This article was downloaded by: [University of New Hampshire]
On: 06 October 2014, At: 13:30
Publisher: Taylor & Francis
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK

Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Synthesis of Optically Pure Terminal Epoxide and 1,2-Diol via Hydrolytic Kinetic Resolution Catalyzed by New Heterometallic Salen Complexes

Santosh Singh Thakur [a] , Shu-Wei Chen [a] , Wenji Li [a] , Chang-Kyo Shin [a] , Yoon-Mo Koo [b] & Geon-Joong Kim [a]

[a] Department of Chemical Engineering , Inha University , Incheon, South Korea

[b] Department of Biological Engineering, ERC for Advanced Bioseparation Technology , Inha University , Incheon, South Korea

Published online: 22 Sep 2006.

To cite this article: Santosh Singh Thakur , Shu-Wei Chen , Wenji Li , Chang-Kyo Shin , Yoon-Mo Koo & Geon-Joong Kim (2006) Synthesis of Optically Pure Terminal Epoxide and 1,2-Diol via Hydrolytic Kinetic Resolution Catalyzed by New Heterometallic Salen Complexes, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 36:16, 2371-2383, DOI: 10.1080/00397910600640354

To link to this article: http://dx.doi.org/10.1080/00397910600640354

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the “Content”) contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at http://www.tandfonline.com/page/terms-and-conditions

Synthetic Communications®, 36: 2371–2383, 2006

ISSN 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910600640354

Synthesis of Optically Pure Terminal Epoxide and 1,2-Diol via Hydrolytic Kinetic Resolution Catalyzed by New Heterometallic Salen Complexes

Santosh Singh Thakur, Shu-Wei Chen, Wenji Li,
and Chang-Kyo Shin
Department of Chemical Engineering, Inha University, Incheon,
South Korea

Yoon-Mo Koo
Department of Biological Engineering, ERC for Advanced Bioseparation
Technology, Inha University, Incheon, South Korea

Geon-Joong Kim
Department of Chemical Engineering, Inha University, Incheon,
South Korea

Abstract: The inactive chiral (salen)Co complex is easily activated by $InCl_3$ and $TlCl_3$ Lewis acids by forming heterometallic salen complexes. These complexes show very high catalytic activity for the synthesis of enantiomerically enriched terminal epoxides (>99% ee) and 1,2-diols simultaneously via hydrolytic kinetic resolution. Strong synergistic effects of different Lewis acids, Co-In and Co-Tl, were exhibited in the catalytic process. The system described is very simple and efficient.

Keywords: Asymmetric catalysis, chiral catalyst, heterometallic complexes, hydrolytic kinetic resolution, terminal epoxides

Received in Japan January 13, 2006

Address correspondence to Geon-Joong Kim, Department of Chemical Engineering, Inha University, Incheon, South Korea. E-mail: kimgj@inha.ac.kr

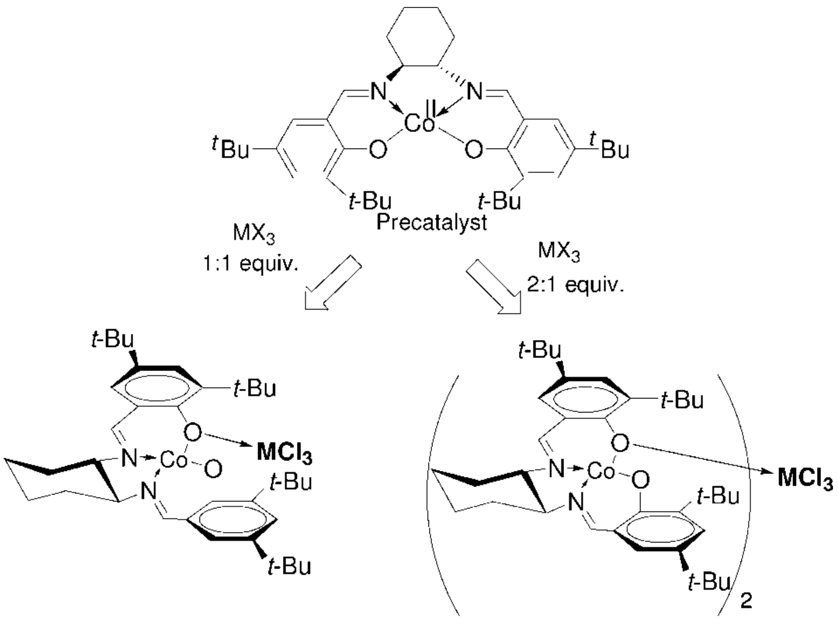
INTRODUCTION

Homo- and heterodinuclear complexes have enormous potential to revolutionize asymmetric catalysis. They can activate both partners of bimolecular reaction simultaneously, overcome entropy barriers associated with bringing the two reagents together, minimize the energy barrier that arises from solvent shell rearrangements during the reaction, and recognize prochiral faces or groups within the reagent through predetermination of the reaction trajectory.[1] Quite recently, several groups have made significant progress toward the design and use of chiral homo- and heterobimetallic complex for asymmetric catalysis.[2–7]

