# Catalytic Enantioselective *meso*-Epoxide Ring Opening Reaction with Phenolic Oxygen Nucleophile Promoted by Gallium Heterobimetallic Multifunctional Complexes

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**Abstract:** The catalytic enantioselective *meso*-epoxide ring opening reaction with phenolic oxygen nucleophile (4-methoxyphenol) is described for the first time herein. This reaction was first found to be promoted by (*R*)-GaLB (Ga = gallium, L = lithium, B = (*R*)-BINOL), giving a variety of epoxide opening products in good to high ee (67−93% ee). However, chemical yield was only modest (yield 31−75%), despite the use of more than 20 mol % GaLB. This was due to the undesired ligand exchange between BINOL and 4-methoxyphenol, which resulted in the decomplexation of GaLB. Application of various known chiral ligands such as 6,6′-bis((triethylsilyl)ethynyl)-BINOL and $H_8$-BINOL were examined, but satisfactory results were not obtained. To overcome this problem a novel linked-BINOL containing coordinative oxygen atom in the linker has been developed. By linking two BINOL units in GaLB, the stability of the Ga-complex was greatly improved. Using 3−10 mol % (*R*,*R*)-Ga-Li-linked-BINOL complex, a variety of epoxide opening reactions were found to proceed smoothly, affording products in analogous ee (66−96% ee) and in much higher yield (yield 67−94%) compared to (*R*)-GaLB. The structure of the LiCl free Ga-Li-linked-BINOL complex was elucidated by X-ray analysis. This is the first X-ray data for an asymmetric catalyst containing gallium. The possible mechanism of the entitled reaction is also discussed, based on the X-ray structure of the Ga-complex.

## Introduction

The catalytic enantioselective *meso*-epoxide ring opening reaction is an attractive method in asymmetric synthesis,[1] since it simultaneously constructs two contiguous stereogenic centers. A few years ago, we reported an asymmetric epoxide ring opening reaction with *t*BuSH catalyzed by a Ga-Li-bis(binaphthoxide) complex (**1**: GaLB, Figure 1) in up to 90% yield and 97% ee.[2a] Recently several chiral asymmetric catalyst systems have been reported which promote enantioselective *meso*-epoxide ring opening in high enantiomeric excess utilizing various nucleophiles, such as trialkylsilyl azide,[3] trimethylsilyl cyanide,[4] aryllithium,[5] halides,[6] and alkylamine.[7] Oxygen nucleophiles such as alcohols, phenols, and carboxylic acids can also be the candidates for this type of reactions. The enantioselective epoxide opening reactions with such oxygen nucleophiles are very useful methods to provide valuable chiral building blocks such as 1,2-diol derivatives.[8] Quite recently Jacobsen et al. reported excellent kinetic resolutions of racemic terminal epoxides with water[9,10b] and phenols[10] by using a

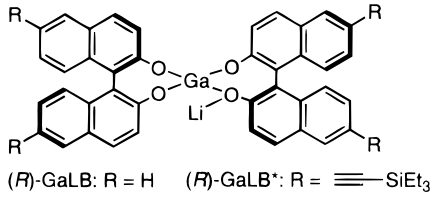


**Figure 1.** Proposed structure of (*R*)-Ga-Li-bis(binaphthoxide) (GaLB, **1**) and (*R*)-Ga-Li-bis((6,6′-bis(triethylsilyl)ethynyl)binaphthoxide) (GaLB*, **15**).

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(1) Review: (a) Hodgson, D. M.; Gibbs, A. R.; Lee, G. P. *Tetrahedron* **1996**, *52*, 14361. (b) Willis, M. C. *J. Chem. Soc., Perkin Trans 1* **1999**, 1765.

(2) (a) Iida, T.; Yamamoto, N.; Sasai, H.; Shibasaki, M. *J. Am. Chem. Soc.* **1997**, *119*, 4783. This reaction was used in the synthesis of a useful chiral phosphinite, sulfur ligand, see: (b) Evans, D. A.; Campos, K. R.; Tedrow, J. S.; Michael, F. E.; Gagné, M. R. *J. Org. Chem.* **1999**, *64*, 2994.

(3) (a) Nugent, W. A. *J. Am. Chem. Soc.* **1992**, *114*, 2768. For mechanistic study by Nugent: (b) McCleland, B. W.; Nugent, W. A.; Finn, M. G. *J. Org. Chem.* **1998**, *63*, 6656. (c) Martinez, L. E.; Leighton, J. L.; Carsten, D. H.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1995**, *117*, 5897. For mechanistic studies by Jacobsen: (d) Hansen, H. B.; Leighton, J. L.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1996**, *118*, 10924. (e) Konsler, R. G.; Jörn, K.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1998**, *120*, 10780.

(4) (a) Cole, B. M.; Shimizu, K. D.; Krueger, C. A.; Harrity, J. P. A.; Snapper, M. L.; Hoveyda, A. H. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1668. (b) Shimizu, K. D.; Cole, B. M.; Krueger, C. A.; Kuntz, K. W.; Snapper, M. L.; Hoveyda, A. H. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1704.

(5) Oguni, N.; Miyagi, Y.; Itoh, K. *Tetrahedtron Lett.* **1998**, *39*, 9023.

(6) (a) Nugent, W. A. *J. Am. Chem. Soc.* **1998**, *120*, 7139. (b) Denmark, S. E.; Barsanti, P. A.; Wong, K.-T.; Stavenger, R. A. *J. Org. Chem.* **1998**, *63*, 2428.

(7) Sagawa, S.; Abe, H.; Hase, Y.; Inaba, T. *J. Org. Chem.* **1999**, *64*, 4962.

(8) For an alternative approach to the synthesis of optically active 1,2-diols by the catalytic asymmetric dihydroxylations of olefins, which was realized by Sharpless, K. B., et al., see: Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless K. B. *Chem. Rev.* **1994**, *94*, 2483.

(9) Tokunaga, M.; Larrow, J. F.; Kakiuchi, F.; Jacobsen, E. N. *Science* **1997**, *277*, 936.

(10) (a) Ready, J. M.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1999**, *121*, 6086. (b) Annis, D. A.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1999**, *121*, 4147.

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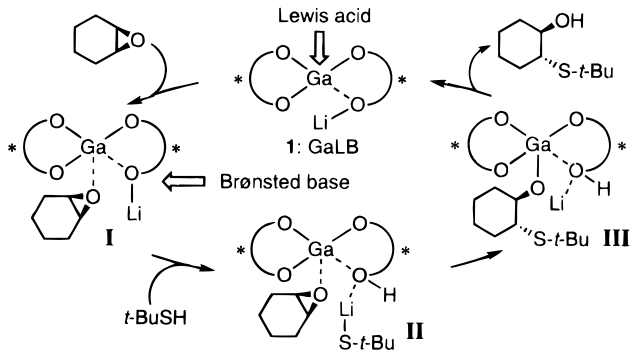
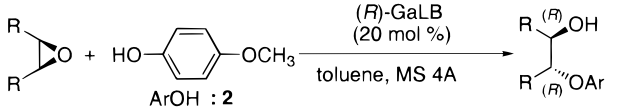
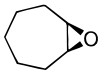
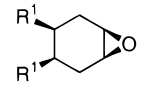
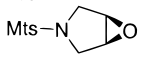
**Scheme 1.** Working Model for the Ring Opening of Cyclohexene Oxide with *t*-BuSH Catalyzed by GaLB (**1**)




(salen)-Co catalyst. The (salen)-Co catalyst was also utilized for the enantioselective ring opening of *meso*-epoxides with carboxylic acid.[11] However, in the latter case the (salen)-Co catalyst left room to be improved in terms of substrate generality—only 2 *meso*-epoxides were ring-opened in high enantiomeric excess and others in moderate (<80%) ee's. So development of practical methods for the asymmetric ring opening of *meso*-epoxides with oxygen nucleophiles has been well desired.[12] The key issue to achieve this type of reaction is how to overcome the normal poor reactivity of oxygen nucleophiles toward epoxides. From the analogy of our and other groups' works, the activation of both epoxides and nucleophiles seems to be very important to obtain products in good yield and ee.[2a,3,6a,9,10,12] We speculated that it might be possible to develop the catalytic enantioselective *meso*-epoxide ring opening reactions with oxygen nucleophiles by using heterobimetallic multifunctional catalysts[13] in a similar manner as with *t*BuSH. A proposed working model for the GaLB catalyzed epoxide opening reaction with *t*BuSH is shown in Scheme 1. We believe that gallium center metal would act as a Lewis acid and activate epoxides (I), while at the same time, the lithium binaphthoxide moiety would function as a Brønsted base to activate *t*BuSH (II). Activated nucleophile would then react with epoxide to give III. Proton exchange between gallium alkoxide and an aromatic hydroxyproton leads to the epoxide opening adduct and regeneration of catalyst. Considering the Brønsted basicity of the alkali-metal binaphthoxide moiety in the heterobimetallic complex (p$K_a$ value of BINOL = ~10), phenolic oxygen nucleophiles (p$K_a$ value of 4-methoxyphenol = 10.2) might also be activated to react with epoxides in a similar catalytic cycle as *t*BuSH (p$K_a$ value of *t*BuSH = 10.6). Herein we report an efficient catalytic enantioselective ring opening of various *meso*-epoxides with 4-methoxyphenol promoted by gallium heterobimetallic catalysts. *These systems afforded optically active 1,2-diol monoethers with broad generality in up to 94% yield and in up to 96% ee.*

**Table 1.** Enantioselective Ring Opening of Various *meso*-Epoxides with 4-Methoxyphenol (2) Promoted by GaLB




| entry | epoxide | product | ArOH (eq) | temp (°C) | time (h) | yield[a] (%) | ee[b] (%) |
|---|---|---|---|---|---|---|---|
| 1 |  | **3** **9** | 1.2 (1.2)[c] | 50 (50)[c] | 72 (72)[c] | 48 (60)[c] | 93 (94)[c] |
| 2 |  | **3** **9** | 2.4 | 50 | 72 | 41 | 86 |
| 3 |  | **3** **9** | 5.0 | 50 | —[d] | —[d] | —[d] |
| 4 |  | **3** **9** | 1.2 | 85 | 72 | 52 | 76 |
| 5 |  | **4** **10** | 1.2 (1.2)[c] | 50 (50)[c] | 72 (72)[c] | 75 (73)[c] | 86 (89)[c] |
| 6 |  | **5** **11** | 1.2 | 50 | 72 | 31 | 67 |
| 7 |  | **6** **12** | 1.2 (1.2)[c] | 50 (50)[c] | 72 (72)[c] | 70 (69)[c] | 87 (92)[c] |
| 8[e] |  | **7** **13** | 1.2 | 50 | 96 | 34 | 80 |
| 9[f] |  | **8** **14** | 1.2 | 50 | 160 | 51 | 90 |

[a] Isolated yield. [b] Determined by HPLC analysis. [c] GaLB* (20 mol %) was used. [d] No reaction. [e] $R^1 = CH_2OSiPh_2tBu$. [f] 30 mol % catalyst was used. Mts = 2,4,6-trimethylbenzenesulfonyl.

