CHO \quad + \quad \overset{O}{\underset{R^2}{\|}} \quad \xrightarrow[\text{THF, -20 °C}]{\substack{(R)\text{-LLB} \\ (20 \text{ mol \%})}} \quad R^1 \overset{OH}{\underset{}{}} \overset{O}{\underset{R^2}{\|}}$$

5a; $R^1$ = *t*-Bu          6a: $R^2$ = Ph          7a; $R^1$ = *t*-Bu, $R^2$ = Ph
5b; $R^1$ = *c*-$C_6H_{11}$     6b: $R^2$ = 1-naphthyl     7b; $R^1$ = *c*-$C_6H_{11}$, $R^2$ = Ph
5c; $R^1$ = *i*-Pr          6c: $R^2$ = $CH_3$          7c; $R^1$ = *i*-Pr, $R^2$ = Ph
5d; $R^1$ = $PhCH_2C(CH_3)_2$  6d: $R^2$ = Et          7d; $R^1$ = *t*-Bu , $R^2$ = 1-naphthyl
5e; $R^1$ = $Ph(CH_2)_2$                              7e; $R^1$ = $PhCH_2C(CH_3)_2$, $R^2$ = Ph
                                                      7f; $R^1$ = $Ph(CH_2)_2$ , $R^2$ = Ph
                                                      7g; $R^1$ = $PhCH_2C(CH_3)_2$, $R^2$ = $CH_3$
                                                      7h; $R^1$ = *t*-Bu, $R^2$ = $CH_3$
                                                      7i; $R^1$ = $PhCH_2C(CH_3)_2$, $R^2$ = Et

| entry | aldehyde | ketone | product | time (h) | yield (%) | ee (%) |
|-------|----------|--------|---------|----------|-----------|--------|
| 1 | **5a** | **6a** (10 equiv) | **7a** | 91 | 81 | 91 |
| 2[a] | **5b** | **6a** (8 equiv) | **7b** | 169 | 72 | 44 |
| 3 | **5c** | **6a** (8 equiv) | **7c** | 277 | 59 | 54 |
| 4 | **5a** | **6b** (8 equiv) | **7d** | 253 | 55 | 76 |
| 5 | **5d** | **6a** (7.4 equiv) | **7e** | 87 | 90 | 69 |
| 6 | **5e** | **6a** (10 equiv) | **7f** | 72 | 28 | 52 |
| 7 | **5d** | **6c** (10 equiv) | **7g** | 185 | 82 | 74 |
| 8 | **5a** | **6c** (10 equiv) | **7h** | 100 | 53 | 73 |
| 9 | **5d** | **6d** (50 equiv) | **7i** | 185 | 71 | 94 |

[a]The reaction was carried out at -30 °C.

3.    Enantioselective    Ring    Opening    of    Epoxides    with    Thiols    Catalyzed    by    a    Gallium•Lithium•Bis(binaphthoxide) Complex

The enantioselective ring opening of symmetrical epoxides is an attractive and quite powerful technique for asymmetric synthesis.    Since a pioneering report by Whitesell,(5) various types of stoichiometric or catalytic asymmetric epoxide openings have been reported.(6)    However, few practical methods have been found, and those that are generally are require the use of silylated compounds as nucleophiles. As a result, the possibility of achieving catalytic asymmetric epoxide ring openings using nonsilylated nucleophiles such as RSH, ROH, HCN, and $HN_3$ was considered.    In 1985, Yamashita and Mukaiyama reported a catalytic asymmetric epoxide opening by thiols using a zinc tartrate catalyst.(7)    To the best of our knowledge, however this is the only example of a useful method for obtaining synthetically versatile β-hydroxy sulfides in an optically active form by way of an epoxide opening.    Mukaiyama's catalyst, however, is still unsatisfactory in terms of broad usefulness, selectivity, and reactivity.    The goal of the present experiment was therefore to find a more efficient technique for obtaining a catalytic asymmetric ring opening of symmetrical epoxides with thiols using a newly prepared asymmetric complex: gallium•lithium•bis(binaphthoxide) (**8**, GaLB).    This catalyst should also be useful for catalytic asymmetric epoxide openings with other nonsilylated nucleophiles.