The high selectivity factors (k_{rel} values) across a wide range of terminal epoxides provide efficient enantioselective kinetic resolution of terminal epoxides with water (i.e., hydrolytic kinetic resolution, HKR).[8] In the asymmetric ring opening of epoxides catalyzed by chiral [(salen)Co] complexes,[9] the reaction involved two separate chiral salen–metal species in the rate-limiting step of the reaction, and subsequently, very efficient oligomeric catalysts were developed based on this principle.[10] However, complicated multistep synthesis of oligomeric catalysts[10] and solubility problems during HKR make it a less attractive strategy. With this approach, we thought an easily synthesized heterometallic chiral salen complex might provide a better catalyst, which would exhibit a faster rate of reaction and high enantioselectivity. As part of our ongoing research toward the design of di- and multinuclear chiral (salen)Co catalysts,[11] herein we report the catalytic activity of new, easily synthesized, heterometallic chiral (salen)Co-MCl_3 catalyst (Scheme 1) for the enantioselective hydrolytic kinetic resolution of terminal epoxides. Comparisons with their monomeric analogue have also been discussed.

RESULTS AND DISCUSSION

The formation of a heterometallic new complex can be viewed from a UV-vis spectrophotometer. The complexes show the new characteristic UV-vis absorption band at 370 nm, and a band at 420 nm, due to precatalyst (salen)Co, disappeared. Vibrational circular dichroism (VCD) spectroscopy has been applied to elucidate the stereochemistries of chiral molecules, including the accurate estimation of enantiomeric excess and their absolute configurations.[12] In the present study, VCD spectra were used to elucidate the stereochemistries of chiral **1a**–**2a** complexes. The shift in peak position of **1a** and **2a** shows the existence of two independent systems with the chiral (salen)Co precatalyst (Fig. 1). The FAB-mass spectra of **1a** and dinuclear **2a** provide direct evidence of formation of two distinct complexes. Compound **2a** showed molecular mass of more than 1418 and monomer complex **1a** of more than 780.



1a= In
1b= Tl

M= In, Tl

2a=In
2b=Tl

Scheme 1.

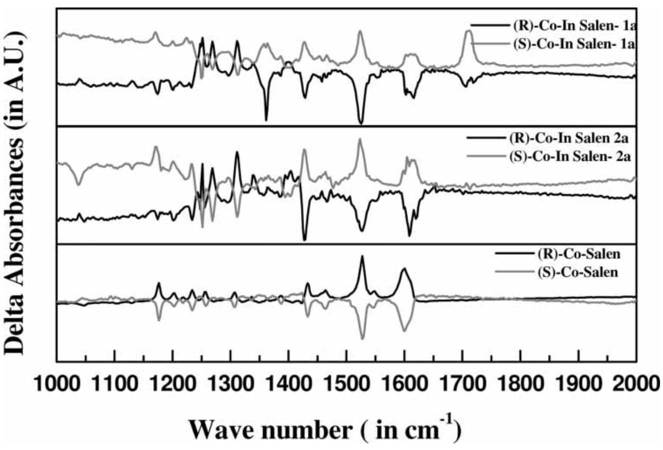


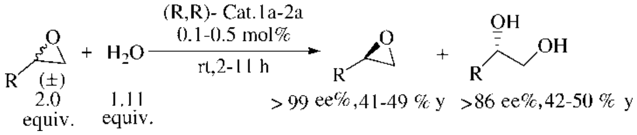
Figure 1. Monitoring of formation of **1a** and **2a** by vibration circular dichroism (VCD) spectra and comparison with Co(salen) complex.