## Results and Discussion

**A. Catalytic Enantioselective Epoxide Ring Opening Reaction with 4-Methoxyphenol Promoted by Gallium Heterobimetallic Complexes.** As phenolic oxygen nucleophile, we chose 4-methoxyphenol (**2**) because the corresponding 1,2-diol monoether adducts can be converted easily into 1,2-diols.[14] However, in general, reactions of epoxides with oxygen nucleophiles are rather difficult, and therefore the epoxide ring opening with phenolic oxygen nucleophiles is quite challenging. In fact, the reaction of cyclohexene oxide (**3**) with 4-methoxyphenol (**2**) using catalytic and/or stoichiometric amounts of BuLi, NaO*t*Bu, KO*t*Bu, $K_2CO_3$, and $Cs_2CO_3$ at 50 °C did not proceed at all. Similarly Lewis acids such as $BF_3 \cdot Et_2O$ or $ZnCl_2$ were also ineffective for this reaction. After several attempts we found that the reaction proceeded by using $ZnCl_2$ (2 equiv; Lewis acid) and $Et_3N$ (5 equiv; Brønsted base) at the same time, although chemical yield was only 6% after 23 h. These results are quite consistent with our initial assumption that dual activation of both substrates is very important.

Encouraged by the results mentioned above, we next examined the epoxide opening reaction with 4-methoxyphenol using (*R*)-GaLB which was effective in the thiol case. We were pleased to find that the reaction of **3** with **2** proceeded in the presence of (*R*)-GaLB (20 mol %) and MS 4A (toluene, 50 °C) to afford 1,2-diol monoether **9** in 48% yield and in 93% ee (Table 1, entry 1). GaLB catalyst was applicable to several

(11) Jacobsen, E. N.; Kakiuchi, F.; Konsler, R. G.; Larrow, J. F.; Tokunaga, M. *Tetrahedtron Lett.* **1997**, *38*, 773.

(12) Quite recently Jacobsen reported an asymmetric intramolecular cyclization of *meso*-epoxy alcohol using the (salen) Co catalyst. Wu, M. H.; Hansen, K. B.; Jacobsen, E. N. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 2012.

(13) For review, see: (a) Shibasaki, M.; Sasai, H.; Arai, T. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 6, 1236. (b) Steinhagen, H.; Helmchen, G. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 5, 2339. For recent representative examples, see: (c) Arai, T.; Sasai, H.; Yamaguchi, K.; Shibasaki, M. *J. Am. Chem. Soc.* **1998**, *120*, 441. (d) Gröger, H.; Saida, Y.; Sasai, H.; Yamaguchi, K.; Martens, J.; Shibasaki, M. *J. Am. Chem. Soc.* **1998**, *120*, 3089. (e) Emori, E.; Arai, T.; Sasai, H.; Shibasaki, M. *J. Am. Chem. Soc.* **1998**, *120*, 4043. (f) Yoshikawa, N.; Yamada, Y. M. A.; Das, J.; Sasai, H.; Shibasaki, M. *J. Am. Chem. Soc.* **1999**, *121*, 4168.

(14) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; Wiley: New York, 1991; p 46.

unfuntionalized and funtionalized *meso*-epoxides affording products in good to high ee (67−93% ee), although chemical yields were only modest (31−75% yield). The results are summarized in Table 1 (entries 1 and 5−9). The addition of MS 4A, which might assist the dissociation of products from the catalyst, was extremely effective in enhancing the reaction rate. The reaction of cyclohexene oxide in the absence of MS 4A afforded product **9** in only 5% yield but in 95% ee.[15]

The GaLB catalyzed epoxide ring opening gave products in good to excellent ee's, but chemical yield was only modest despite the use of more than 20 mol % catalyst. Attempts to increase the reactivity of GaLB by using more equivalents of 4-methoxyphenol (**2**) or by heating the reaction mixture at higher temperature failed. When 2.4 mol equiv of **2** was used, both chemical yield and ee of **9** decreased (yield 41%, 86% ee, Table 1, entry 2). In the presence of 5.0 mol equiv of **2**, the reaction did not proceed at all (entry 3). Even at higher temperature (85 °C) chemical yield was still moderate and ee decreased (yield 52%, 76% ee, entry 4). These results can probably be attributed to an undesired ligand exchange between BINOL and 4-methoxyphenol (**2**), resulting in the decomplexation of the GaLB and the formation of unavoidable side products.[16] So preparation of a more stable gallium heterobimetallic complex seemed to be the solution to this problem. Therefore we started to examine various modified BINOLs as chiral ligands. After several attempts,[17] we found that the use of GaLB* (Figure 1, **15**), which was prepared from (*R*)-6,6′-bis((triethylsilyl)ethynyl)binaphthol, slightly improved the yield of the ring opening of **3** (60% yield) without loss in enantiomeric excess (94% ee) (Table 1, entry 1 in parentheses).[19] This may be due to the higher stability of GaLB* with respect to ligand exchange than that of GaLB. However, this GaLB* complex was also not stable enough to suppress the undesired ligand exchange completely, and so the use of as much as 20 mol % catalyst was needed to obtain products in acceptable yield.

To develop more efficient catalysts, we then prepared a number of new gallium complexes with various known chiral ligands.[20] Among those, the gallium complexes prepared from (*R*)-5,5′,6,6′,7,7′,8,8′-octahydro-BINOL ($H_8$-BINOL)[24] showed much higher catalytic activities for the present reaction. The proposed structure of the Ga-Na-bis($H_8$-binaphthoxide) complex (**16**: GaSO) is shown in Scheme 2. The reaction of **3** with **2** catalyzed by GaSO proceeded smoothly in toluene at 50 °C in only 4 h to afford **9** (73% yield), albeit in modest ee (56% ee). A wide range of *meso*-epoxides could be subjected to GaSO catalyzed ring opening with **2** to give products in good to excellent yields (except entry 6, Table 2) although the enantioselectivities were only modest (34−58% ee). The results are summarized in Table 2. In contrast to heterobimetallic gallium binaphthoxide complex (GaLB), sodium was the most suitable alkali metal to make the heterobimetallic gallium $H_8$-binaphthoxide complex effective.[25] It seems likely that different Ga−O bond lengths account for the observed alkali metal ion effects. Furthermore GaSO and GaLB catalysts seem to be equipped with characteristic dihedral angles of the axial biaryl groups.[26] Difference in dihedral angles between $H_8$-BINOL and BINOL may be crucial for enantioselection, resulting in poor ee in the former system.[27]

**Scheme 2.** Preparation of Ga-Na-bis($H_8$-binaphthoxide) (GaSO, **16**)

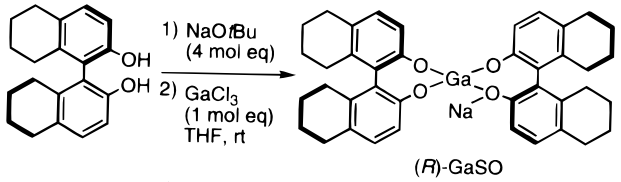
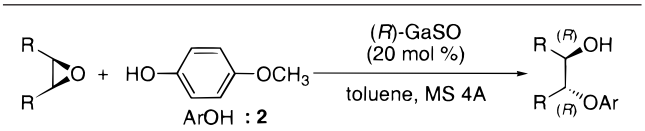



**Table 2.** Enantioselective Ring Opening of Various *meso*-Epoxides with 4-Methoxyphenol (2) Promoted by Ga-Na-bis($H_8$-binaphthoxide) (GaSO)




| entry | epoxide | product | ArOH (eq) | temp (°C) | time (h) | yield [a] (%) | ee [b] (%) |
|---|---|---|---|---|---|---|---|
| 1 | **3** | **9** | 1.2 | 50 | 4 | 73 | 56 |
| 2 | **4** | **10** | 1.2 | 50 | 4 | 77 | 54 |
| 3 | **5** | **11** | 1.2 | 50 | 4 | 67 | 58 |
| 4 | **6** | **12** | 1.2 | 50 | 24 | 90 | 55 |
| 5[c] | **7** | **13** | 1.2 | 50 | 48 | 83 | 43 |
| 6[d] | **8** | **14** | 1.2 | 50 | 19 | 44 | 34 |
| 7 | **17** | **18** | 1.2 | 50 | 7 | 75 | 50 |

[a] Isolated yield. [b] Determined by HPLC analysis. [c] $R^1 = CH_2OSiPh_2tBu$. [d] 30 mol % catalyst was used. Mts = 2,4,6-trimethylbenzenesulfonyl.

## B. Development of a Novel Linked-BINOL for the Improved Catalytic Enantioselective Epoxide Ring Opening

(15) The same phenomenon was observed in GaLB catalyzed enantioselective epoxide opening with *t*BuSH. See ref 2a.

(16) The product from the ring opening of cyclohexene oxide with BINOL was obtained in 24% yield based on BINOL.

(17) The use of (*R*)-6,6′-bis(trimethylsilyl)-, dibromo-, or dimethoxy-BINOL, 3,3′-dimethyl-, or difluoro-BINOL, 3-hydroxymethyl-BINOL,[18] and 4,4′-dibromo- or dimethyl-BINOL gave less satisfactory results.

(18) Bougauchi, M.; Watanabe, S.; Arai, T.; Sasai, H.; Shibasaki, M. *J. Am. Chem. Soc.* **1997**, *119*, 2329.

(19) Another application of 6,6′-bis((triethylsilyl)ethynyl)binaphthol is in catalytic asymmetric nitroaldol reactions: (a) Sasai, H.; Tokunaga, T.; Watanabe, S.; Suzuki, T.; Itoh, N.; Shibasaki, M. *J. Org. Chem.* **1995**, *60*, 7388. (b) Takaoka, E.; Yoshikawa, N.; Yamada, Y. M. A.; Sasai, H.; Shibasaki, M. *Heterocycles* **1997**, *46*, 157.

