

Synthesis of Chiral Intermediates Catalyzed by New Chiral Polymeric (Salen) Cobalt Complexes Bearing Lewis Acidic Metal Halides

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The new type of heterometallic chiral polymer salen complexes have been synthesized and it has been found that group 13 metal salts (AlCl_3 , GaCl_3 and InCl_3) combined to cobalt salen unit played the crucial role in the asymmetric kinetic resolution of racemic epoxides. Polymeric salen catalysts showed very high reactivity and enantioselectivity for the asymmetric ring opening of terminal epoxide with diverse nucleophiles. They provide the enantiopure useful chiral intermediates such as chiral terminal epoxides and α -aryloxy alcohols in one-step process. An efficient methodology for providing very high enantioselectivity can be achieved in the synthesis of valuable chiral building blocks *via* our catalytic system by combination of various asymmetric ring opening reactions.

Key Words : Chiral polymeric salen, Chiral intermediates, Terminal epoxides, Kinetic resolution

Introduction

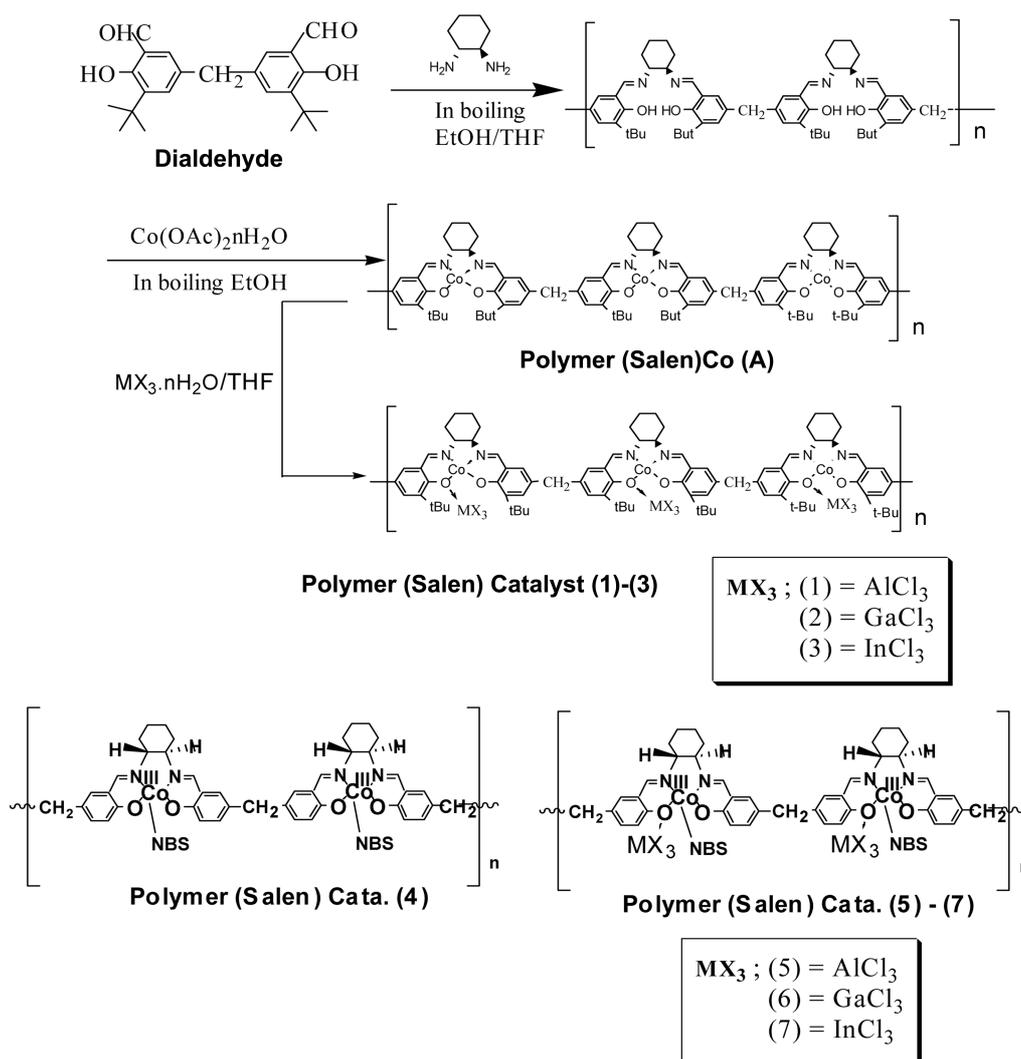
Terminal epoxides are the most important subclass for organic synthesis.¹ As a consequence, the preparation of optically pure terminal epoxides has long stood as a most significant target for asymmetric, chiral building-block synthesis.² Hydrolytic Kinetic Resolution (HKR) provides very efficient, scalable and practical manner to prepare stereochemically enriched terminal epoxides.^{3,4} Remarkable progress had been made in the use of chiral catalysts to synthesize valuable enantioenriched intermediates of the academic and pharmaceutical interests.⁵⁻⁷ Pursuant to our own efforts directed toward the designing of the catalyst system for the HKR, we have synthesized the new chiral Co (salen) GaCl_3 catalysts showing very high enantioselectivity for the HKR of terminal epoxides.⁸⁻¹⁰ In the asymmetric ring opening of epoxides catalyzed by chiral (salen) Co complexes,¹¹ the reaction involved two separate chiral salen-metal species in the rate limiting step of the reaction and subsequently, very efficient oligomeric,¹² dendrimeric,¹³ polymeric¹⁰ and supported^{14,15} type catalysts have been developed based on this principle. The oligomeric (salen) Co catalyst exhibited very high reactivity and enantioselectivity for the terminal epoxides ring opening with phenols *via* a kinetic resolution process, however multi-step synthesis was required for such oligomeric cobalt-salen catalysts.^{16,17}

As a part of our ongoing research on the development of highly active catalysts for asymmetric transformation, our group has reported the highly efficient polymeric (salen) Co bearing Lewis acid such as BF_3 for the enantioselective ring opening of terminal epoxides with H_2O .⁹ Herein we report the catalytic activity of new polymeric chiral (salen)-Co- MX_3 catalyst for the enantioselective kinetic resolution of terminal epoxides by nucleophile H_2O and phenol derivatives. The polymeric salen complexes modified with 13 group salts in the structure has never been used as a catalyst in the ring opening of terminal epoxides to obtain

the variety of chiral intermediates, particularly in the reaction using phenol derivatives as a nucleophile. The polymeric catalysts showed remarkably enhanced reactivity and may be employed in substantially lower loadings to obtain the enantio-enriched products without suffering solubility problem as well as their deactivation.