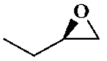
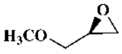
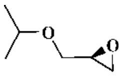
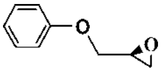
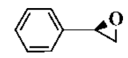
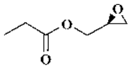
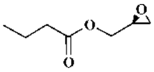
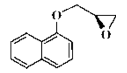
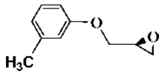
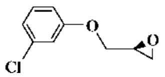
Many authors have been reported that oxygen atoms of the metal complexes of the Schiff bases are able to coordinate to the transition and group 13 elements to form bi- and trinuclear complex.[13] On these bases, possible structure of chiral (salen)Co-In/Co-Tl complexes is depicted in Scheme 1. The catalytic activities of the heterometallic catalysts **1a** and **2a** for of the representative diverse racemic terminal epoxides are shown in Table 1. The HKR of propylene and butylene oxide proved to be an efficient reaction, requiring only 0.1 mol% catalyst under solvent-free conditions (entries 1 and 2). Glycidol (entry 3) needs solvent THF to optimize the HKR. Epichlorohydrin (entry 4) is a readily available C-3 unit, which is widely employed in organic and polymer synthesis.[14] Glycidyl methyl ether, glycidyl isopropyl ether, glycidyl α-naphthyl ether (entries 5, 6, and 11), and glycidyl phenyl ether and their m-CH_3 and m-Cl derivatives (entries 7, 12, and 13) underwent resolution in excellent yield, employing 0.2 mol% of the catalyst. The kinetic resolutions of glycidyl propionate and glycidyl butyrate (entries 9 and 10) were effected in a straightforward manner. Styrene oxide (entry 8) and its derivatives are among the most useful terminal epoxides from a synthetic standpoint and are therefore particularly important candidates for the HKR reaction. Resolution of styrene oxide was possible using water-miscible solvents such as THF and 0.5 mol% of catalyst for a longer reaction time. The HKR of the styrene oxide might be plagued by conflicting steric and electronic factors influencing regioselectivity in the epoxide ring-opening reaction; consequently, a high catalyst loading amount and a longer reaction time required. The order of reactivity for the heterometallic complexes were found to be **2a** > **2b** > **1a** > **1b.** It is quite obvious from Figures 2 and 3 that the bimetallic complex **2a** or **2b** catalyst amount (0.05 mol%) is half of the monomeric complex **1a** or **1b** (0.1 mol%), but it shows twice the activity of their monomeric analogue. This fact clearly indicates that **2a** or **2b** is not a physical mixture of the monomeric Co-In/Co-Tl and precatalyst but that it possesses real dimeric nature.

The catalyst prepared from hydrated $MCl_3 \cdot nH_2O$ exhibited similar activity and enantioselectivity for the present study. In a control experiment, the heterometallic complexes, treated with excess of water and worked up, are found to have similar reactivity and selectivity (Scheme 2). This reveals that there is no dissociation of Co-In/Tl complex during HKR reaction. It appears that Cl^- ions are also coordinated to In/Tl metals during synthesis of **1a**–**2b** and consequently formed stable complexes. The UV-vis spectrum of the catalyst during the HKR reaction is also in favor of this fact (Fig. 4). Neither precatalyst (salen)Co nor In/$TlCl_3$ alone induce any HKR reaction. However, **2a** or **2b** could be generated readily in situ by suspension of the precatalyst in epoxide or epoxide/solvent and addition of monomer (salen)Co-MCl_3 complex.

Kinetic experiment of the HKR of epichlorohydrin (ECH) was carried out as a model reaction (Table 2). The two-term rate equation involving both intra- and intermolecular components [Eq. (1)] could be

Table 1. HKR of terminal epoxides catalyzed by the heterometallic catalyst



Entry	Recovered epoxides[a]	Catalyst/catalyst loading (mol%)[b]		Time (h)	% Yield (ee)[c]
1		**1a**	0.1	4	44 (99.3)
		2a	0.1	2	45 (99.5)
2		**1a**	0.1	7	45 (99.2)
		2a	0.1	3	48 (99.6)
3[d]		**1a**	0.1	11	42 (98.5)
		2a	0.1	6	44 (98.9)
4		**1a**	0.1	3	43 (99.8)
		2a	0.1	2	47 (99.9)
5		**1a**	0.2	4	45 (99.4)
		2a	0.2	2	49 (99.6)
6		**2a**	0.3	5	43 (99.5)
7		**2a**	0.2	3	42 (99.7)
8[d]		**2a**	0.5	5	41 (98.8)
9		**2a**	0.2	3	44 (99.6)
10		**2a**	0.2	3	45 (99.5)
11[e]		**2a**	0.2	5	42 (96.7)
12[e]		**2a**	0.2	2	43 (99.4)
13[e]		**2a**	0.2	2	45 (99.1)

[a] Isolated yield is based on racemic epoxides (theoretical maximum = 50%).
[b] Loading on a per [Co] basis with regard to racemic epoxides.
[c] ee percentage was determined by chiral GC or chiral HPLC.
[d] THF was used as a solvent.
[e] Solvents CH_2Cl_2:THF = 2:1.