(20) The use of 10,10′-dihydroxy-9,9′-biphenanthryl,[21] 3,3′-dihyroxy-4,4′-biphenanthryl (BIPOL),[22] and α,α,α′,α′-tetraphenyl-2-methyl-2-phenyl-1,3-dioxolane-4,5-dimethanol (TADDOL)[23] gave unsatisfactory results.

(21) Toda, F.; Tanaka, K. *J. Org. Chem.* **1988**, *53*, 3607.

(22) Yamamoto, K.; Nada, K.; Okamoto, K. *J. Chem. Soc., Chem. Commun.* **1985**, 1065.

(23) (a) Seebach, D.; Beck, A. K.; Imwinkelried, R.; Roggo, S.; Wonnacott, A. *Helv. Chim. Acta* **1987**, *70*, 954. (b) Narasaka, K.; Iwasawa, N.; Inoue, M.; Yamada, T.; Nakashima, M.; Sugimori, J. *J. Am. Chem. Soc.* **1989**, *111*, 5340.

(24) Cram, D. J.; Helgeson, R. C.; Peacock, S. C.; Kaplan, L. J.; Domeier, L. A.; Moreau, P.; Koga, K.; Mayer, J. M.; Chao, Y.; Siegel, M. G.; Hoffman, D. H.; Sogah, G. D. Y. *J. Org. Chem.* **1978**, *43*, 1930.

(25) Ga-Li-bis($H_8$-binaphthoxide) (39% yield, 33% ee) and Ga-K-bis($H_8$-binaphthoxide) (58% yield, 52% ee) gave less satisfactory results.

(26) By comparison with Takaya's catalytic enantioselective hydrogenations with the $H_8$-(*S*)-[2,2′-bis(diphenylphosphanyl)-1,1′-binaphthyl] complex ($H_8$-BINAP): Uemura, T.; Zhang, X.; Matsumura, K.; Sayo, N.; Kumobayashi, H.; Ohta, T.; Nozaki, K.; Takaya, H. *J. Org. Chem.* **1996**, *61*, 5510.

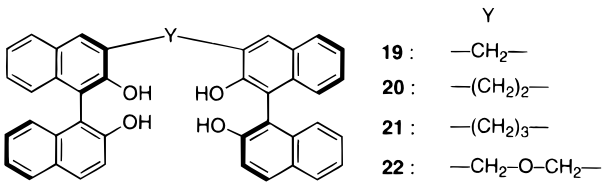
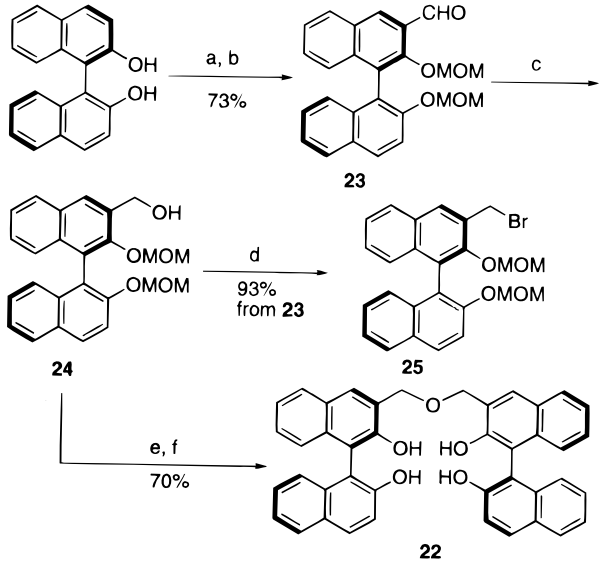



**Figure 2.** Linked-BINOLs (**19**−**22**).

**Reaction.** As described above, we have achieved success in carring out catalytic enantioselective *meso*-epoxide opening reaction with phenolic oxygen nucleophile for the first time utilizing heterobimetallic catalyst GaLB, GaLB* (high ee but modest yield), and GaSO (high yield but modest ee).[28] However, to make this methodology synthetically useful, it is indispensable to develop a new catalyst which affords epoxide opening adducts both in high chemical yield and in high ee even with reduced amounts of catalyst. In this section we report our efforts in this direction utilizing a novel linked-BINOL concept.

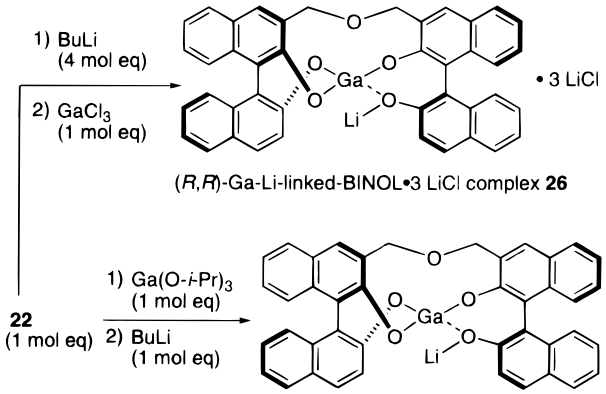
We assumed that by linking two BINOL units in GaLB the complex would become more stable against ligand exchange without any adverse effects on the asymmetric environment. As a first trial, we designed carbon linked-BINOLs (Figure 2, **19**−**21**).[29] One of the key issues for designing the linked-BINOLs is the length of its linker. The linker should be relatively short to limit the flexibility of BINOL units since details of the geometry might be crucial for enantioselection. We prepared Ga-Li-carbon-linked-BINOL complexes using **19**, **20**, and **21**; however, none of these were effective in the enantioselective epoxide opening reaction of **3** with **2** (**19**, yield 28%, 27% ee; **20**, yield 43%, 10% ee; **21**, yield 40%, −1% ee).[30] We assumed that these unsatisfactory results might be attributed to the undesired oligomeric structure of these linked-BINOL complexes. With carbon linker, each BINOL unit of linked-BINOLs would rotate freely during the formation of Ga-complexes and so they would not settle down to the desired monomeric species. To overcome this problem, we then designed a novel oxygen-containing linked-BINOL (Figure 2, **22**). This new linked-BINOL **22** was designed by considering the related works by Cram et al. regarding crown ether incorporating chiral BINOL units.[32a] We supposed that the oxygen atom in the linker might coordinate to gallium during the Ga-complex formation, thus helping the formation of the desired monomeric Ga-complex. The preparation of **22** is shown in Scheme 3. Starting from (*R*)-BINOL, **24** and **25** could easily be prepared on a multigram scale following our procedure.[18,29a] Coupling reaction between **24** and **25** proceeded smoothly. After deprotection of the MOM group and 2 times recrystallization, (*R*,*R*)-linked-BINOL **22** was obtained on a gram scale (total yield 47% from (*R*)-BINOL). Complex **26** (prepared from $GaCl_3$ (1 mol equiv), **22** (1 mol equiv), and BuLi (4 mol equiv): Scheme 4) was found to be far more stable than GaLB and very effective for the epoxide opening reaction. The results are summarized in Table 3. Unlike GaLB, complex **26** was stable even in the presence of excess 4-methoxyphenol (**2**) and/or at higher temperature. By using complex **26**, the catalyst amount could be reduced for the first time. Under the optimized conditions (toluene, 75 °C, 3 equiv of **2**), **6** reacts with **2** smoothly in the presence of 10 mol % catalyst, half the amount

**Scheme 3.** Synthesis of Oxygen Containing (*R*,*R*)-Linked-BINOL **22**[a]




[a] (a) NaH, MOMCl, DMF, 0 °C, 5 h; (b) i) BuLi, TMEDA, THF, −78 to 0 °C; (ii) DMF, −78 to 0 °C; (c) $NaBH_4$, THF, MeOH, 0 °C, 15 min; (d) (i) MsCl, toluene, AcOEt, 0 °C, 90 min; (ii) LiBr, DMF, room temperature, 10 min; (e) (i) NaH, THF, DMF, 0 °C, 60 min; (ii) **25**, room temperature, 64 h; (f) $TsOH \cdot H_2O$, $CH_2Cl_2$, MeOH, 40 °C, 36 h.

**Scheme 4.** Preparation of (*R*,*R*)-Ga-Li-linked-BINOL·3 LiCl Complex **26** and LiCl Free (*R*,*R*)-Ga-Li-linked-BINOL Complex **36**




(27) For other examples in which $H_8$-binaphthyl ligands gave better results than binaphthyl ligands, see, for the Ti($H_8$-binaphthoxide) complex: (a) Chan, A. C. S.; Zhang, F.-Y.; Yip, C.-W. *J. Am. Chem. Soc.* **1997**, *119*, 4080. For the [Rh(2,2′-bis(diphenylphosphinoamino)-$H_8$-binaphthyl)COD]$BF_4$ complex: (b) Zhang, F.-Y.; Pai, C.-C.; Chan, A. C. S. *J. Am. Chem. Soc.* **1998**, *120*, 5808.

(28) The result was reported previously, see: Iida, T.; Yamamoto, N.; Matsunaga, S.; Woo, H.-G.; Shibasaki, M. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 7, 2223.

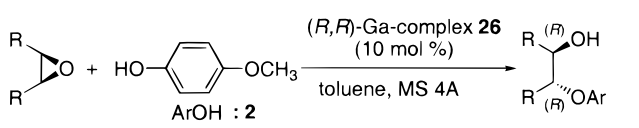
(29) The synthesis of the carbon linked-BINOLs **19** and **20** were reported previously, see: (a) Vogl, E. M.; Matsunaga, S.; Kanai, M.; Iida, T.; Shibasaki, M. *Tetrahedron Lett.* **1998**, *39*, 7917. For other group's related works using **19**: (b) Ishitani, H.; Kitazawa, T.; Kobayashi, S. *Tetrahedron Lett.* **1999**, *40*, 2161. For the synthesis of **21** ($n = 3$), see the supporting information.

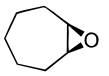
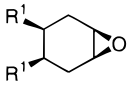
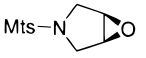
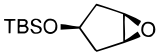
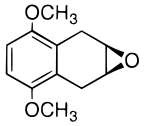
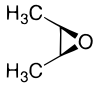
(30) In the case of **20** ($n = 2$), we could not get reproducibility for the data reported in ref 29a (yield 37%, 86% ee). We found that the results were very sensitive to the amount of BuLi used in the preparation of the catalyst. By adding a small excess (0.5 equiv) of BuLi, the result was greatly improved and **9** was obtained in 69% yield, 99% ee. However, this catalyst system was not effective for other epoxides at all and gave unsatisfactory results (yield <50%). Furthermore a positive nonlinear effect[31] was observed in this catalyst system, suggesting the oligomeric structure of the Ga-Li-carbon-linked-BINOL complex. For detailed results and discussion, see the supporting information (Table S-1, Table S-2, and Figure S-1).