Experimental

Preparation of catalysts. The desired polymeric (salen)Co complexes were synthesized according to reported procedure.¹⁰ The polymeric salen ligand could be synthesized by the reaction between dimeric dialdehyde and chiral diaminocyclohexane in boiling ethanol as shown in Scheme 1. The dimeric dialdehyde was obtained in 50% yield by treating 3-tert-butyl-2-hydroxybenzaldehyde with trioxane and sulfuric acid in acetic acid solution as synthesized by Janssen *et al.*¹⁸ The molecular weight of obtained polymer (salen)sample was about 10,000.¹⁰ For the typical synthesis of polymer salen catalyst (**2**), to a solution of hydrated gallium chloride $\text{GaCl}_3 \cdot n\text{H}_2\text{O}$ (8.28 mmol, 1.0 equiv.) in tetrahydrofuran (THF, 25 mL), polymer (salen) Co(**A**) (8.28 mmol, 1.0 equiv.; calculation based on per Co unit) was added and stirred in open atmosphere at room temperature. As soon as the chiral (salen)Co was added the color of solution changes from brick red to dark olive green. The solution was stirred at room temperature for 1 h. The resulting powder sample was collected after subsequent washing with THF and CH_2Cl_2 (MC) concentrated under reduced pressure. The crude solid was worked up with H_2O and MC (Yield = 98-99% as a dark green solid powder). In addition, anhydrous gallium (III) chloride (8.28 mmol, 1.0 equiv.) could be treated in a similar manner, as mentioned above. In the case of anhydrous salt source, methylene chloride (MC) was used as a solvent in place of THF. The samples were dried to powder after washing with CH_2Cl_2 , THF and MeOH. In addition, to obtain the polymer salen



Scheme 1. The structure of polymer salen catalyst used in PKR and HKR of racemic epoxides.

catalyst (5)-(7), polymer (salen)Co (A) or polymer salen catalyst (1)-(3) was treated by 4-nitrobenzene sulfonic acid (NBS; 1.2 equivalent based on Co unit) under air atmosphere in THF for 2 hrs, respectively.

Materials and analysis. All reagents and solvents were purchased from Aldrich or TCI Inc., and they were used without further purification. ^1H NMR and ^{13}C NMR were recorded using 400 MHz FT-NMR spectrometer (VARIAN UNITYINOVA400) at ambient temperature. Optical rotation measurements were conducted using a JASCO DIP 370 digital polarimeter. Vibrational Circular Dichroism (VCD) spectra were measured in Chiral-irTM (ABB Bomem Inc.) using Bomem GRAMS-32 software. The IR spectra were determined with a PERKIN-ELMER Spectrum 2000 Explorer. Gas chromatographic analyses were performed on Hewlett-Packard 5890 Series II instrument equipped with a FID detector using a chiral column (CHIRALDEX G-TA and A-TA, 20 m \times 0.25 mm id (Astec) and a HP 3396 integrator with HP Chem Station software for data analysis. HPLC analyses were performed on a YOUNGLIN instrument using a Chiralcel[®] OD Chiral column (24 cm \times 0.46

cm i.d.; Chiral Technologies, Inc.) and Regis (*S,S*) Whelk-O1 at 254 nm.

General procedure for kinetic resolution reaction by nucleophiles. In a representative reaction of epichlorohydrin (ECH) with phenol (or water), the polymeric catalyst (0.05 mmol, 0.5 mol %), (\pm)-ECH (0.93 g, 10 mmol) and solvent such as *tert*-butyl methyl ether (TBME) (or THF) were charged in an oven dried 25 mL flask, and the reaction mixture was stirred in at open atmosphere at ambient temperature. After addition of phenol (4.5 mmol, 0.45 equiv.) or water (5.5 mmol, 0.55 equiv.), the resultant solution was stirred for 15 hrs and monitored by chiral GC and HPLC. The products were identified/characterized by IR, ^1H NMR, ^{13}C NMR.

Results and Discussion

Asymmetric ring opening of racemic epoxides with phenol derivatives. The results obtained in the asymmetric ring opening of terminal epoxides with phenol derivatives catalyzed by polymer (salen) Co-(Al, Ga, In)Cl₃ are sum-

Table 1. Asymmetric ring opening of terminal epoxides with phenol derivatives catalyzed by heterometallic polymer (salen) complexes