$$GaCl_3 \quad + \quad \overset{OLi}{\underset{OLi}{}} \quad \xrightarrow[\text{rt, 3 h}]{\text{THF}} \quad \text{(R)-GaLB}$$

(2 mol eq)                    **8**:  ($R$)-GaLB
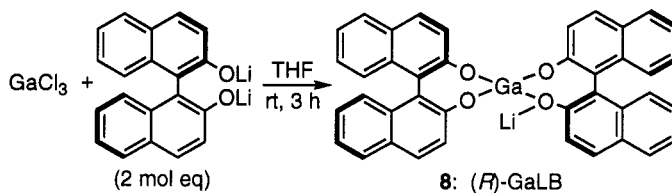
Scheme 4.    Preparation of ($R$)-GaLB (**8**)

It was thought that these complexes would prove to be useful for the catalytic asymmetric opening of **9** with a nucleophile such as PhCH$_2$SH.   However, LnMB or ALB showed only low catalytic activity, resulting in 1-10% yield of 2-(benzylthio) cyclohexanol, although modest to high ee values (27-86% ee) were observed.   In order to develop more reactive catalysts, new heterobimetallic asymmetric complexes using group 13 elements (B, Ga, In) other than Al were prepared.   Of these, (*R*)-GaLB (**8**), which was readily prepared from GaCl$_3$, (*R*)-BINOL (2 mol equiv to GaCl$_3$), and BuLi (4 mol equiv to GaCl$_3$) in THF, showed a high catalytic activity for the present reaction.   The structure of **8** is proposed, as shown in Scheme 4.   The $^{13}$C-NMR spectrum of GaLB was similar to that of ALB, the structure of which has been unequivocally determined by X-ray crystallography. (1)   After many attempts, the use of sterically hindered thiols, such as **10** in the presence of dried MS 4A, were found to be effective for achieving a highly enantioselective opening of epoxides.   A possible role of the MS 4A may be to assist decomplexation of the product from the catalysts, resulting in an enhanced overall reaction rate.   The results are summarized in Table 4.

TABLE 4.   Catalytic Asymmetric Ring Openings of Symmetrical Epoxides with *t*-BuSH (**10**) Catalyzed by (*R*)-GaLB with MS 4A

| entry | epoxide | MS 4A[a] (g) | time (h) | product | yield (%) | ee (%) |
|-------|---------|--------------|----------|---------|-----------|--------|
| 1 | | 9 | none | 65 | **17** | 35 | 98 |
| 2 | | 9 | 0.2 | 9 | **17** | 80 | 97 |
| 3 | | 11 | 0.2 | 36 | **18** | 74 | 95 |
| 4 | TBDPSO / TBDPSO | 12 | 0.2 | 12 | **19** | 83 | 96 |
| 5 | TBDPSO / TBDPSO | 13 | 0.2 | 137 | **20** | 64 | 91 |
| 6 | | 14 | 0.2 | 24 | **21** | 89 | 91 |
| 7[b] | Tr–N | 15 | 0.2 | 20 | **22** | 92 | 93 |
| 8 | TrO / TrO | 16 | 2.0 | 48 | **23** | 89 | 82 |

[a] Weight per 0.1 mmol of GaLB. [b] Carried out at 40 °C.