(31) For review see: Girard, C.; Kagan, H. B. *Angew. Chem., Int. Ed.* **1998**, *37*, 2922.

(32) (a) Helgeson, R. C.; Tarnowski, T. L.; Cram, D. J. *J. Org. Chem.* **1979**, *44*, 2538. For review about BINOL, see also: (b) Pu, L. *Chem. Rev.* **1998**, *98*, 2405.

**Table 3.** Enantioselective Ring Opening of Various *meso*-Epoxides with 4-Methoxyphenol (**2**) Promoted by Ga-Li-Linked-BINOL Complex (**26**)



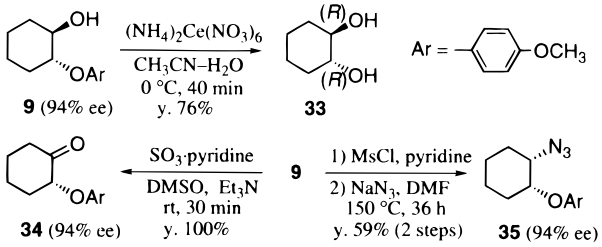

| entry | epoxide | product | ArOH (eq) | temp (°C) | time (h) | yield [a] (%) | ee [b] (%) |
|---|---|---|---|---|---|---|---|
| 1 |  | **3** **9** | 3.0 | 75 | 96 | 72 | 91 |
| 2 |  | **4** **10** | 3.0 | 60 | 63 | 88 | 85 |
| 3 |  | **5** **11** | 3.0 | 75 | 108 | 82 | 66 |
| 4 |  | **6** **12** | 3.0 (1.2)[c] | 75 (75)[c] | 36 (117)[c] | 94 (80)[c] | 85 (91)[c] |
| 5[d] |  | **7** **13** | 3.0 | 60 | 96 | 72 | 79 |
| 6[e] |  | **8** **14** | 3.0 | 60 | 160 | 77 | 78 |
| 7 |  | **27** **30** | 3.0 | 60 | 48 | 67 | 87 |
| 8 |  | **28** **31** | 2.0 | 60 | 70 | 85 | 96 |
| 9 |  | **29** **32** | 3.0 | 60 | 140 | 72 | 91 |

[a] Isolated yield. [b] Determined by HPLC analysis. [c] 3 mol % catalyst was used. [d] $R^1 = CH_2OSiPh_2tBu$. [e] 30 mol % catalyst was used. Mts = 2,4,6-trimethylbenzenesulfonyl.

of GaLB, to afford **12** (36 h, yield 94%, 85% ee, entry 4). Entries 1−5 show that the new catalyst **26** (10 mol %) afforded products (**9**−**13**) in analogous ee's (66−91%) but in much higher chemical yields (72−94%) compared to GaLB (20 mol %, Table 1). After the reaction ligand **22** was recovered in almost quantitative yield by extracting with 1 N aq NaOH. This situation was very different for the GaLB catalyzed reaction because BINOL itself reacted with epoxide. The catalyst **26** was also effective for epoxides **27** and **28** (entry 7, yield 67%, 87% ee; entry 8, yield 85%, 96% ee). It is noteworthy that even the reaction between **2** and the less reactive acyclic epoxide **29** proceeded with this catalyst (entry 9, yield 72%, 91% ee). Importantly, using only 3 mol % of catalyst **26**, epoxide **6** gave **12** in 80% yield and in 91% ee; however, the reaction time was long (117 h, entry 4 in parentheses). It seems that all of these results can be attributed to the stability of complex **26**, obtained by linking the two BINOL units in GaLB. The stable catalyst **26** remained unchanged during the course of the reaction, whereas GaLB was decomposed by severe ligand exchange with 4-methoxyphenol and the reaction stopped on the way.

As shown in Scheme 5, epoxide ring-opened product **9** was transformed into various useful intermediates in organic synthesis. Corresponding 1,2-diol **33** was readily obtained in 76% yield from **9** by treatment with ammonium cerium(IV) nitrate (CAN).[33] In addition, since **9** was obtained as a monoprotected diol, it could also be converted into α-aryloxyketone **34** and *β*-aryloxy azide **35** without any reduction in its optical purity.

**Scheme 5.** Transformations of **9** into the Optically Active 1,2-Diol **33**, Ketone **34**, and Azide **35**



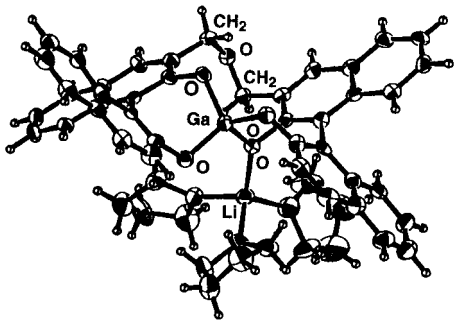




**Figure 3.** X-ray structure of LiCl-free Ga-Li-linked-BINOL **36**.

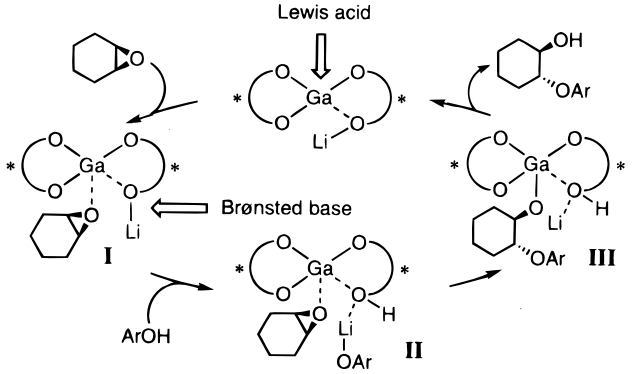
**C. Catalyst Structure and the Mechanism of the Epoxide Opening Reaction.** Having succeeded in improving the catalytic enantioselective epoxide opening reaction, we then turned our attention to the elucidation of the catalyst structure. Although $^{13}C$ NMR,[34] FAB mass (GaLB: $M^+ = 644$ for $Ga^{69}$ and 646 for $Ga^{71}$), and (−)-LDI TOF mass (Ga-Li-linked-BINOL **26**: $M - Li^+ = 679$ for $Ga^{69}$) data suggested the assumed monomeric structures, all attempts to obtain X-ray grade crystal of these catalysts, prepared from $GaCl_3$, were unsuccessful. After several trials, we succeeded in getting an X-ray grade crystal of LiCl free Ga-Li-linked-BINOL complex. The LiCl free Ga-Li-linked-BINOL complex (**36**) was prepared from Ga(O-*i*-Pr)$_3$ (1 mol equiv), linked-BINOL **22** (1 mol equiv), and BuLi (1 mol equiv) (Scheme 4), and the crystal of **36** was grown from toluene solution in the presence of a small amount of THF and diethyl ether. This crystal of **36** also catalyzed the ring opening reaction of epoxide **3** to give **9** (20 mol % catalyst, toluene, 50 °C, 40 h, yield 85%), although in somewhat lower ee (74%) compared to catalyst **26**. By treating this crystal with 3 mol equiv of LiCl in THF prior to use, the enantiomeric excess increased to 90%, suggesting the formation of the same catalyst as the one from $GaCl_3$. The role of LiCl is not clear, but it is well-known that lithium halide functions effectively as an achiral additive to increase enantioselectivity.[35] Therefore it might be possible that LiCl could coordinate to the Ga-Li-linked-BINOL complex, slightly affecting the asymmetric environment of the complex in solution phase. As shown in Figure 3, Ga-Li-linked-BINOL complex has a monomeric tetracoordinated structure, which is similar to the structure of Al-Li-bis(binaphthoxide)-

(33) Fukuyama, T.; Laird, A. A.; Hotchkiss, L. M. *Tetrahedron Lett.* **1985**, *26*, 6291.

(34) $^{13}C$ NMR of GaLB gave only 10 peaks in aromatic region, suggesting symmetric structure of GaLB. $^{13}C$ NMR chart of GaLB is available. See the supporting information.

(35) Sugasawa, K.; Shindo, M.; Noguchi, H.; Koga, K. *Tetrahedron Lett.* **1996**, *37*, 7377 and references therein.

**Scheme 6.** Working Model for the Ring Opening of Cyclohexene Oxide with 4-Methoxyphenol (**2**, ArOH) Catalyzed by Gallium Heterobimetallic Complexes




$(thf)_3$ complex (ALB).[36] This is the first X-ray crystal analysis of an asymmetric catalyst containing gallium, and this result also strongly supports the proposed monomeric structures of other gallium heterobimetallic catalysts which were reported by our group[2a,37] and others.[38]

On the basis of mechanistic studies of other asymmetric reactions catalyzed by various heterobimetallic complexes,[13a,13d,13f,36,39] especially those of ALB,[36,39b] which has a group 13 element Al as a center metal, it is quite reasonable to consider that group 13 element Ga would also function as a Lewis acid in a similar manner as Al to activate epoxides[40] and lithium binaphthoxide would act as a Brønsted base to activate 4-methoxyphenol. Furthermore, as mentioned previously (section A), dual activation of both epoxides and 4-methoxyphenol seems very important. So the proposed catalytic cycle for the present epoxide opening reaction appears to be reasonable (Scheme 6). In the *meso*-epoxide ring opening reaction, fixing the position of epoxides coordinating to the Lewis acid and controlling the orientation of nucleophiles are necessary to achieve high enantiomeric induction. Based on the X-ray structure of LiCl free (*R*,*R*)-Ga-Li-linked-BINOL complex **36** and the absolute configuration of the product obtained by this catalyst (74% ee for (*R*,*R*)-**9**), enantiomeric induction in the present system can be understood by assuming the transition state in Figure 4.[41] Due to the steric hindrance, the epoxide coordinating to gallium would be fixed in (A) form rather than (B) form. Lithium binaphthoxide then activates and controls the orientation of ArOH **2** so that lithium phenoxide should attack the epoxide selectively from one side to afford (*R*,*R*)-1,2-diol monoether.[42]

## Conclusion

In conclusion, we have succeeded in carrying out the first catalytic enantioselective *meso*-epoxide ring opening reaction with phenolic oxygen nucleophile by utilizing heterobimetallic multifunctional catalysts. A novel linked-BINOL containing a coordinative oxygen atom in its linker was developed for preparing a more stable gallium heterobimetallic complex. By using this Ga-Li-linked-BINOL complex, the present reaction was greatly improved to afford 1,2-diol monoethers in up to 94% yield and in up to 96% ee. These 1,2-diol monoethers could easily be converted not only into optically active 1,2-diols but also into other chiral compounds. Furthermore we have succeeded in getting X-ray data of LiCl free Ga-Li-linked-BINOL complex. This is the first X-ray analysis of an asymmetric catalyst containing gallium. Although more detailed mechanistic studies are needed for clear understanding, these X-ray data contribute a lot to understanding the mechanism of various reactions catalyzed by other gallium heterobimetallic complexes as well as the mechanism of the present epoxide opening reaction. The linked-BINOL has opened up the possibility of developing various catalysts containing several types of Lewis acidic metals other than gallium. In addition, we consider that this new linked-BINOL concept makes it easy to develop a solid-phase asymmetric catalyst that contains several BINOL units.[43] These are now under intense investigation in our group.