Entry	R ¹	R ²	Catalyst	Yield (%) ^b	Ee (%) ^c
1	H	CH ₂ Cl	1	38	88
2	H	CH ₂ Cl	2	39	86
3	H	CH ₂ Cl	3	42	90
4	H	CH ₂ Cl	4	39	92
5	H	CH ₂ Cl	5	42	96
6	H	CH ₂ Cl	6	41	94
7	H	CH ₂ Cl	7	43	97
8	H	CH ₃	7	41	95
9	H	C ₂ H ₅	7	39	93
10	H	CH ₃ -O-CH ₂	7	41	94
11	3-Cl	CH ₂ Cl	4	38	89
12	3-Cl	CH ₂ Cl	5	40	93
13	3-Cl	CH ₂ Cl	6	38	91
14	3-Cl	CH ₂ Cl	7	43	95
15	3-Cl	CH ₃	7	42	95
16	3-Cl	C ₆ H ₅ -O-CH ₂	7	38	96
17	3-Cl	CH ₃ -O-CH ₂	7	40	95
18	3-CH ₃	CH ₂ Cl	1	36	86
19	3-CH ₃	CH ₂ Cl	5	39	91
20	3-CH ₃	CH ₂ Cl	6	37	89
21	3-CH ₃	CH ₂ Cl	7	41	96
22	3-CH ₃	C ₂ H ₅	5	43	92
23	3-CH ₃	CH ₃ -O-CH ₂	5	40	90

^aCatalyst loading on a per Co basis relative to racemic epoxide. ^bIsolated yield. ^cee % was determined by chiral HPLC or chiral GC. Products were characterized by ¹H and ¹³C NMR and found to be similar to that reported.¹¹⁻¹⁴

marized in Table 1. Both the electron-poor or rich phenols reacted with ECH enantioselectively to provide the corresponding α -aryloxy alcohols in good yield and high ee%. As can be seen from Table 1, a series of terminal epoxides reacted with a various phenol derivatives to offer corresponding optically enriched alcohols (upto 97ee%). These reactions occurred in a good yield when low loading (0.5-1.0 mol%) of catalyst was employed. The catalyst (5) and (7) (entry 5, 7, 16, 21) exhibited superior ee's (93-99ee%) to the catalyst (1) and (2). The identity of the counter anion and the oxidation state of cobalt for this new chiral salen complex proved to be an important in this work, displaying the superior activity with the NBS anion.

In Table 1, it is evident that the polymeric salen catalyst (7) exhibits the highest activity and selectivity among others. The order of reactivity of catalysts was observed as follows; (7) > (5) \approx (6) > (4) > (3) > (1). 3-Chlorophenol (3-CP) acts as an excellent nucleophile for the kinetic resolutions of ECH, phenyl glycidyl ether (PGE), propylene oxide (PO) and butylene glycidyl methyl ether (entry 14-17). Overall,

Table 2. Effect of solvent on the kinetic resolution of epichlorohydrin with phenol

Entry	Solvent	Catalyst type	Yield (%) ^b	Ee (%) ^c
1	TBME	4	38	93
2	TBME	7	41	98
3	CH ₃ CN	4	35	80
4	CH ₃ CN	7	37	88
5	CH ₂ Cl ₂	7	35	81
6	1, 4-Dioxane	7	38	85
7	THF	7	40	86
8	<i>n</i> -Hexane	4	37	72
9	<i>n</i> -Hexane	7	39	79

^a0.5 mol% Catalyst loading on a per Co basis relative to racemic epoxide. ^bIsolated yield. ^cee % was determined by chiral HPLC or chiral GC. Reaction time; 12 h.

Table 3. Asymmetric ring opening of ECH with phenol derivatives catalyzed by polymer salen complexes catalysts

Entry	R ¹	R ²	Catalyst ^a	Yield (%) ^b	ee (%)
1	3-CH ₃	CH ₂ Cl	4 (cycle 1)	38	91
2 ^a	3-CH ₃	CH ₂ Cl	4 (cycle 2)	37	83
3 ^b	3-CH ₃	CH ₂ Cl	4 (cycle 3)	39	90
4	3-CH ₃	CH ₂ Cl	7 (cycle 1)	40	97
5 ^b	3-CH ₃	CH ₂ Cl	7 (cycle 2)	38	96
6	H	CH ₂ Cl	7 (cycle 1)	41	98
7 ^a	H	CH ₂ Cl	7 (cycle 2)	39	92
8 ^b	H	CH ₂ Cl	7 (cycle 3)	39	97

The catalyst structure is shown in Scheme 1. ^aThe catalyst is used without regeneration. ^bCatalyst is regenerated by 4-NBS

phenols with wide range of electronic properties participated in the ring opening reaction with good yield and ee's.

It was found that the solvent plays crucial role in this reaction. In the typical example during the reaction of ECH with 3-methyl phenol, the effect of polar and nonpolar solvents was examined, and a non-polar solvent such as TBME was found to be the most effective as indicated in Table 2. The heterometallic complex of polymeric chiral (salen) Co-AlCl₃ showed more active than that of chiral (salen) Co-GaCl₃ possibly due to the higher Lewis acidity.

It has been investigated that there was no leaching of the monomer units from the polymer backbone during the kinetic resolution after subsequent washing with solvent. The liquid mixture containing the product was transparent

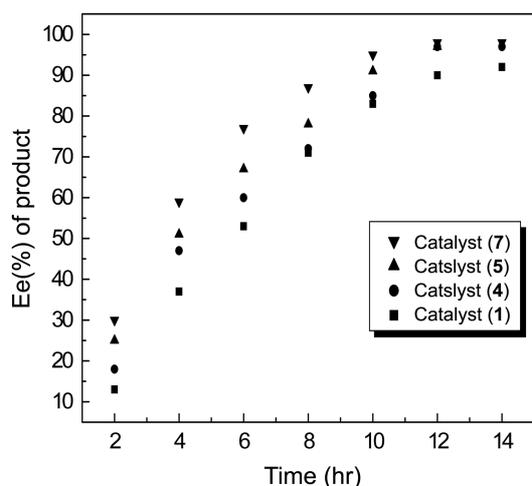


Figure 1. The catalytic activity of Polymer (salen) Co-MX₃ catalysts for the asymmetric ECH ring opening with phenol using 0.7 mol % catalyst at room temperature.

during the reaction and it could be easily separated by filtration. The greatly increased activities and recyclability of catalysts were investigated on the polymer salen catalyst and the obtained results are summarized in Table 3.