A working model for the catalytic asymmetric epoxide opening is shown in Scheme 5.   GaLB (**8**) appears to act as an asymmetric multifunctional catalyst, with a lithium binaphthoxide moiety functioning as a Brønsted base, activating **10** and controlling the orientation of the resulting lithium thiolate by chelation.   In contrast, significant enantioselectivity was not detected when **24** was used instead.   In addition, a gallium metal appears to function as a Lewis acid, activating and also controlling the orientation of **9**, presumably due to coordination of an axial lone pair, allowing for the cleavage of C-O bond by backside attack (**II**).   On this basis, the likely absolute configuration of **17** can be predicted to be 1(*R*),2(*R*), and in fact (*R*)-GaLB did indeed give 1(*R*),2(*R*)-products in every case.   Since six-membered S$_N$2-like transition states are not usually seen for epoxide opening reactions, probably due to bond angle problems, the geometry (**II**) is suggested as a working model that provides a way to correlate these results.   The alkoxide intermediate (**III**) thus produced may then abstract a proton from an acidic OH group to afford **17** and regenerate GaLB, thereby completing the catalytic cycle.
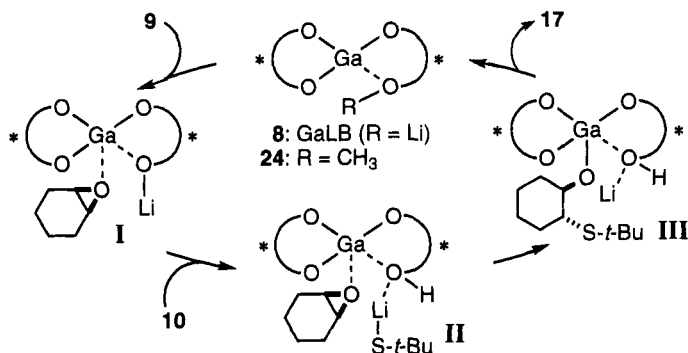
Scheme 5. Working Model for the Ring Opening of Cyclohexane Oxide (**9**)
with *t*-BuSH (**10**) Catalyzed by GaLB (**8**)

This methodology has been applied to the synthesis of **28**, an important intermediate in the synthesis of prostaglandins. As shown in Scheme 6, epoxide **25** gave **26** with 91% ee in 90% yield by reaction with *t*-BuSH (**10**) in the presence of (*S*)-GaLB (10 mol %) and MS 4A (rt, 96 h). Oxidation of **26** gave α-sulfinyl ketone **27**, and subsequent pyrolysis afforded (*R*)-**28** in 77% overall yield.(8)
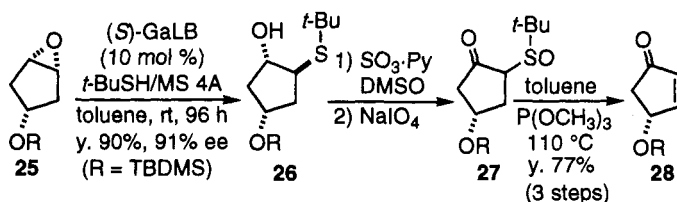


Scheme 6. Catalytic Asymmetric Synthesis of **28**

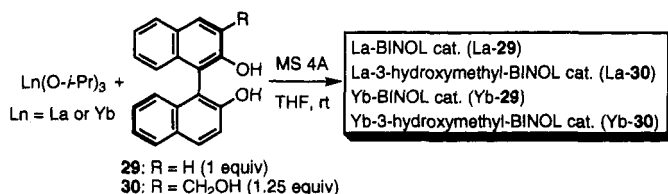Further applications using ROH, HCN and/or $HN_3$ are under study.

### 4. Catalytic Asymmetric Epoxidation of α,β-Unsaturated Ketones Promoted by Lanthanoid Complexes.

Catalytic asymmetric epoxidations are some of the most important asymmetric processes. In 1980, Shapless *et al.* reported a stoichiometric asymmetric epoxidation of allylic alcohols, a method which was later developed into a catalytic process.(9) Moreover, catalytic asymmetric epoxidations of unfunctionalized olefins using salen-manganese complexes have been reported independently by Jacobsen *et al.*, Katsuki *et al.*, and Mukaiyama *et al.*(10) In striking contrast to these successful achievements, an efficient catalytic asymmetric epoxidation of enones *with broad generality* has not been developed.(11) Quite recently, Enders and coworkers reported a very impressive and practical asymmetric epoxidation of enones using a stoichiometric amount of *N*-methyl pseudoephedrine as a chiral source.(12) We have developed an efficient catalytic asymmetric epoxidation of enones using lanthanoid complexes, which is the first example of a catalytic process applicable to various enones.