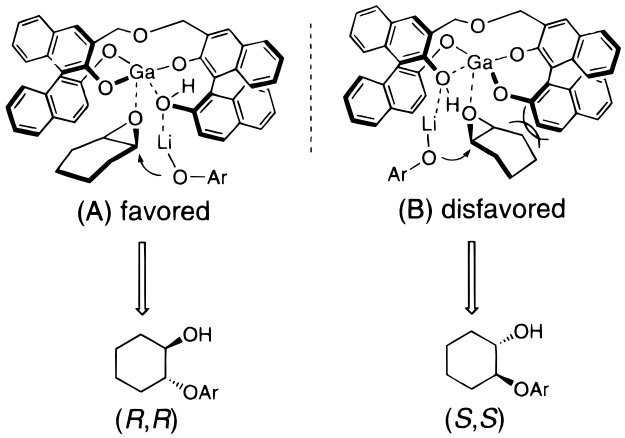



**Figure 4.** Working transition state model for *meso*-epoxide opening reaction promoted by gallium heterobimetallic complexes.

## Experimental Section

**General.** Infrared (IR) spectra were recorded on a JASCO FT/IR 410 Fourier transform infrared spectrophotometer. NMR spectra were recorded on a JEOL JNM-LA500 spectrometer, operating at 500 MHz for $^1H$ NMR and 125.65 MHz for $^{13}C$ NMR. Chemical shifts in $CDCl_3$ were reported downfield from TMS (=0) for $^1H$ NMR. For $^{13}C$ NMR, chemical shifts were reported on the scale relative to $CHCl_3$ (77.00 ppm for $^{13}C$ NMR) as an internal reference. Optical rotations were measured on a JASCO P-1010 polarimeter. EI mass spectra were measured on JEOL JMS-DX303 or JMS−BU20 GCmate. LDI-TOF mass spectra were measured on Shimadzu MALDI IV. Column chromatography was performed with silica gel Merck 60 (230−400 mesh ASTM). The enantiomeric excess (ee) was determined by HPLC analysis. HPLC was performed on JASCO HPLC systems consisting of the following: pump, 880-PU or PU-980; detector, 875-UV or UV-970, measured at 254 nm; column, DAICEL CHIRALPAK AS, AD,

(36) Arai, T.; Yamada, Y. M. A.; Yamamoto, N.; Sasai, H.; Shibasaki, M. *Chem. Eur. J.* **1996**, *2*, 1368.

(37) Ga-Na-bis(binaphthoxide) (GaSB) complex was used for catalytic asymmetric Michael reaction; see ref 36.

(38) Ford, A.; Woodward, S. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 335.

(39) (a) Sasai, H.; Arai, T.; Satow, Y.; Houk, K. N.; Shibasaki, M. *J. Am. Chem. Soc.* **1995**, *117*, 6194. (b) Arai, T.; Sasai, H.; Aoe, K.; Okamura, K.; Date, T.; Shibasaki, M. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 5, 104.

(40) ALB can also promote the epoxide opening reaction with **2**, although the result was inferior to GaLB and **26**. Epoxide **3** gave **9** in 20% yield and 72% ee (20 mol % ALB, toluene, MS 4A, 50 °C, 115 h).

(41) LiCl effect as an achiral additive to enhance enantiomeric excess has already been discussed in this section. However, since its role is not yet clear, LiCl is not included into the proposed transition state.

(42) Probably in the case of GaSO, $H_8$-BINOL has a larger dihedral angle and so fixation of epoxides might not be rigid enough, thus resulting in low enantiomeric excess.

(43) With two nonlinked BINOL units, the relative spatial relationship between two BINOL units on the resin should be finely controlled to make an active catalytic species formation possible. However, such control probably is not so easy. Seebach reported various polymer supported Ti-TADDOL catalysts. The polymer supported Ti catalysts afforded products in comparable ee with homogeneous analogues in the reaction where the active species was a Ti:TADDOL = 1:1 complex. On the other hand, the catalysts gave products only in poor ee in the reaction where the active species was different from the Ti:TADDOL = 1:1 complex. See: Seebach, D.; Marti, R. E.; Hintermann, T. *Helv. Chim. Acta* **1996**, *79*, 1710.

DAICELCHIRALCEL OD or OJ; mobile phase, hexane-2-propanol; flow rate, 0.50−1.0 mL/min. Reactions were carried out in dry solvents under an argon atmosphere, unless otherwise stated. Tetrahydrofuran (THF) and diethyl ether were distilled from sodium benzophenone ketyl. Toluene was distilled from sodium. $GaCl_3$ and $Ga(O\text{-}i\text{-}Pr)_3$ were purchased from Kojundo Chemical Laboratory Co., Ltd., 5-1-28, Chiyoda, Sakado-shi, Saitama 350-0214, Japan (fax, ++(81)-492-84-1351). Other reagents were purified by the usual methods.

**Procedure for the Preparation of (*R*)-Ga-Li-bis(binaphthoxide) Complex (GaLB: 1).** To an ice-cooled solution of (*R*)-binaphthol (1.145 g, 4.00 mmol) in THF (24 mL) was added BuLi (5.00 mL, 8.00 mmol, 1.60 M in hexane), and the mixture was stirred at 0 °C for 10 min and at room temperature for 30 min. The resultant solution was added to a mixture of $GaCl_3$ (4.67 mL, 2.00 mmol, 0.428 M in diethyl ether) and THF (15 mL) at room temperature. The reaction mixture was then stirred at room temperature for 3 h. This catalyst solution can be stored for a couple of months under argon at room temperature. $^{13}C$ NMR (THF, external $D_2O$ was used to obtain lock signal) $\delta$ 121.0, 121.3, 124.0, 125.2, 126.3, 127.0, 127.3, 128.4, 134.6, 157.4; FAB-MS, *m*/*z* 653 (for $^{71}Ga$) and 651 (for $^{69}Ga$) [$M^+$ + Li], 646 (for $^{71}Ga$) and 644 (for $^{69}Ga$) [$M^+$].

**General Procedure for the Catalytic Enantioselective Epoxide Ring Opening Reactions with 4-Methoxyphenol using GaLB 1.** A mixture of powdered MS 4A (400 mg), dried at 180 °C under reduced pressure (ca. 5 mmHg) for 6 h prior to use, and a 0.05 M solution of (*R*)-GaLB **1** (4.0 mL, 0.20 mmol, prepared by the procedure described above) was evaporated in vacuo to remove the solvents. A solution of 4-methoxyphenol (**2**) (149 mg, 1.2 mmol) in toluene (2.0 mL) and cyclopentene oxide (**4**) (87.5 $\mu$L, 1.0 mmol) was added to the residue at room temperature, and the mixture was stirred at 50 °C for 72 h. The resultant mixture was diluted with diethyl ether (30 mL) and filtered over a Celite pad to remove MS 4A. The filtrate was washed successively with 5% aq citric acid (10 mL), 1 N aq NaOH (10 mL), saturated aq $NH_4Cl$ (10 mL), and brine (10 mL) and then dried over $MgSO_4$. After evaporation of the volatiles, the residue was purified by flash column chromatography ($SiO_2$, hexane/acetone 10/1) to give **10** (157 mg, 0.75 mmol, yield 75%) in 86% ee as a colorless oil.

**Procedure for the Preparation of (*R*)-Ga-Na-bis($H_8$-binaphthoxide) Complex (GaSO: 16).** To an ice-cooled solution of (*R*)-$H_8$-BINOL (294 mg, 1.00 mmol) in THF (11.52 mL) was added *t*-BuONa (4.48 mL, 2.00 mmol, 0.446 M in THF) and the mixture was stirred at room temperature for 30 min. The resultant suspension was added to a mixture of $GaCl_3$ (1.00 mL, 0.500 mmol, 0.500 M in diethyl ether) and THF (3.00 mL) at room temperature. The mixture was stirred for 10 h at room temperature. Then the resultant suspension was kept standing at the same temperature until NaCl salt precipitated. The supernatant solution was used as (*R*)-GaSO catalyst (0.025 M). This catalyst can be stored for couple of months under argon at room temperature.

**General Procedure for the Catalytic Enantioselective Epoxide Ring Opening Reactions with 4-Methoxyphenol Using GaSO 16.** A mixture of powdered MS 4A (200 mg), dried at 180 °C under reduced pressure (ca. 5 mmHg) for 6 h prior to use, and a 0.025 M supernatant of (*R*)-GaSO **16** (4.0 mL, 0.10 mmol, prepared by the procedure described above) was evaporated in vacuo to remove the solvents. A solution of 4-methoxyphenol (**2**) (74.5 mg, 0.60 mmol) in toluene (2.0 mL) and cyclohexene oxide (**3**) (51 $\mu$L, 0.50 mmol) was added to the residue at room temperature, and the mixture was stirred at 50 °C for 4 h. The resultant mixture was diluted with diethyl ether (30 mL) and filtered over a Celite pad to remove MS 4A. The filtrate was washed successively with 5% aq citric acid (10 mL), 1 N aq NaOH (10 mL), saturated aq $NH_4Cl$ (10 mL), and brine (10 mL) and then dried over $MgSO_4$. After evaporation of the volatiles, the residue was purified by flash column chromatography ($SiO_2$, hexane/acetone 15/1) to give **9** (81.1 mg, 0.365 mmol, yield 73%) in 56% ee as colorless solid.