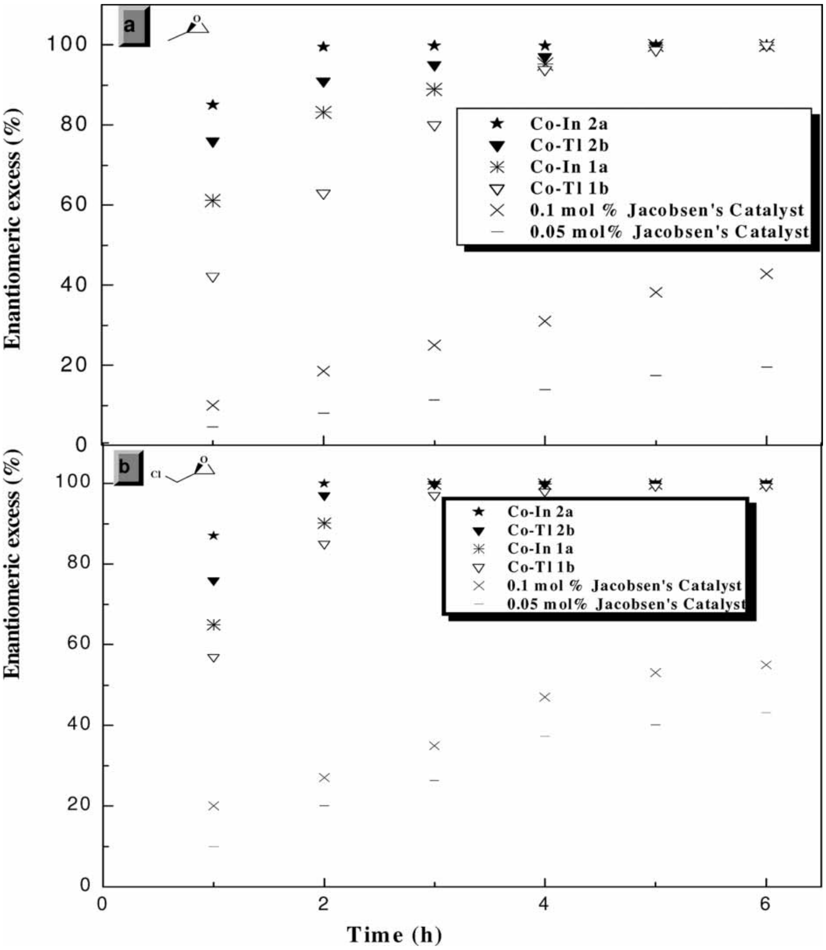


Figure 2. Comparison of catalytic activity of the heterometallic catalyst with Jacobsen's on the HKR of (a) epoxy propane and (b) epichlorohydrine. Catalyst loading amount is 0.1 mol% per [Co] unit for the heterometallic catalyst.

implemented.[11a,15] Analysis of such plots

$$\text{rate} \propto k_{\text{intra}}[\text{catalyst}] + k_{\text{inter}}[\text{catalyst}]^2 \qquad (1)$$

with rate data obtained with heterometallic catalysts **1a–2b** explicitly lead to the linear correlations with positive slopes and nonzero y-intercepts, consistent with participation of both inter- and intramolecular pathway for the HKR (Fig. 5). Similar analyses of rate data obtained with the reported Co-Al monomeric catalyst,[11a] Co-Ga monomeric catalyst,[11d] and Jacobsen's catalyst[8] revealed y-intercepts of zero, reflecting the absence of any

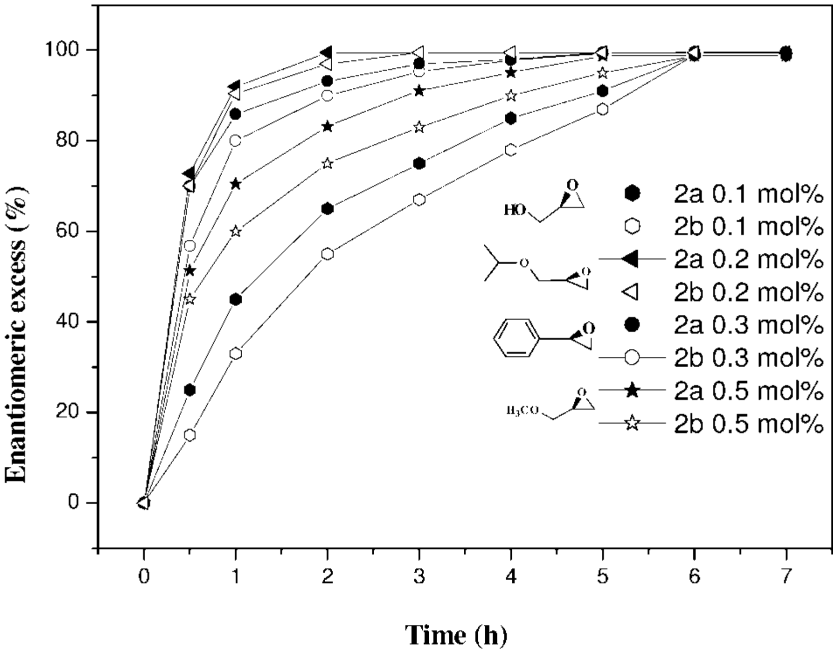


Figure 3. Catalytic activity of heterometallic complexes **2a** and **2b** for representative terminal epoxides using catalytic amount of 0.1–0.5 mol% (per Co unit) at ambient temperature.

first-order pathway for these complexes. With Co-In catalyst **2a**, a maximum value for intramolecular and intermolecular rate constants was obtained showing highest reactivity and enantioselectivity.