Of the several kinds of heterobimetallic asymmetric catalysts previously developed, LSB, ALB, and GaSB have been found to be very useful for catalytic asymmetric Michael reactions.(1) It was thought that these chiral catalysts would be useful for the asymmetric epoxidation of enones using hydroperoxides such as *tert*-butyl hydroperoxide (TBHP) and cumene hydroperoxide (CMHP) on mechanistic grounds of epoxidations. As expected, the reaction of **31** with TBHP (2 equiv) in the presence of LSB (10 mol %) in THF at room temperature for 10 h was found to give **32** with 83% ee and in 92% yield. However LSB, like ALB and GaSB, was unfortunately not useful for many other enones. Next to be considered, therefore, was the possibility that an alkali metal-free lanthanum complex of the type known to be effective for catalytic asymmetric Michael reactions might also be useful in this case. The catalytic suspension of the La-BINOL complex was prepared from La(O-*i*-Pr)₃ and (*R*)-BINOL (**29**) (1 molar equiv) in the presence of MS 4A (Scheme 7). As expected it was found that treatment of **31** with TBHP (1.5 equiv) in the presence of 10 mol % of the La-BINOL complex (La-**29**) in THF at rt for 0.5 h afforded **32** with 62% ee in 90% yield. Moreover, the use of CMHP instead of TBHP improved the asymmetric epoxidation, giving **32** with 83% ee in 93% yield (5 mol % of La-**29**). In marked contrast to LSB, this type of chiral lanthanum catalyst was found to be applicable to a range of enone substrates. Thus, **33** was converted to **34** with 86% ee and in

93% yield, and **35** was transformed to **36** with 85% ee in 85% yield (Table 5, entries 1, 4, and 6). After several attempts, it was found that the use of (R)-3-hydroxymethyl-BINOL (**30**) instead of **29** substantially improved the catalytic asymmetric epoxidations (Table 5, entries 2, 3, 5, and 7). Namely, excellent yields of **32**, **34**, and **36** were obtained with 91, 94, and 83% ee, respectively.

In contrast to the results presented above, the enones shown in Table 5 (entries 8, 9, 10, and 11) were best converted to the corresponding epoxides by using the ytterbium complex generated from Yb(O-i-Pr)$_3$, (R)-**30**, and MS 4A in THF at 40 ℃ for 1 h (Scheme 7, Yb-**30**). That is, treatment of **37** with TBHP (1.5 equiv) in the presence of 5 mol % of Yb-**30** in THF at rt for 96 h was found to give **38** with 94% ee in 83% yield. Gratifyingly, **40**, **42**, and **44** were obtained with 88, 88, and 91% ee, respectively, and in excellent yields. In contrast, the use of either Yb-**29** catalyst or La-CMHP system afforded **38** with less satisfactory results. It seems likely that the difference in ionic radius between lanthanum and ytterbium, as well as the difference in Lewis acidities, accounts for the observed center metal effects.



Ln(O-i-Pr)$_3$ +
Ln = La or Yb

MS 4A
THF, rt

La-BINOL cat. (La-29)
La-3-hydroxymethyl-BINOL cat. (La-30)
Yb-BINOL cat. (Yb-29)
Yb-3-hydroxymethyl-BINOL cat. (Yb-30)

**29**: R = H (1 equiv)
**30**: R = CH$_2$OH (1.25 equiv)

Scheme 7. Preparation of Chiral Lanthanoid-BINOL Derivatives Catalysts

TABLE 5. Catalytic Asymmetric Epoxidations Using Alkali Metal Free Lanthanoid Complexes



**31, 32**: R$^1$ = Ph, R$^2$ = Ph　　　　**39, 40**: R$^1$ = Ph, R$^2$ = i-Pr
**33, 34** : R$^1$ = i-Pr, R$^2$ = Ph　　　**41, 42**: R$^1$ = Ph(CH$_2$)$_2$, R$^2$ = CH$_3$
**35, 36** : R$^1$ = Ph, R$^2$ = o-MOMOC$_6$H$_4$　**43, 44**: R$^1$ = CH$_3$(CH$_2$)$_4$, R$^2$ = CH$_3$
**37, 38**: R$^1$ = Ph, R$^2$ = CH$_3$