To investigate the effect of catalyst structure on the reactivity, PKR of (\pm) ECH with phenol was performed in the presence of catalysts (1)-(7), and the level of reactivity is shown in Figure 1. All catalysts have afforded 1-chloro-3-phenoxy-2-propanol in highly enantioenriched form with in 16hs. The catalysts (5) and (7) led to more than 98% enantioselectivity at 12 hs. As Co^{II} salen was oxidized to Co^{III} by treatment of NBS in air, it became more active and enantioselective as compared to that having no NBS anion. Camphorsulfonic acid or *p*-toluenesulfonic acid treated chiral salen catalyst was less enantioselective in this reaction. However, the polymer catalyst (1) containing no NBS anion also showed a high reactivity in PKR of racemic epoxides as compared to catalyst (5) as can be seen in Figure 1, and then almost similar high enantioselectivity was provided with a prolonged reaction time.

The ring opening of racemic ECH with 3-chloro phenol(3-CP) is monitored by IR spectroscopy and the result is shown in Figure 2. The disappearance of reactant 3-CP can be identified by the observation of decrease in phenolic OH peak (3200 to 3500 cm⁻¹), and the appearance of new aliphatic OH peak (2800 to 3000 cm⁻¹) was found with the prolonged reaction time. In the band range of 1000-1600 cm⁻¹, appearance of new peaks was also found through the formation of (*S*)-[*m*-chloro phenoxy]-3-chloropropan-2-ol product For this analysis, the product was collected by extraction with *n*-hexane from the system. The liquid type reactant and product could be easily recovered by *n*-hexane extraction from the salen catalyst.

Kinetic resolution of racemic epoxides by nucleophile water. The catalytic activities of polymeric catalysts for HKR of representative racemic terminal epoxides are examined and the results are summarized in Table 4. The

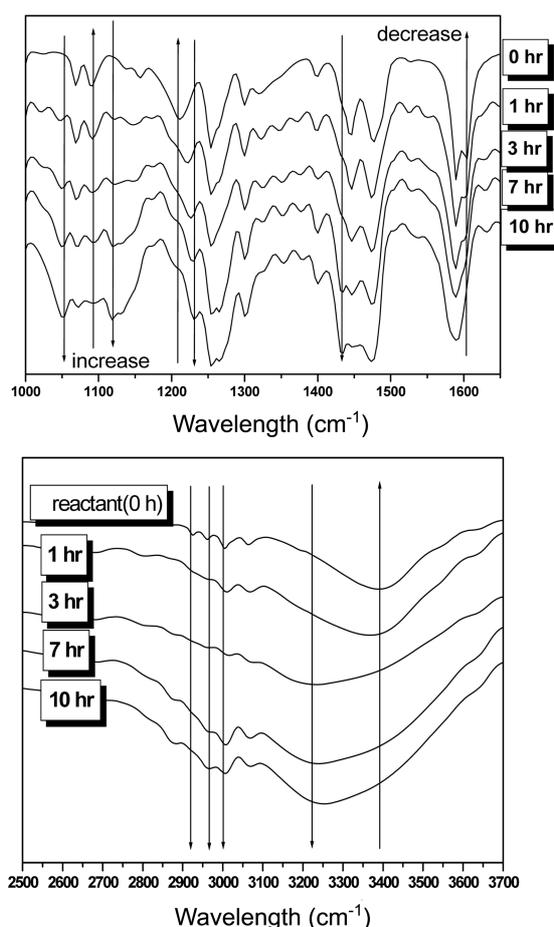
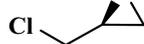
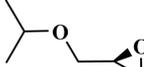
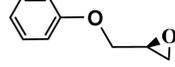
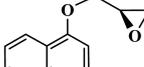
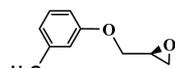
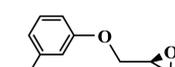
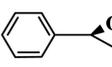
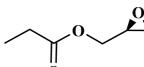
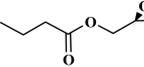


Figure 2. IR Spectra change during the ring opening reaction of ECH with 3-chlorophenol.

HKR of PO and butylene oxide proved to be efficient, requiring less than 0.5 mol % catalyst under solvent free conditions. The aromatic epoxides and their derivatives are very useful ones from a synthetic standpoint, and are therefore particularly important candidate for the HKR reaction. Resolution of styrene oxide (entry 18, 19) was efficient in the presence of water-miscible solvent such as THF and 0.4 mol % of catalyst. The HKR of styrene oxide might be plagued by conflicting steric and electronic factors influencing regioselectivity in the epoxide ring opening reaction. Under a similar catalyst-loading based on the [Co] unit, the polymeric catalyst (1) gives lower activity and selectivity than catalysts (2) and (3). ECH (entry 8-11) is a readily available C-3 unit that is widely employed in organic and polymer synthesis. Its optically pure form is the most important chiral building block in the synthesis of useful pharmaceutical intermediates. Glycidyl isopropyl ether, glycidyl α -naphthyl ether (entry 12, 13 and 18, 19 respectively), and PGE and its *m*-CH₃ and *m*-Cl derivatives (entry 14-17, 20 and 21), underwent resolution in excellent yield employing 0.6 mol % of catalysts. The kinetic resolutions of glycidyl propionate and glycidyl butyrate (entry 24 and 25) were also efficient in a straightforward manner. Especially, the oxidation of chiral salen complexes from Co^{II} to Co^{III}