Lewis acids play a crucial role in the asymmetric catalysis.[1b,16] In our present finding Co-In **1a** and Co-Tl **1b** act as heterometallic complexes, exhibiting two different Lewis acid centers, Co and In[17a–c] and Co and Tl,[17d] which show a strong synergistic effect. The intramolecular pathway for the catalysts **1a** and **1b** could be explained on the basis of the proposed Scheme 3, which may be similar to the enantioselective ring opening of epoxides with 4-methoxyphenol catalyzed by Ga heterobimetallic reported by Iida et al.[2c] The central metal atom Co appears to activate and control the orientation of epoxide and stereoselectively bind only one enantiomer, and the latter seems to activate and control the orientation of

$$\text{Catalysts } \mathbf{1a\text{-}2b} \xrightarrow[\text{excess of } H_2O]{\text{treated with}} \begin{array}{c}\text{Work up}\\ \text{with } CH_2Cl_2\end{array} \xrightarrow{\hspace{3em}} \begin{array}{c}\text{Shows same reactivity}\\ \text{and selectivity}\end{array}$$

Scheme 2.

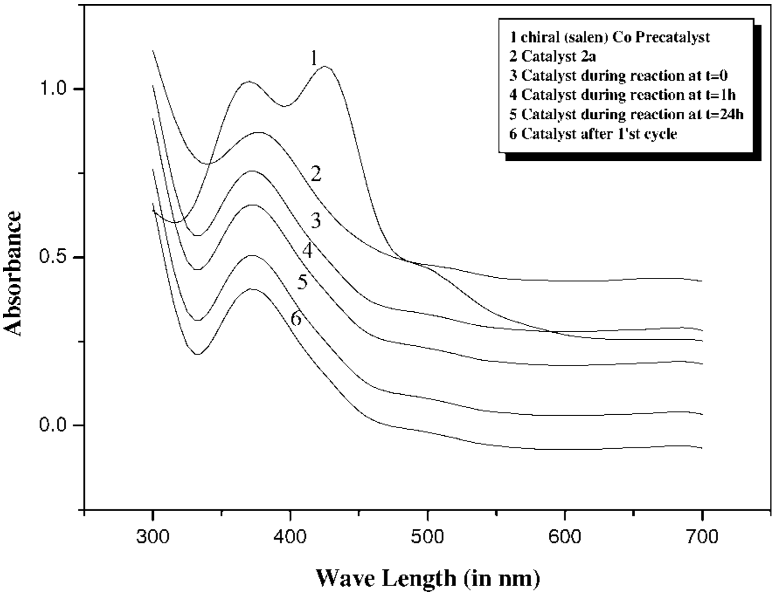


Figure 4. The UV-vis spectral analysis of the catalyst during and after the HKR of racemate methyl glycidyl ether.

nucleophlie H_2O by enabling an enantioselective ring opening of epoxides with nucleophiles. The intermolecular mechanism for **1a**–**2b** may follow the earlier report.[11a,15] Although the HKR reaction is easily carried out with Co(II) complexes, it appears that the reactive species is in fact Co(III).[18]

In summary, readily available chiral (salen)Co, the presence of multiple Lewis acid centers, and a low catalyst loading amount are some of the special features of the heterometallic salen catalyst used in the present investigation. The role of group 13 elements for the activation of the precatalyst, catalyst recyclability, scalability, heterogenization, and use of

Table 2. Kinetic data for the HKR of racemic ECH catalyzed by **1a**–**2b**

Catalyst	No. of (salen)Co unit	k_{intra} $(\text{min}^{-1}\times 10^{-2})^a$	k_{inter} $(\text{M}^{-1}\times\text{min}^{-1})^a$
Co-Al	1		1.0
1a	1	49.8	15.2
2a	2	66.0	22.0
1b	1	49.3	12.1
2b	2	61.3	21.0

[a] Calculated from Fig. 5. using Eq. 1.