**Procedure for the Preparation of (*R*,*R*)-Ga-Li-linked-BINOL Complex 26.** To a stirred solution of (*R*,*R*)-linked-BINOL **22** (1.09 g, (15.5 w/w % diethyl ether and hexane), 1.5 mmol), in THF (22.7 mL) at 0 °C was added BuLi (4.0 mL, 6.0 mmol, 1.50 M in hexane) and the mixture was stirred at 0 °C for 2 h. $GaCl_3$ (3.3 mL, 1.5 mmol, 0.455 M in diethyl ether) was then added at 0 °C. After stirring for 90 min at 0 °C, the reaction mixture became a white suspension and was then stirred at room temperature for another 90 min. The resultant suspension was used as (*R*,*R*)-Ga-Li-linked-BINOL catalyst. This catalyst suspension can be stored for at least 1 month under an argon atmosphere at 0 °C. $GaCl_3$ can be stored as diethyl ether solution for several months at −20 °C.

**General Procedure for the Catalytic Enantioselective Epoxide Ring Opening Reactions with 4-Methoxyphenol Using Ga-Li-linked-BINOL Complex 26.** A mixture of powdered MS 4A (100 mg), dried at 180 °C under reduced pressure (ca. 5 mmHg) for 6 h prior to use, and a 0.05 M suspension of (*R*,*R*)-Ga-Li-linked-BINOL complex **26** (1.0 mL, 0.05 mmol, prepared by the procedure described above) was evaporated *in vacuo*. A solution of 4-methoxyphenol (**2**) (186 mg, 1.5 mmol) in toluene (2.0 mL) and cyclopentene oxide (**4**) (43.7 $\mu$L, 0.50 mmol) was added to the residue at room temperature, and the mixture was stirred at 75 °C for 96 h. The resultant mixture was diluted with diethyl ether (30 mL) and filtered over a Celite pad to remove MS 4A. The organic layer was washed successively with 5% aq citric acid (10 mL), 1 N aq NaOH (15 mL × 2), saturated aq $NH_4Cl$ (10 mL), and brine (10 mL) and then dried over $MgSO_4$. After evaporation, the residue was purified by flash column chromatography ($SiO_2$, hexane/diethyl ether 5/1) to give **10** (91.8 mg, 0.44 mmol, yield 88%) in 85% ee as a colorless oil. Linked-BINOL **22** was recovered in the following manner: aq NaOH layers were acidified with 1 N aq HCl and then extracted with diethyl ether (20 mL). The organic layer was washed with saturated aq $NaHCO_3$ (10 mL) and brine (10 mL) and then dried over $MgSO_4$. After evaporation, the residue was purified by flash column chromatography ($SiO_2$, hexane/diethyl ether 2/1) to give **22** in quantitative yield.

**Synthesis of the 1,2-Diol Monoethers 9−14, 18, and 30−32 Using Gallium Heterobimetallic Complexes.** The absolute configurations of **9** and **10** were determined by converting them into known chiral diols. **12** was transformed into **9** and **14** was transformed into a known compound.[44a] Mosher's method[44b] was used for **11**, **13**, **18**, and **31**. The absolute configurations of **30** and **32** have not yet been determined.

**(1*R*,2*R*)-2-(4-Methoxyphenyloxy)cyclohexanol (9)**: colorless solid; mp 84−86 °C; IR (KBr) $\nu$ 3398, 2933, 2056, 1982 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.21−1.43 (m, 4 H), 1.73 (m, 2 H), 2.02−2.17 (m, 2 H), 2.62 (br, 1 H), 3.68 (ddd, *J* = 4.6, 8.6, 10.5 Hz, 1 H), 3.76 (s, 3 H), 3.84 (ddd, *J* = 4.6, 8.6, 10.5 Hz, 1 H), 6.79−6.92 (m, 4 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 23.9, 24.0, 29.3, 32.0, 55.7, 73.5, 83.6, 114.6, 118.1, 151.7, 154.4; MS *m*/*z* 222 [$M^+$]; $[\alpha]_D^{25}$ −56.6° (*c* 1.10, $CHCl_3$); HPLC (DAICEL CHIRALCEL OJ, 2-propanol/hexane 1/9, flow 1.0) $t_R$ 14.2 and 16.5 min. Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 69.95; H, 8.29.

**(1*R*,2*R*)-2-(4-Methoxyphenyloxy)cyclopentanol (10)**: colorless oil; IR (neat) $\nu$ 3408, 2954, 1507 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.58−1.84 (m, 4 H), 2.01−2.16 (m, 3 H), 3.75 (s, 3 H), 4.28 (m, 1 H), 4.43 (m, 1 H), 6.83 (m, 4 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 21.0, 29.8, 32.5, 55.7, 77.2, 85.2, 114.6, 116.6, 151.9, 153.8; MS *m*/*z* 208 [$M^+$]; $[\alpha]_D^{25}$ −36.0° (*c* 1.08 $CHCl_3$); HPLC (DAICEL CHIRALPAK AS, 2-propanol/hexane 1/9, flow 1.0) $t_R$ 10.1 and 25.5 min; HRMS [$M^+$] calcd for $C_{12}H_{16}O_3$, 208.1100; found, 208.1099.

**(1*R*,2*R*)-2-(4-Methoxyphenyloxy)cycloheptanol (11)**: colorless solid; mp 89−91 °C; IR (KBr) $\nu$ 3457, 2936, 1509 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.42−1.76 (m, 8H), 1.89−2.00 (m, 2 H), 2.70 (br, 1 H), 3.77 (s, 3 H), 3.86 (dt, *J* = 4.0, 8.5 Hz, 1 H), 3.96 (dt, *J* = 3.1, 8.9 Hz, 1 H), 6.84 (m, 4 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 22.27, 22.34, 27.3, 28.2, 31.8, 55.7, 75.9, 85.7, 114.8, 117.8, 151.5, 154.3; MS *m*/*z* 236 [$M^+$]; $[\alpha]_D^{23}$ −28.1° (*c* 0.206 $CHCl_3$ (67% ee)); HPLC (DAICEL CHIRALPAK AD, 2-propanol/hexane 1/9, flow 1.0) $t_R$ 13.0 and 16.0 min; HRMS [$M^+$] calcd for $C_{14}H_{20}O_3$, 236.1413; found, 236.1412.

**(1*R*,2*R*)-2-(4-Methoxyphenyloxy)-4-cyclohexen-1-ol (12)**: colorless solid; mp 98−100 °C; IR (KBr) $\nu$ 3376, 2925, 1508 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 2.08−2.22 (m, 2 H), 2.55−2.63 (m, 2 H), 3.77 (s, 3 H), 4.02 (ddd, *J* = 5.9, 9.2, 9.2 Hz, 1 H), 4.19 (ddd, *J* = 5.7, 9.2, 9.2 Hz, 1 H), 5.52−5.56 and 5.59−5.62 (m, 1 H each), 6.82−6.94 (m, 4 H);

(44) (a) Ballini, R.; Marcantoni, E.; Petrini, M. *J. Org. Chem.* **1992**, *57*, 1316. (3*S*,4*S*)-1-Benzyl-3,4-bis(methoxymethoxy)pyrrolidine: $[\alpha]_D^{20}$ + 11.9° (*c* 2.4, $CHCl_3$). (b) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543. Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Org. Chem.* **1991**, *56*, 1296.

$^{13}$C NMR ($CDCl_3$) $\delta$ 30.3, 32.5, 55.7, 69.9, 79.6, 114.7, 117.9, 123.8, 124.6, 151.7, 154.5; MS *m*/*z* 220 [$M^+$]; $[\alpha]_D^{25}$ −56.5° (*c* 0.74 $CHCl_3$ (47% ee)); HPLC (DAICEL CHIRALCEL OJ, 2-propanol/hexane 1/9, flow 1.0) $t_R$ 18.5 and 26.3 min; HRMS [$M^+$] calcd for $C_{13}H_{16}O_3$, 222.1100; found, 222.1099.

**(1*R*,2*R*,4*R*,5*S*)-4,5-bis((*tert*-Butyldiphenylsilyloxy)methyl)-2-(4-methoxyphenyloxy)cyclohexanol (13)**: colorless foam; IR (neat) $\nu$ 3437, 2930, 1507 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 0.96 (s, 9H), 0.98 (s, 9H), 1.37 (m, 1 H), 1.45 (m, 1 H), 1.97 (m, 1 H), 2.21 (br s, 1 H), 2.59 (m, 1 H), 3.48 (d, $J$ = 6.4 Hz, 2 H), 3.68 (dd, $J$ = 9.8, 10.1 Hz, 1 H), 3.74 (s, 3 H), 3.73−3.81 (m, 3 H), 4.19 (ddd, $J$ = 4.3, 8.5, 11.6 Hz, 1 H), 6.75 (dt, $J$ = 4.0, 9.2 Hz, 2 H), 6.91 (dt, $J$ = 3.7, 9.2 Hz, 2 H), 7.24−7.42 (m, 12 H), 7.52−7.62 (m, 8H); $^{13}$C NMR ($CDCl_3$) $\delta$ 19.1, 26.8, 29.8, 30.9, 37.5, 39.8, 55.7, 62.1, 65.6, 73.3, 80.0, 114.7, 117.8, 127.66, 127.72, 129.6, 129.7, 133.4, 133.5, 135.5, 151.8, 154.3; MS *m*/*z* 758 [$M^+$]; $[\alpha]_D^{21}$ −13.9° (*c* 1.07 $CHCl_3$ (80% ee)); HPLC (DAICEL CHIRALPAK AD, 2-propanol/hexane 1/99, flow 1.0) $t_R$ 21.0 and 26.0 min; HRMS [$M^+$] calcd for $C_{47}H_{58}O_5Si_2$, 758.3823; found, 758.3821.