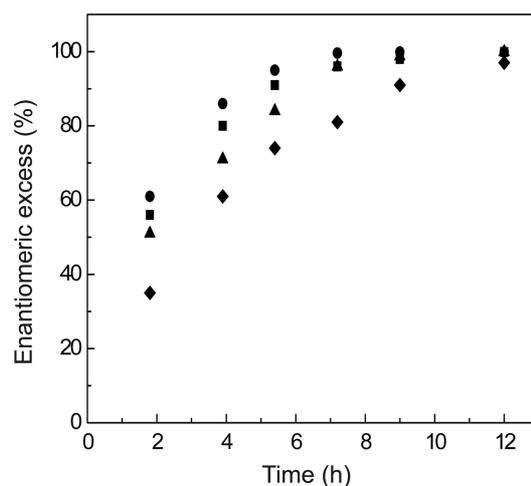
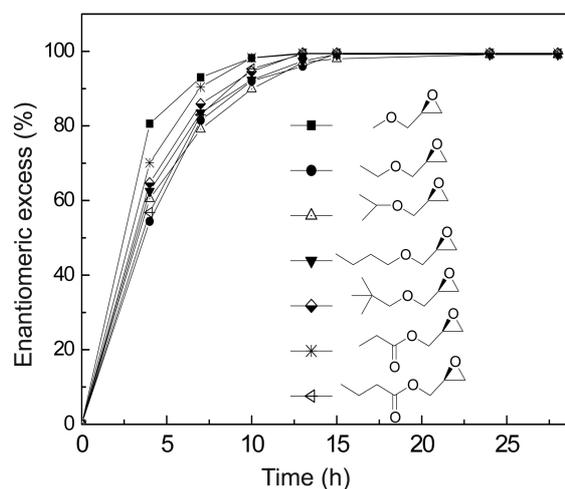
Table 4. HKR of terminal epoxides catalyzed by the various polymeric salen catalysts

Entry	Recovered Epoxides ^a	Catalyst/Catalyst Loading (mol%) ^b	% Yield (ee) ^c
1		1 0.6	33 (95)
2		2 0.6	35 (97)
3		3 0.6	36 (99)
4		4 0.6	35 (97)
5		5 0.6	34 (98)
6		6 0.6	37 (98)
7		7 0.6	35 (99)
8		3 0.6	37 (>99)
9		4 0.6	37 (>98)
10		5 0.5	38 (>99)
11		7 0.5	36 (>99)
12		4 0.6	39 (99)
13		7 0.5	38 (99)
14		1 0.6	39 (95)
15		3 0.6	40 (98)
16		5 0.6	38 (>98)
17		7 0.6	36 (>98)
18 ^d		3 0.6	37 (97)
19 ^d		7 0.6	35 (96)
20 ^d		7 0.5	36 (98)
21 ^d		7 0.6	35 (99)
22 ^c		4 0.9	35 (97)
23 ^c		7 0.8	36 (97)
24		7 0.6	37 (>98)
25		7 0.6	38 (98)

^aIsolated yield is based on racemic epoxides (theoretical maximum value = 50%). ^bLoading is based on a [Co] unit. ^cee % was determined by chiral GC or chiral HPLC. THF was used as a solvent. ^dSolvents CH₂Cl₂: THF = 2:1, Reaction time; 15 hrs.

with NBS in air was also effective in HKR as well as in PKR of epoxides.

As described in Table 1, the catalyst (6) and (7) exhibited a slight higher level of reactivity than (2) and (3), respectively. The catalytic activities of polymeric salen catalyst (4)-(7) were examined to investigate the effect of NBS treatment and the type of added metal salts. The variation of enantiomeric excess% with time in HKR of ECH is shown in Figure 3. For all catalysts, the racemic substrates were kinetically

**Figure 3.** The activities of different catalysts in the asymmetric HKR reaction of racemate ECH (for catalyst (7); ●, (6); ■, (5); ◆, (4); ▲, 0.7 mol % at ambient temp).**Figure 4.** The catalytic activity of the polymer catalyst (3) for asymmetric HKR of terminal epoxides using 0.7 mol % catalyst at ambient temp.

well resolved to give an optically pure epoxide within 12 h. The NBS-treated polymeric InCl₃-salen (7) has afforded the most superior reactivity and enantioselectivity for HKR of ECH relative to the catalysts (4)-(6). Only NBS-treated polymeric salen catalyst (4) exhibited relatively lower reaction rates than polymer salen (5)-(7) having 13-group metal chlorides. However, almost similar high enantioselectivity (upto 99%ee) was provided with a prolonged reaction time using those salen catalysts.

As the same manner, the linear-type polymer salen (3) having Indium chloride was examined in HKR reaction of epoxides. Figure 4 shows the activities of catalyst (3) for the HKR reaction of racemate glycidol derivatives. The optically pure isomers of various glycidol derivatives could be obtained by HKR of racemates using new polymeric salen catalysts containing Indium chloride salt. This salen catalyst (3) showed unique catalytic activities. Under a standard condition employing 0.7 mol % catalyst (3) and 0.6 equi-