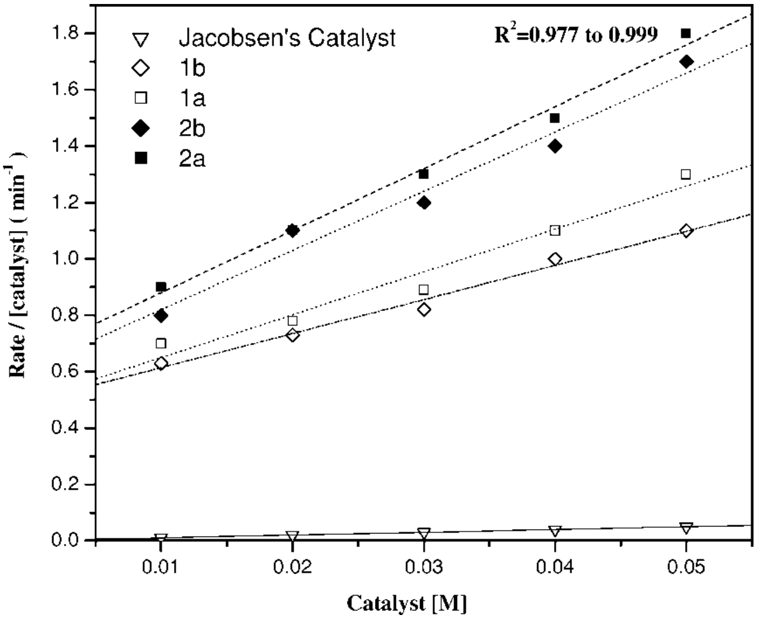
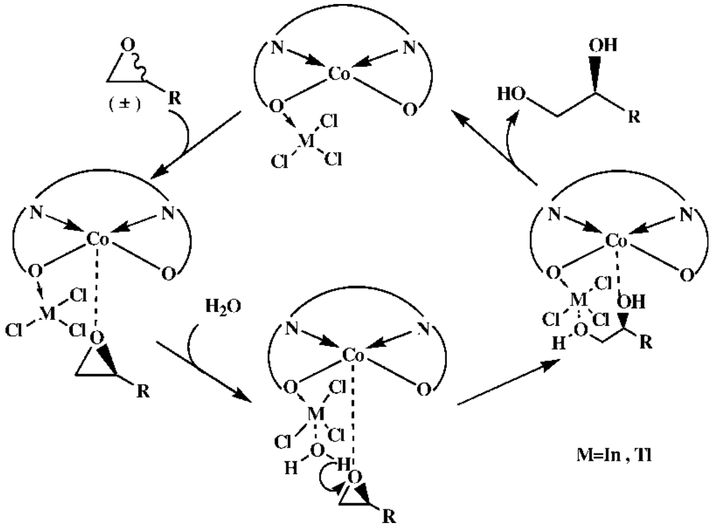


Figure 5. Initial rate kinetics for the asymmetric HKR of the ECH catalyzed by the **1a**–**2b** complexes.



Scheme 3. Possible working model for the HKR of terminal epoxides catalyzed by Co-In and Co-Tl heterometallic complexes.

the catalyst for other asymmetric catalytic reactions are focus of our ongoing studies.

EXPERIMENTAL

General

All ^{1}H NMR and ^{13}C NMR data were recorded using a 400-MHz FT NMR spectrophotometer (Varian Unity Nova 400) at ambient temperature. Optical rotation measurements were conducted using a Jasco DIP 370 digital polarimeter. Gas chromatography analyses were performed on Hewlett-Packard 5890 series II instruments equipped with FID detectors using chiral column (Chiraldex G-TA and A-TA, 20-m × 0.25-mm id, Astec) and HP 3396 integrators with HP Chem Station software for data analysis. Chiral HPLC analyses were performed on Younglin instrument using a Chiralcel® OD column (24-cm × 0.46-cm i d; Chiral Technologies, Inc.) and Regis (S,S)Whelk-O1 at 254 nm. UV spectra were recorded on UV-vis spectrophotometer (Optizen 2120 UV) interfaced with a PC using Optizen View 3.1 software for data analysis. VCD was measured in ChiralirTM (ABB Bomem Inc.) with a pathlength of 94 μ set at 8-cm^{-1} resolution and a spectral collection time of 1 h using Bomem GRAMS-32 software. All reagents were purchased from Aldrich, Fluka, and TCI. ($\pm$)-(α-Naphthyl) glycidyl ether was prepared by a known method[19] and confirmed by ^{1}H NMR,^{13}C NMR, and elemental analysis. The general method for the HKR and kinetic analysis are the same as cited literature.[8,11a]

Synthesis of the Heterometallic Complexes 1 and 2

(R,R)-SalenCo (5.0 g, 8.28 mmol, 1.0 equiv.) was added to a solution of hydrated Indium chloride (2.428 g, 8.28 mmol, 1.0 equiv.) in tetrahydrofuran (30 mL), and the mixture was stirred for 1 h in an open atmosphere at room temperature. As soon as the chiral (salen)Co was added, the color of the solution changed from brick red to dark olive green. The resulting solution was concentrated under reduced pressure. The crude solid was worked up with H_2O and CH_2Cl_2. Yield was 98–99% as a dark green solid powder. UV-vis shows strong absorbance at 370 nm. The characteristic absorption band of precatalyst (salen)Co(II) at 420 nm disappeared. For complex **1a**, FAB-mass was calculated (779.83) and observed (780.6). Complex **2a** was prepared by stirring 2:1 equiv. of the precatalyst (salen)Co(II) and hydrated Indium chloride respectively in THF solvent for 1 h. FAB-mass was calculated (1418) and observed (1419). A similar procedure has been adopted for the synthesis of **1b** and **2b**.