| entry | enone | epoxide | Ln cat. (mol %) | ROOH (1.5 eq) | time (h) | yield (%) | ee (%) |
|---|---|---|---|---|---|---|---|
| 1 | **31** | **32** | La - **29** (5) | CMHP | 6 | 93 | 83 |
| 2 | **31** | **32** | La - **30** (5) | CMHP | 7 | 93 | 91 |
| 3 | **31** | **32** | La - **30** (1) | CMHP | 44 | 95 | 89 |
| 4 | **33** | **34** | La - **29** (5) | CMHP | 12 | 93 | 86 |
| 5 | **33** | **34** | La - **30** (5) | CMHP | 7 | 95 | 94 |
| 6 | **35** | **36** | La - **29** (5) | CMHP | 20 | 85 | 85 |
| 7 | **35** | **36** | La - **30** (5) | CMHP | 96 | 78 | 83 |
| 8 | **37** | **38** | Yb - **30** (5) | TBHP | 96 | 83 | 94 |
| 9 | **39** | **40** | Yb - **30** (8) | TBHP | 159 | 55 | 88 |
| 10 | **41** | **42** | Yb - **30** (8) | TBHP | 118 | 91 | 88 |
| 11 | **43** | **44** | Yb - **30** (8) | TBHP | 67 | 71 | 91 |

Although we have not succeeded in determining the structure, it was found that an almost 1:1 ratio of Ln(O-i-Pr)$_3$ (Ln = La or Yb) and **29** gave the maximum enantiomeric excesses (Fig. 2). The $^{13}$C-NMR spectrum of La-**29** was quite obscure, suggesting that both the chiral Yb-**29** catalyst and the La-**29** catalyst exist as oligomers. Moreover, we have succeeded in obtaining asymmetric amplification of the catalytic asymmetric epoxidation (Fig. 3). Thus the structure **45** is tentatively proposed. It is likely that the oligomeric structure of these lanthanoid-BINOL catalysts may play a key role in these catalytic asymmetric epoxidations of enones. That is, a Ln-alkoxide moiety in the catalysts appears to act as a Brønsted base, activating a hydroperoxide moiety so as to make possible a Michael reaction, and at the same time another Ln metal ion seems to act as a Lewis acid, both activating and controlling the orientation of the enone. Such a mechanism, analogous to those for enzymatic methods, may explain why various epoxides can be synthesized with good enantiomeric excesses even at rt.(13)　As in the preliminary studies, the use of *cis-*

unsaturated ketones were converted to the corresponding epoxides with high ees without the significant isomerzation of an olefinic double bond.    Futher studies are under investigation.
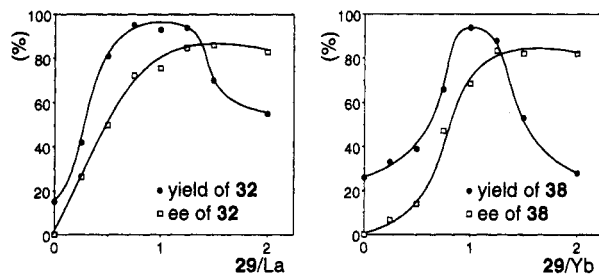


Fig. 2.    Influence of the ratio of Ln(O-*i*-Pr)$_3$ and **29** on yield and ee.    Left: epoxidation of **31** catalyzed by La-**29** catalyst.    Right: epoxidation of **37** catalyzed by Yb-**29** catalyst.
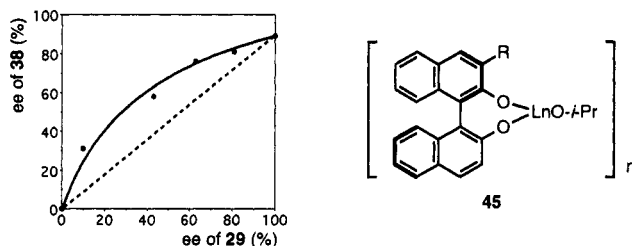


Fig. 3. Left: Asymmetric Amplification in the Epoxidation of **37** Catalyzed by Yb-**29** catalyst. Right: Tentative Structure of the Asymmetric Catalyst

## 5.    Summary and Outlook

Attempts to develop conceptually new heterobimetallic asymmetric catalysts such as LnMB, AMB, and GaMB have proven successful.    These catalysts function as both Brφnsted bases and also as Lewis acids, making possible various efficient catalytic asymmetric reactions in a manner analogous to enzyme chemistry.    Several such catalytic asymmetric reactions are now being investigated for potential industrial applications.    The successful development and application of the heterobimetallic concept has opened up a new field in asymmetric catalysis, and a wide range of applications may well ensue.    Moreover, the attempt to develop homopolymetallic asymmetric catalysts, as discussed in section 4, have also been successful.

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