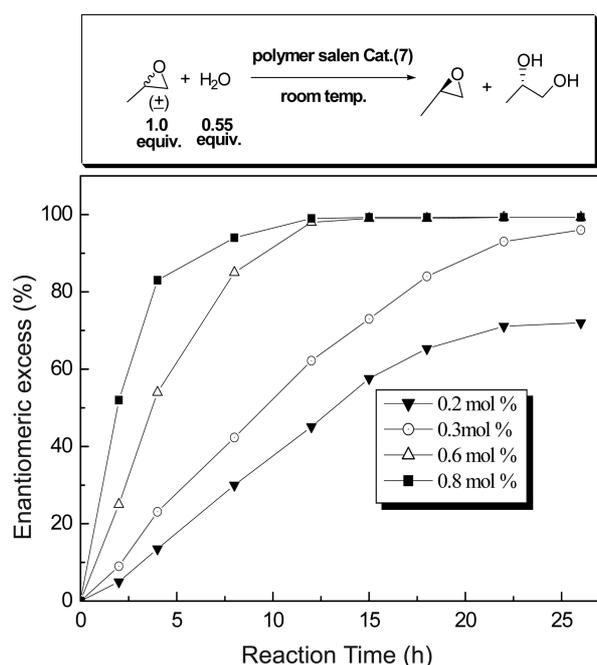
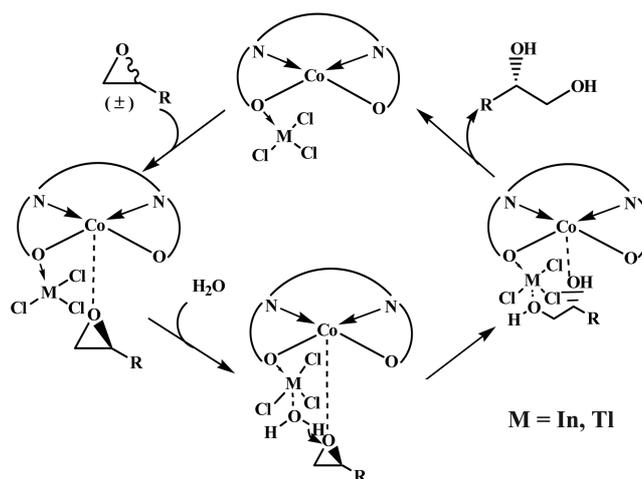


Figure 5. The effect of loading amount of polymer (salen) catalyst (7) on the enantioselectivity in HKR of racemic propane oxide.

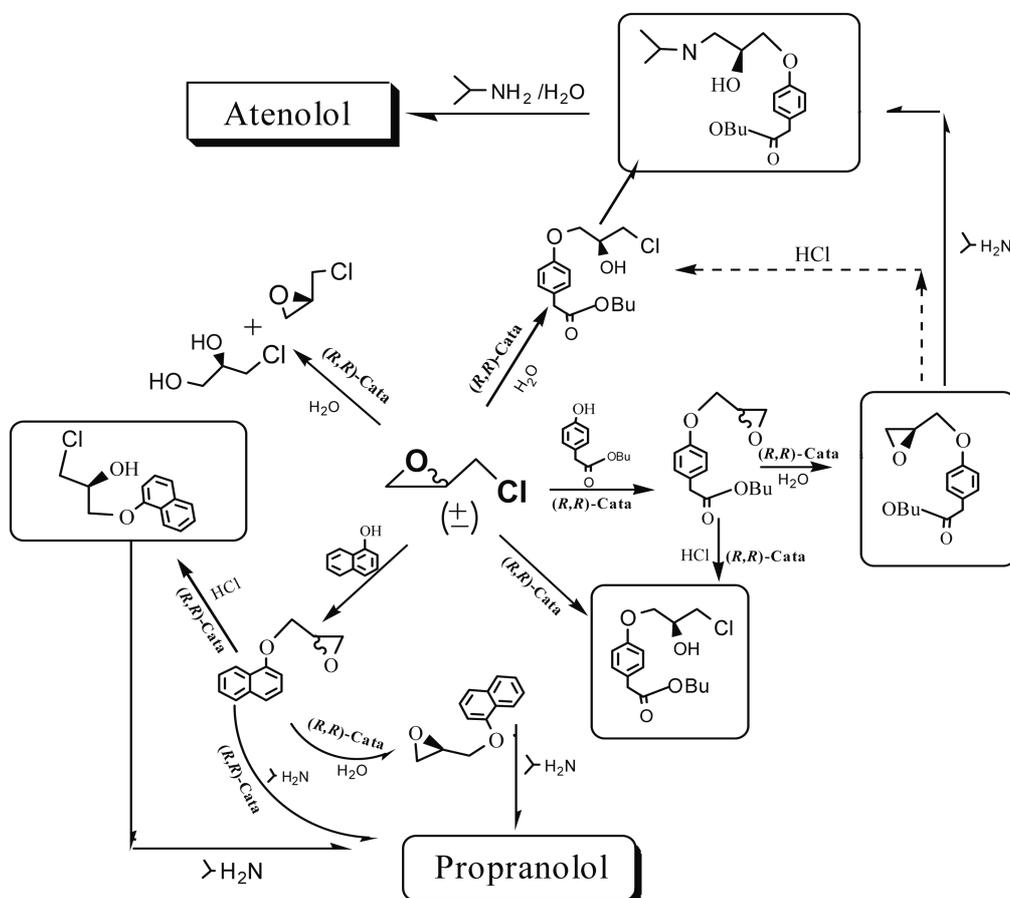
valent H_2O , various optically pure glycidyl ether and ester compounds could be recovered with $>99\%$ ee in a high



Scheme 2. Possible working model for the asymmetric ring opening of terminal epoxides by nucleophiles, catalyzed by 13 group metal salt-containing heterometallic salen complexes.

isolated yield as shown in Figure 4.

The effects of metal halide source on the catalytic activities were investigated in HKR of ECH. The reactivity for the polymeric salen complexes were dependent on the type of anchoring metal salts, and The activity order of catalyst found in HKR of racemic epoxides was as follows;



Scheme 3. Synthesis of chiral intermediates catalyzed by Heterobimetallic salen catalyst.

Co-InCl₃ catalyst (7) > Co-GaCl₃ (6) > Co-AlCl₃ (5) > Co-GaCl₃ (2) catalyst (4) > Co-AlCl₃ (1). Neither precatalyst (salen)Co (A) nor 13-group MX₃ salts alone exhibits any ring opening reactivity of epoxides in the presence of nucleophiles.

The HKR of 1,2-epoxy propane was investigated using the chiral catalyst (7) at different substrate/catalyst mole ratios and the results are summarized in Figure 5. The ee% of epoxide increased with the high loading of catalyst at the same reaction time. When the substrate-to-catalyst ratio is so high, the efforts to recycle the chiral catalysts become superfluous. The reaction with catalyst (7) at 0.3 mol % level led to 98 % ee for epoxide after 25 h.