**(1*R*,2*R*)-4-(4-Methoxyphenyloxy)-1-(2,4,6-trimethylphenylsulfonyl)-3-pyrrolidin-3-ol (14)**: MS 4A was used without prior activation; colorless solid; IR (KBr) $\nu$ 3449, 2960, 1509, 1315, 1146 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 2.31 (s, 3 H), 2.64 (s, 6H), 3.36 (dd, $J$ = 2.0, 11.5 Hz, 1 H), 3.42 (br s, 1 H), 3.53 (dd, $J$ = 4.0, 12.0 Hz, 1 H), 3.76 (s, 3 H), 3.81 (dd, $J$ = 5.0, 11.5 Hz, 1 H), 4.38 (m, 1 H), 4.64 (m, 1 H), 6.81 (s, 4 H), 6.96 (s, 2 H); $^{13}$C NMR ($CDCl_3$) $\delta$ 20.9, 22.8, 50.0, 52.7, 55.7, 73.8, 82.0, 114.8, 116.9, 131.9, 132.3, 140.2, 142.8, 150.6, 154.6; MS *m*/*z* 391 [$M^+$]; $[\alpha]_D^{27}$ −19.6° (*c* 1.04 $CHCl_3$ (79% ee)); HPLC (DAICEL CHIRALCEL OD, 2-propanol/hexane 1/9, flow 1.0) $t_R$ 26.4 and 31.6 min; HRMS [$M^+$] calcd for $C_{20}H_{25}O_5$, 391.1453; found, 391.1450.

**(2*R*,3*R*)-2-Hydroxy-3-(4-methoxyphenyloxy)-1,4-butanediol Bis-(triphenylmethyl) Ether (18)**: colorless foam; $^1$H NMR ($CDCl_3$) $\delta$ 2.51 (d, $J$ = 6.1 Hz, 1 H), 3.16 (dd, $J$ = 6.1, 9.2 Hz, 1 H), 3.24 (dd,; $J$ = 6.4, 9.2 Hz, 1 H), 3.28 (dd, $J$ = 5.2, 10.8 Hz, 1 H), 3.45 (dd, $J$ = 5.5, 10.1 Hz, 1 H), 3.76 (s, 3 H), 4.06 (m, 1 H), 4.42 (dt, $J$ = 3.4, 4.0 Hz, 1 H), 6.71−6.78 (m, 4 H), 7.17−7.25 (m, 18H), 7.33−7.39 (m, 12 H); $^{13}$C NMR ($CDCl_3$) $\delta$ 55.7, 62.8, 64.0, 70.9, 78.0, 86.8, 87.1, 114.5, 114.7, 117.5, 127.0, 127.2, 127.3, 127.78, 127.81, 127.9, 128.6, 128.7, 143.76, 143.81, 152.5, 154.2; MS *m*/*z* 712 [$M^+$]; $[\alpha]_D^{23}$ +1.9° (*c* 0.579 $CHCl_3$ (50% ee)); HPLC (DAICEL CHIRALCEL OD, 2-propanol/hexane 1/9, flow 0.8) $t_R$ 28.0 and 35.0 min.

**(1*R*,2*R*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)-2-(4-methoxyphenyloxy)-cyclopentanol (30)**: colorless oil; IR (neat) $\nu$ 3508, 2930, 1507 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 0.10 (s, 6H), 0.90 (s, 9H), 1.86 (ddd, $J$ = 1.5, 1.8, 14.0 Hz, 1 H), 1.97 (ddd, $J$ = 4.3, 4.7, 15.0 Hz, 1 H), 2.05 (ddd, $J$ = 4.9, 4.9, 14.0 Hz, 1 H), 2.34 (dddd, $J$ = 1.8, 1.8, 7.0, 15.0 Hz, 1 H) 3.24 (br s, 1 H), 3.75 (s, 3 H), 4.19 (brd, $J$ = 4.9 Hz, 1 H), 4.51−4.53 (m, 1 H), 4.71−4.73 (m, 1 H), 6.80−6.87 (m, 4 H); $^{13}$C NMR ($CDCl_3$) $\delta$ −5.0, −4.9, 17.9, 25.7, 41.5, 42.2, 55.7, 74.3, 77.0, 84.8, 114.7, 116.3, 151.9, 153.8; MS *m*/*z* 338 [$M^+$]; $[\alpha]_D^{25}$ −6.2° (*c* 1.08 $CHCl_3$(87% ee)); HPLC (DAICEL CHIRALPAK AD, 2-propanol/hexane 1/9, flow 1.0) $t_R$ 9.9 and 10.9 min; HRMS [$M^+$] calcd for $C_{30}H_{18}O_4Si$, 338.1913; found, 338.1906.

**(1*R*,2*R*)-5,8-Dimethoxy-3-(4-methoxyphenyloxy)-1,2,3,4-tetrahydronaphthalene-2-ol (31)**: colorless foam; mp 155−156 °C; IR (KBr) $\nu$ 3406, 2942, 1508 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 2.56 (dd, $J$ = 9.2, 17.1 Hz, 1 H), 2.64 (dd, $J$ = 9.2, 17.7 Hz, 1 H), 3.37 (dd, $J$ = 6.1, 17.1 Hz, 1 H), 3.38 (dd, $J$ = 5.5, 17.7 Hz, 1 H), 4.15 (ddd, $J$ = 6.1, 9.2, 9.2 Hz, 1 H), 4.32 (ddd, $J$ = 5.5, 9.2, 9.2 Hz, 1 H), 6.63 (d, $J$ = 8.9 Hz, 1 H), 6.65 (d, $J$ = 8.9 Hz, 1 H), 6.83−6.98 (m, 4 H); $^{13}$C NMR ($CDCl_3$) $\delta$ 28.1, 30.4, 55.5, 55.7, 69.8, 79.2, 107.4, 107.7, 114.8, 117.9, 123.7, 124.1, 151.1, 151.2, 151.8, 154.5; MS *m*/*z* 330 [$M^+$] 207; $[\alpha]_D^{25}$ −131.93° (*c* 0.42, $CHCl_3$ (96% ee)); HPLC (DAICEL CHIRALCEL OD, 2-propanol/hexane 1/9, flow 0.5) $t_R$ 39.0 and 42.7 min. Anal. Calcd for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 68.89; H, 6.59.

**(2*R*,3*R*)-3-(4-Methoxyphenyloxy)-2-butanol (32)**: colorless oil; IR (neat) $\nu$ 3433, 2976, 1507 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.18 (d, $J$ = 6.1 Hz, 3 H), 1.22 (d, $J$ = 6.1 Hz, 3 H), 2.63 (br s, 1 H), 3.75 (s, 3 H), 3.79 (dq, $J$ = 6.1, 6.4 Hz, 1 H), 3.98 (dq, $J$ = 6.1, 6.4 Hz, 1 H), 6.79−6.86 (m, 4 H); $^{13}$C NMR ($CDCl_3$) $\delta$ 15.6, 18.4, 55.6, 70.9, 80.3, 114.7, 117.8, 151.6, 154.3; MS *m*/*z* 196 [$M^+$]; $[\alpha]_D^{26}$ −52.3° (*c* 1.93, $CHCl_3$ (91% ee)); HPLC (DAICEL CHIRALPAK AS, 2-propanol/hexane 1/9, flow 1.0) $t_R$ 7.3 and 28.9 min; HRMS [$M^+$] calcd for $C_{11}H_{16}O_3$, 196.1099; found, 196.1104.

**Synthesis of Linked-BINOL 22. 2,2′-Bis(methoxymethyloxy)-1,1′-binaphthalene-3-carboxaldehyde (23).** To a stirred solution of MOM-protected (*R*)-binaphthol (32.05 g, 85.6 mmol), in THF (320 mL) at −78 °C was added TMEDA (15.5 mL, 103 mmol) and then BuLi (60.8 mL, 96.7 mmol, 1.59 M in hexane) over 15 min. The mixture was warmed to 0 °C and stirred for 30 min. After cooling to −78 °C, DMF (7.58 mL, 103 mmol) in THF (40 mL) was added dropwise over 10 min. The mixture was stirred at the same temperature for 30 min and then was warmed to 0 °C and stirred for further 40 min. The resultant yellow solution was quenched with saturated aq $NH_4Cl$ (50 mL). After addition of 1 N aq HCl (50 mL), the solution was extracted with diethyl ether (500 mL), and the combined organic layers were washed with saturated aq $NaHCO_3$ (50 mL) and brine and then dried over $MgSO_4$. The solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography ($SiO_2$, hexane/ethyl acetate 10/1) to give **23** (26.03 g, 64.7 mmol, yield 76%). **23** has already been reported. See ref 18.

**3-Hydroxymethyl-2,2′-bis(methoxymethyloxy)-1,1′-binaphthalene (24).** To an ice-cooled solution of **23** (5.15 g, 12.8 mmol) in THF (80 mL)/$CH_3OH$ (80 mL) was added $NaBH_4$, and the mixture was stirred at 0 °C for 15 min. $H_2O$ was added and the mixture was concentrated under reduced pressure and then extracted with ethyl acetate (100 mL × 2). The combined organic extracts were washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was then dried in vacuo to afford **24** as a colorless foam, which was used for the next step without further purification. **24** has already been reported. See ref 18.

**3-Bromomethyl-2,2′-bis(methoxymethyloxy)-1,1′-binaphthalene (25).** To an ice-cooled solution of crude **24** in toluene (50 mL)/ethyl acetate (50 mL) were added successively $Et_3N$ (7.14 mL, 51.2 mmol) and MsCl (1.98 mL, 25.6 mmol). The mixture was stirred at 0 °C for 90 min. The resultant suspension was filtered to remove solid $Et_3NH^+Cl^-$ and the solid was washed with ethyl acetate (50 mL). The combined filtrate and washings were cooled to 0 °C and then LiBr (11.1 g, 128 mmol) and DMF (100 mL) were added. The mixture was stirred at room temperature for 10 min. It was diluted with diethyl ether (200 mL) and washed with water (100 mL × 2), 1 N aq HCl (50 mL × 2), saturated aq $NaHCO_3$ (50 mL), and brine. It was dried over $MgSO_4$ and evaporated in vacuo to give **25** as a colorless solid (5.568 g, 11.9 mmol, yield 93% from **23**) which was pure enough to be used in next step without further purification. **25** has already been reported. See ref 29a.

**3,3″-(Oxydimethylene)-di-1,1′-bi-2-naphthol (22).** To a stirred solution of **24** (4.0 g, 9.89 mmol), in THF (50 mL)/DMF (30 mL) at 0 °C, was added NaH in oil (482 mg, 12.6 mmol as 60% purity). The mixture was stirred at the same temperature for 60 min, and then **25** (4.62 g, 9.89 mmol) in DMF (30 mL) was added. The mixture was stirred at room temperature for 64 h and then cooled to 0 °C and quenched with $H_2O$. It was diluted with diethyl ether (400 mL), washed with $H_2O$ (100 mL) and brine (100 mL), and then dried over $MgSO_4$. After evaporation of solvent, the residue was purified by flash column chromatography ($SiO_2$, hexane/ethyl acetate 4/1) to give MOM-protected linked-BINOL (6.63 g (4.0 w/w % ethyl acetate was included based on $^1$H NMR), 8.04 mmol, yield 82%) as a yellow foam.