REFERENCES

1. (a) Ojima, I, *Catalytic Asymmetric Synthesis*, 2nd Ed.; Ojima, I., Eds.; Wiley: New York, 2000; (b) Jacobsen, E. N.; Pfaltz; Yamamoto, A. H., Eds. *Comprehensive Asymmetric Catalysis*; Springer: Heidelberg, 1999.
2. (a) Shibasaki, M.; Kanai, M.; Funabashi, K. Recent progress in asymmetric two-center catalysis. *Chem. Commun.* **2002**, 1989–1999; (b) Shibasaki, M.; Yoshikawa, N. Lanthanide complexes in multifunctional asymmetric catalysis. *Chem. Rev.* **2002**, *102*, 2187–2210; (c) Iida, T.; Yamamoto, N.; Matsunaga, S.; Woo, H.-G.; Shibasaki, M. Enantioselective ring opening of epoxides with 4-methoxyphenol catalyzed by gallium heterobimetallic complexes: An efficient method for the synthesis of optically active 1,2-diol monoethers. *Angew. Chem. Int. Ed.* **1998**, *37*, 2223–2225; (d) Matsunaga, S.; Yoshida, T.; Morimoto, H.; Kumagai, N.; Shibasaki, M. Direct catalytic asymmetric Mannich-type reaction of hydroxyketone using a Et_2Zn/linked-BINOL complex: Synthesis of either anti- or syn-amino alcohols. *J. Am. Chem. Soc.* **2004**, *126*, 8777–8785.
3. (a) Trost, B. M.; Yeh, V. S. C. A dinuclear Zn catalyst for the asymmetric nitroaldol (Henry) reaction. *Angew. Chem. Int. Ed.* **2002**, *41*, 861–863; (b) Trost, B. M.; Mino, T. Desymmetrization of meso 1,3- and 1,4-diols with a dinuclear zinc asymmetric catalyst. *J. Am. Chem. Soc.* **2003**, *125*, 2410–2411; (c) Trost, B. M.; Terrell, M. L. R. A direct catalytic asymmetric Mannich-type reaction to syn-amino alcohols. *J. Am. Chem. Soc.* **2003**, *125*, 338–339.
4. Belokon, Y. N.; North, M.; Maleev, V. I.; Voskoboev, N. V.; Moskalenko, M. A.; Peregudov, A. S.; Dmitriev, A. V.; Ikonnikov, N. S.; Kagan, H. B. Homogeneous catalysis: In situ formation of a heterobimetallic chiral [(salen)TiI^V]/[(salen)V^V] catalyst for the asymmetric addition of TMSCN to benzaldehyde. *Angew. Chem. Int. Ed.* **2004**, *43*, 4085–4089.
5. Kobayashi, S.; Arai, K.; Shimizu, H.; Ihori, Y.; Ishitani, H.; Yamashita, Y. A novel dinuclear chiral niobium complex for Lewis acid catalyzed enantioselective reactions: Design of a tridentate ligand and elucidation of the catalyst structure. *Angew. Chem. Int. Ed.* **2005**, *44*, 761–764.
6. Yang, M.; Zhu, C.; Yuan, F.; Huang, Y.; Pan, Y. Enantioselective ring-opening reaction of meso-epoxides with ArSeH catalyzed by heterometallic Ti-Ga-Salen system. *Org. Lett.* **2005**, *7*, 1927–1930.
7. Gandelman, M. K.; Jacobsen, E. N. Highly enantioselective catalytic conjugate addition of N-heterocycles to a,b-unsaturated ketones and imides. *Angew. Chem. Int. Ed.* **2005**, *44*, 2393–2397.
8. Tokunaga, M.; Larrow, J. F.; Kakiuchi, F.; Jacobsen, E. N. Asymmetric catalysis with water: Efficient kinetic resolution of terminal epoxides by means of catalytic hydrolysis. *Science* **1997**, *277*, 936–938.
9. Furrow, M. E.; Schaus, S. E.; Jacobsen, E. N. Practical access to highly enantioenriched C-3 building blocks via hydrolytic kinetic resolution. *J. Org. Chem.* **1998**, *63*, 6776–6777.
10. (a) Ready, J. M.; Jacobsen, E. N. A practical oligomeric [(salen)Co] catalyst for asymmetric epoxide ring-opening reactions. *Angew. Chem. Int. Ed.* **2002**, *41*, 1374–1377; (b) White, D. E.; Jacobsen, E. N. New oligomeric catalyst for the hydrolytic kinetic resolution of terminal epoxides under solvent-free conditions. *Tetrahedron: Asymmetry* **2003**, *14*, 3633–3638.
11. (a) Thakur, S. S.; Li, W.; Kim, S. J.; Kim, G.-J. Highly reactive and enantioselective kinetic resolution of terminal epoxides with H_2O and HCl catalyzed by

new chiral (salen)Co complex linked with Al. *Tetrahedron Lett.* **2005**, *46*, 2263–2266; (b) Shin, C. K.; Kim, S. J.; Kim, G.-J. New chiral cobalt salen complexes containing Lewis acid BF$_3$: A highly reactive and enantioselective catalyst for the hydrolytic kinetic resolution of epoxides. *Tetrahedron Lett.* **2004**, *45*, 7429–7433; (c) Kim, G.-J.; Lee, H.; Kim, S.-J. Catalytic activity and recyclability of new enantioselective chiral Co–salen complexes in the hydrolytic kinetic resolution of epichlorohydrine. *Tetrahedron Lett.* **2003**, *44*, 5005–5008; (d) Thakur, S. S.; Li, W.; Shin, C. K.; Kim, G.-J. Enantioselective hydrolytic kinetic resolution of 1,2-epoxy-3-phenoxy propane derivatives by new chiral (salen) cobalt complexes. *Catal. Lett.* **2005**, *104*, 151–156; (e) Kwon, M.; Kim, G.-J. Synthesis of polymeric salen complexes and application in the enantioselective hydrolytic kinetic resolution of epoxides as catalysts. *Catal. Today* **2003**, *87*, 145–151.