In the ring opening reaction by nucleophiles using chiral salen complexes, the reported mechanistic study suggests that the catalysts display simultaneous activation of epoxides and nucleophiles by two different catalyst molecules *via* cooperative bimetallic mechanism. Alternatively, it means that the possibility of linking two salen units together in a bimetallic complex to enforce cooperative action like in the oligomeric or dendrimeric structures. The chiral salen units should be constructed and linked with flexible tethers to enforce cooperative catalysis. Whereas the cooperative reaction route may be restricted in our case using linear-type polymer salens, because the backbones of polymeric salen catalysts are rigid. However the polymeric catalysts exhibited an unusual high activity in catalysis with a small loading amount. Lewis acids play a crucial role in the asymmetric catalysis and it is known they can activate the epoxides during the ring opening reaction. In our previous finding, the cobalt-salen catalysts having Al, Ga and InCl₃ salts act as heterometallic complexes providing two different Lewis acid centers with strong synergistic effect.^{8,9} The intramolecular pathway for the polymeric catalysts (1)-(3) could be explained on the basis of proposed reaction mechanism as in Scheme 3. As similar to the enantioselective ring opening of epoxides with 4-methoxy phenol in the presence of Ga

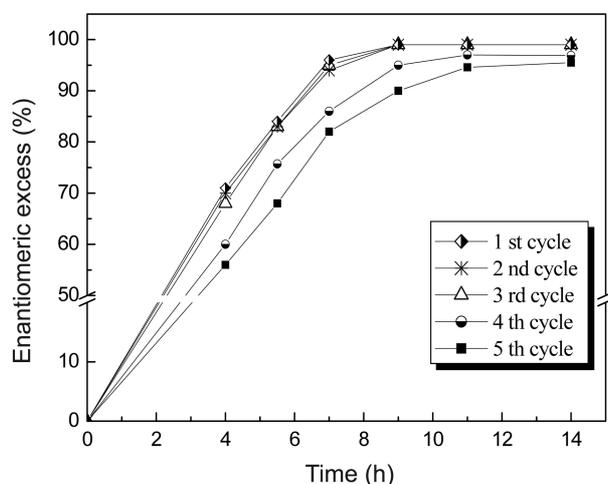


Figure 6. The catalytic activity and recyclability of the polymer salen catalyst (3) in the asymmetric HKR of (±) ECH using, 0.6 equiv. H₂O and 0.7 mol % catalyst at rt.

heterobimetallic catalysts, the central cobalt metal as well as Al, Ga and In appears to activate the epoxides and nucleophiles cooperatively in the same salen unit, providing the fast reaction rates and enantioselectivity.

The heterogeneous catalysts offer practical advantages of the facile separation from reactants and products, as well as recovery and reuse. But some disadvantages may be expected in heterogeneous catalysis in terms of reaction rates and enantioselectivity.

Our polymeric salen catalyst (1-3) could be recovered and reused several times without further treatment after reaction, showing no appreciable loss in its reactivity and enantioselectivity after washing with water and n-hexane (Table 4 and Figure 6). In the case of salen catalyst (4-7), regeneration by NBS is needed after use in HKR reaction to

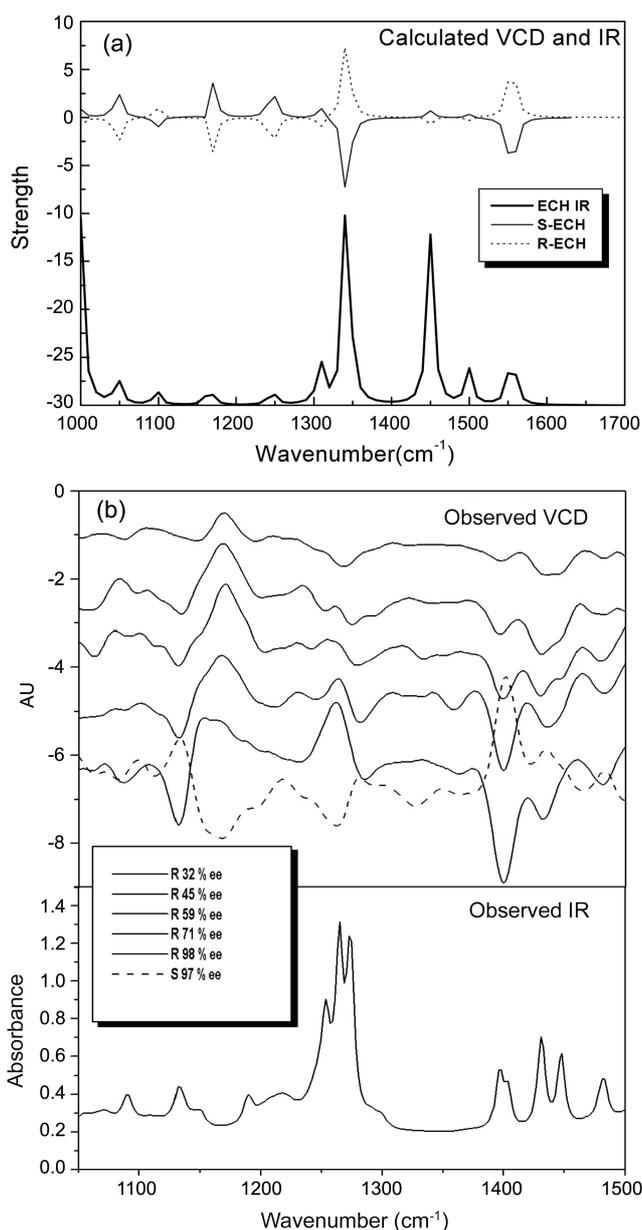


Figure 7. VCD and IR spectra of ECH; theoretical (a), observed (b).