To a stirred solution of this yellow foam (3.01 g, 3.65 mmol) in $CH_2Cl_2$ (40 mL)/$CH_3OH$ (40 mL) was added $TsOH\cdot H_2O$ (300 mg, 1.58 mmol). The solution was stirred at 40 °C for 36 h. It was then diluted with $CH_2Cl_2$ (250 mL), washed with saturated $NaHCO_3$ (100 mL) and brine (100 mL), and dried over $MgSO_4$. After removing the solvent under reduced pressure the residue was purified by flash column chromatography ($SiO_2$, hexane/ethyl acetate 4/1). The product was further purified by recrystallization using diethyl ether/hexane to give **22** (2.03 g, 5.6 w/w % diethyl ether and hexane were included based on $^1$H NMR), 3.12 mmol, yield 85%) as a colorless powder: IR (KBr) $\nu$ 3375, 3069, 1507, 1106 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 5.00 (br s, 2 H), 5.05 (d, $J$ = 12.6 Hz, 2 H), 5.06 (d, $J$ = 12.6 Hz, 2 H), 6.31 (s, 2 H), 7.10 (d, $J$ = 8.3 Hz, 2 H), 7.14 (d, $J$ = 8.5 Hz, 2 H), 7.22 (ddd, $J$ = 1.5, 6.8, 8.3 Hz, 2 H), 7.28−7.38 (m, 8H), 7.85 (d, $J$ = 8.0 Hz, 2 H),

7.87 (d, $J = 7.3$ Hz, 2 H), 7.93 (d, $J = 8.9$ Hz, 2 H), 7.98 (s, 2 H); $^{13}$C NMR ($CDCl_3$) $\delta$ 70.2, 112.1, 112.5, 117.7, 123.7, 124.2, 124.4, 125.6, 127.1, 127.4, 128.2, 128.3, 128.9, 129.3, 130.0, 130.8, 133.4, 133.6, 151.8, 152.2; MS *m*/*z* 614 [$M^+$] 299; $[\alpha]_D^{27} + 67.4°$ (*c* 0.90, $CHCl_3$); HPLC (DAICEL CHIRALPAK AS, 2-propanol/hexane 1/4, flow 0.75) $t_R$ 24.8 and 46.5 min. Anal. Calcd for $C_{42}H_{30}O_5$ (1.00 mol equiv), diethyl ether ($C_4$ $_{H10}$O, 0.265 mol equiv), and hexane ($C_6H_{14}$, 0.200 mol equiv): C, 81.59; H, 5.48. Found: C, 81.30; H, 5.51.

**Transformation of 9 into 1,2-Cyclohexanediol (33), α-Aryloxyketone 34, and *β*-Aryloxy Azide 35. (1*R*,2*R*)-Cyclohexane-1,2-diol (33).** To a stirred solution of **9** (47.5 mg, 0.214 mmol) in $CH_3CN$ (2.0 mL)/$H_2O$ (0.5 mL) at 0 °C was added $(NH_4)_2Ce(NO_3)_6$ (293 mg, 0.534 mmol). The mixture was stirred at the same temperature for 40 min; then 6 N aq HCl was added. The resultant mixture was continuously extracted with $CHCl_3$ for 12 h. The organic layer was washed with brine and then dried over $MgSO_4$. After evaporation, **33** was obtained as a colorless oil (yield 76%). $[\alpha]_D^{25}$ −40° (*c* 0.19, $H_2O$ (94% ee)); literature value $[\alpha]_D^{25}$ −46.5° (*c* 1.6, $H_2O$).[45]

**(2*R*)-2-(4-Methoxyphenyloxy)cyclohexan-1-one (34).** To a stirred solution of **9** (32.0 mg, 0.144 mmol) and $Et_3N$ (60.0 $\mu$L, 0.430 mmol) in DMSO (1.0 mL) was added $SO_3$·pyridine, and the mixture was stirred at room temperature for 30 min. The resultant mixture was poured into ice-cooled water (20 mL) and then extracted with ethyl acetate (10 mL × 3). The combined organic layers were washed with brine and dried over $MgSO_4$. The solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography ($SiO_2$, hexane/ethyl acetate 15/1) to give **34** (32.0 mg, 0.144 mmol, yield 100%) as a colorless solid: IR (KBr) $\nu$ 2944, 1721, 1508 $cm^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.69−1.80 (m, 2 H), 1.97−2.07 (m, 3 H), 2.25−2.36 (m, 2 H), 2.58−2.61 (m, 1 H), 3.73 (s, 3 H), 4.50−4.52 (m, 1 H), 6.76−6.95 (m, 4 H); $^{13}$C NMR ($CDCl_3$) $\delta$ 22.8, 27.8, 34.5, 40.5, 55.7, 81.8, 114.6, 117.0, 151.7, 154.4; MS *m*/*z* 220 [$M^+$]; $[\alpha]_D^{23}$ +60.5° (*c* 0.65, $CHCl_3$ (94% ee)); HPLC (DAICEL CHIRALPAK AD, 2-propanol/hexane 1/99, flow 1.0) $t_R$ 14.6 and 16.9 min; HRMS [$M^+$] calcd for $C_{13}H_{16}O_3$, 220.1099; found, 220.1105.

**(1*S*,2*R*)-1-Azido-2-(4-methoxyphenyloxy)cyclohexane (35).** To a stirred solution of **9** (36.6 mg, 0.163 mmol) in $CH_2Cl_2$ (1.0 mL) at 0 °C were added pyridine (0.5 mL, 6.2 mmol) and MsCl (65 $\mu$L, 0.84 mmol). The mixture solution was stirred at room temperature for 2.5 h. The resultant solution was washed successively with 1 N HCl (10 mL × 2), saturated aqueous $NaHCO_3$ (10 mL), and brine (10 mL) and then dried over $MgSO_4$. After evaporation of solvent, the residue was purified by flash column chromatography ($SiO_2$, hexane/ethyl acetate 10/1) to give the corresponding mesylate as colorless oil. A portion of this mesylate (16.0 mg, 0.0533 mmol) was dissolved in DMF (1.0 mL), and then $NaN_3$ was added at room temperature. The suspension was stirred at 120 °C for 48 h. The reaction mixture was cooled and diluted with $H_2O$ (20 mL) and then extracted with $CH_2Cl_2$ (15 mL × 3). The combined organic layers were dried over $MgSO_4$ and then evaporated *in vacuo*. The residue was purified by flash column chromatography ($SiO_2$, hexane/ethyl acetate 10/1) to give **35** (7.8 mg, yield 59% 2 steps) as colorless oil: IR (neat) $\nu$ 2939, 2097, 1507 $cm^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.32−1.43 (m, 2 H), 1.58−1.73 (m, 4 H), 1.92−2.05 (m, 2 H), 3.61−3.62 (m, 1 H), 3.75 (s, 3 H), 4.29−4.32 (m, 1 H), 6.79−6.83 (m, 2 H), 6.88−6.91 (m, 2 H); $^{13}$C NMR ($CDCl_3$) $\delta$ 21.5, 22.1, 27.3, 27.5, 55.7, 60.6, 77.8, 114.7, 117.8, 151.3, 154.4; MS *m*/*z* 247 [$M^+$]; $[\alpha]_D^{23}$ +2.26° (*c* 0.58, $CHCl_3$(94% ee)); HPLC (DAICEL CHIRALCEL OD, 2-propanol/hexane 1/99, flow 1.0) $t_R$ 7.3 and 9.6 min; HRMS [$M^+$] calcd for $C_{13}H_{17}O_2N_3$, 247.1321; found, 247.1323.

**Preparation of LiCl free (*R*,*R*)-Ga-Li-linked-BINOL Complex for the X-ray Structure Analysis.** To a stirred solution of (*R*,*R*)-linked-BINOL **22** (357.2 mg (14.2 w/w % diethyl ether and hexane included), 0.5 mmol), in THF (4.6 mL) at 0 °C was added Ga(O-*i*-Pr)$_3$ (123.49 mg, 0.5 mmol) in THF (5 mL), and the solution was stirred for 12 h at room temperature. It was cooled to 0 °C and BuLi (0.333 mL, 0.5 mmol, 1.5 M in hexane) was added. The reaction mixture was stirred at room temperature for 3 h. Ga(O-*i*-Pr)$_3$ CANNOT be stored as a THF solution, it should be stored as a toluene solution or powder under an argon atmosphere.

**Preparation of the Crystal of (*R*,*R*)-Ga-Li-linked-BINOL(thf)$_3$.** The LiCl free Ga-Li-linked-BINOL complex **36** in THF (0.05 M, 1 mL) was evaporated in vacuo. The resulting foam was dissolved in toluene (0.4 mL). An X-ray quality crystal of LiCl free Ga-Li-linked-BINOL(thf)$_3$ complex (colorless prism) was grown at room temperature from toluene solution (0.125 M, 0.4 mL) under argon in the presence of a trace amount of THF and diethyl ether.

**(*R*,*R*)-Ga-Li-linked-BINOL(thf)$_3$:** Collected at 135 K; $C_{65}H_{70}O_{10}$-GaLi = 1087.92; colorless prism, $a = 10.013(5)$ Å, $b = 19.02(1)$ Å, $c = 15.34(1)$ Å, $\beta = 106.32(3)°$, $V = 2802(3)$ Å$^3$, monoclinic, $P2_1$ ($Z = 2$), Dx = 1.289 g/cm$^3$, $R$(F) = 0.067. Other than (thf)$_3$, diethyl ether × 1, water × 1, and toluene × 1 were incorporated in the crystal. For data collection and solution and refinement of the structure, see the supporting information.

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**Supporting Information Available:** Detailed results and discussion about the epoxide opening reaction with Ga-Li-carbon-linked-BINOL **20** complex, synthetic scheme for **21**, X-ray structural information for **36**, $^1$H NMR spectra of **22**, $^{13}$C NMR spectra of GaLB, **14**, **22**, **30**−**32**, **34**, **35** (PDF), and an X-ray crystallographic file (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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