12. (a) Spencer, K. M.; Cianciosi, S. J.; Baldwin, J. E.; Freedman, T. B.; Nafie, L. A. *Appl. Spectros.* **1990**, *44*, 235; (b) Freedman, T. B.; Cao, X.; Dukor, R. K.; Nafie, L. A. Absolute configuration determination of chiral molecules in the solution state using vibrational circular dichroism. *Chirality* **2003**, *15*, 743.
13. (a) Atwood, D.; Harvey, M. J. Group 13 compounds incorporating salen ligands. *Chem. Rev.* **2001**, *101*, 37–52, and references cited therein; (b) Atwood, D.; Wei, P. An unusual imine (NC) alkylalumination reaction. *Chem. Commun.* **1997**, 1427–1428; (c) Solari, E.; Corazza, F.; Floriani, C.; Chiesi-Villa, A.; Guastini, C. Polydentate ligand exchange via formation of a dimetallic complex: Crystal structures of [(thf)Fe(acen)MCl$_2$](M = Fe or Zn), [ClFe(salphen)FeCl(thf)$_2$], [Ti(acen)(thf)$_2$][CoCl$_3$(thf)], and [Ti(acen)(thf)$_2$]$_2$ [Fe$_3$Cl$_8$(thf)$_2$][acenN,N-ethylenebis(acetylacetoneiminate),salphen = N,N-O-phenylenebis(salicylideneiminate), and thf = tetrahydrofuran]. *J. Chem. Soc., Dalton Trans.* **1990**, 1345–1355; (d) Gruber, S. J.; Harris, C. M.; Sinn, E. Metal complexes as chelates, II: Binuclear complexes containing similar and dissimilar metal atoms. *Inorg. Chem.* **1968**, *2*, 268–273; (e) Holm, R. H.; Everett, W.; Chakravorty, A. *Prog. Inorg. Chem.* **1966**, *7*, 83–214; (f) Aoi, H.; Ishimori, M.; Tsuruta, T. A study of the kinetic resolution of DL-propylene oxide with optically active Co(I) (salen) type complexes. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 1897–1901.
14. Huber, J. E. *Encyclopedia of Reagents for Organic Synthesis*; Paquuette, L. A., Ed.; Wiley: New York, 1995; Vol. 4, p. 2326.
15. (a) Konsler, R. G.; Karl, J.; Jacobsen, E. N. Cooperative asymmetric catalysis with dimeric salen complexes. *J. Am. Chem. Soc.* **1998**, *120*, 10780–10781; (b) Breinbauer, R.; Jacobsen, E. N. Cooperative asymmetric catalysis with dendrimeric [Co(salen)] complexes. *Angew. Chem. Int. Ed.* **2000**, *39*, 3604–3607.
16. Yamamoto, H., *Lewis Acids in Organic Synthesis*, Ed.; Wiley: New York, 2000; Vol. 1 and 2.
17. For examples using InCl$_3$ and TlCl$_3$ as Lewis acid see, (a) Kobayashi, S.; Busujima, T.; Nagayama, S. A novel classification of Lewis acids on the basis of activity and selectivity. *Chem.—Eur. J.* **2000**, *6*, 3491–3494; (b) Ranu, B. C. Indium metal and its halides in organic synthesis. *Eur. J. Org. Chem.* **2000**, 2347–2356; (c) Sengupta, S.; Mondal, S. InCl$_3$: A new Lewis acid catalyst for reactions with α-diazocarbonyl compounds. *Tetrahedron Lett.* **1999**, *40*, 8685–8688; (d) Uemura, S.; Sohma, K.; Okano, M. Thallium(III) chloride tetrahydrate as a Lewis acid catalyst for aromatic alkylation and acylation. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 860–863.

18. Nielson, L. P. C.; Stevenson, C. P.; Backmond, D. G.; Jacobsen, E. N. Mechanistic investigation leads to a synthetic improvement in the hydrolytic kinetic resolution of terminal epoxides. *J. Am. Chem. Soc.* **2004**, *126*, 1360–1362.
19. Nicholas, B.; ElKoussi, A.; Kano, M.; Nakamura, T. Improved delivery through biological membranes, 26: Design, synthesis, and pharmacological activity of a novel chemical delivery system for adrenergic blocking agents. *J. Med. Chem.* **1988**, *31*, 100–106.