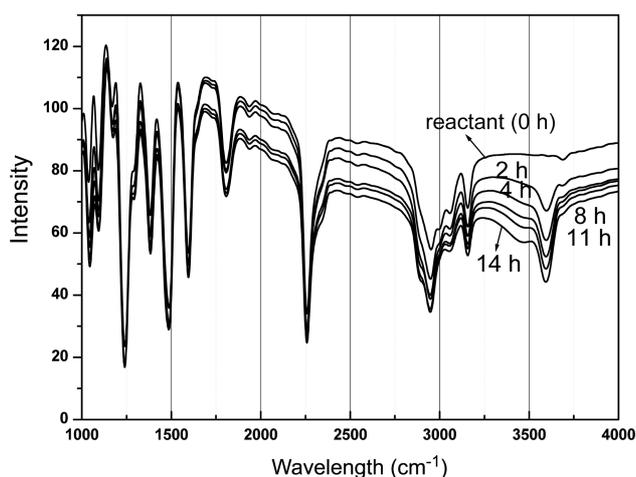


Figure 8. IR Spectra change during the ring opening reaction of phenyl glycidyl ether by water in the presence of polymer salen catalyst (3).

recover the activity of catalyst to the level of new one. On the basis of asymmetric HKR of various epoxides, the chiral (salen) complexes obtained by the present procedure can be applied as an effective recyclable catalyst for the asymmetric HKR reactions.

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 configuration. In the present study VCD spectroscopy was used to determine the ee% and absolute configuration of product in HKR reaction. Optically pure samples as well as racemates were used as references to compare the VCD spectra. The VCD spectra of opposite configuration such as R and S exhibits the reverse absorption peaks and the racemate shows no peaks at all. The VCD spectra were determined *in-situ* during the ring opening reaction of terminal epoxides by water. The theoretical VCD and IR spectra of ECH (Figure 7(a)) could be calculated using DFT/6-31G(b)/B3 LYP program. Figure 7(b) shows that the peaks in the VCD spectra increased with a prolonged reaction time, indicating the increase of produced ECH optical purity. The comparison of observed and calculated spectra showed very high level fidelity, and the absolute configuration of ECH was clearly matched together. The shift in peak position between observed and calculated VCD spectra might be due to solute-solvent interactions. The ee% determined by the VCD and those measured by GC were found to be good agreement within 1% ee.

The ring opening of PGE with water was monitored by IR spectroscopy and the obtained result with reaction time is shown in Figure 8. The liquid type product was recovered during the reaction and identified by IR analysis. The starting reactant PGE has no OH groups in the structure as shown in Figure 8. The observation of increase in OH peak (3200 to 3500 cm^{-1}) confirms the appearance of diol product by hydrolytic epoxide ring opening of PGE.

An efficient strategy for providing very high enantio-

selectivity can be achieved in the synthesis of valuable chiral building blocks *via* our catalytic system by combination of various asymmetric ring opening reactions as shown in Scheme 3. Development of synthetic routes to enantiopure α -aryloxy alcohol through asymmetric ring opening of racemic epoxides with phenol derivatives is potentially attractive. Among α -aryloxy alcohols, β -blockers have a wide range of clinical applications, and the mode of delivery of these drugs becomes crucial. Chiral atenolol and propranolol are one of the important drugs as an antihypertensive agent.⁵⁻⁷ However, there are few methods developed for the synthesis of chiral atenolol and propranolol.

The synthesis of chiral atenolol or propranolol could be applied efficiently and successfully *via* HKR of (\pm)-1-[*p*-(butoxycarbonyl) methyl] phenoxy]-2,3-epoxypropane or (\pm)-1-naphthoxy-2,3-epoxypropane, and it is the new promising strategy in our current study. The HKR of (\pm)-1-[*p*-(butoxycarbonyl) methyl] phenoxy]-2,3-epoxypropane and 1-naphthoxy-2,3-epoxypropane using polymer catalysts led to an optically pure (*S*)-epoxides (>98% ee, >35% yield). Transformation to chiral β -blockers were simply accomplished by ring opening of chiral 1-[*p*-(butoxycarbonyl) methyl] phenoxy]-2,3-epoxypropane and 1-naphthoxy-2,3-epoxypropane after HKR by using our new heterometallic polymer salen catalysts as indicated in Scheme 3.

In addition, atenolol synthesis *via* ring opening of inexpensive racemic ECH with butyl-*p*-hydroxyphenyl acetate as a nucleophile could be performed successfully in this work with high selectivity in good yields. In asymmetric ring opening of ECH with butyl-*p*-hydroxyphenyl acetate by using polymer catalysts completed the reaction at 2 mol% of catalyst loading within 12 h to offer the enantioriched α -aryloxy alcohol product as depicted in Scheme 3.

Conclusion

We have synthesized the new type of heterometallic chiral polymer salen complexes and it has been found that group 13 metal salts combined to Co^{III} salen unit played the crucial role in the asymmetric kinetic resolution of racemic epoxides. More importantly, the Lewis acidic centre of the chiral (salen) Co bonded to another Lewis acid centre (AlCl_3 and GaCl_3) enabled the smooth and efficient asymmetric kinetic resolution to afford the valuable chiral building blocks. Polymeric salen catalysts showed very high reactivity and enantioselectivity for the asymmetric ring opening of terminal epoxide with diverse nucleophiles. They provide the enantiopure useful chiral intermediates such as chiral terminal epoxides and α -aryloxy alcohols in one-step process. An efficient methodology for providing very high enantioselectivity can be achieved in the synthesis of valuable chiral building blocks *via* our catalytic system by combination of various asymmetric ring opening reactions. The stability and recyclability of catalysts appeal to successful use for other catalytic asymmetric reactions between nucleophiles and electrophiles since such processes can provide practical access to chiral materials.

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