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New chiral cobalt salen complexes containing Lewis acid BF_3; a highly reactive and enantioselective catalyst for the hydrolytic kinetic resolution of epoxides

Chang-Kyo Shin,[a] Seong-Jin Kim[b] and Geon-Joong Kim[a,*]

[a]*Department of Chemical Engineering, Inha University, Inchon 402-751, South Korea*
[b]*RStech Corp. #305 Venture Town, 1688-5, Sinil-dong, Daedeok-gu, Daejeon, 306-230, South Korea*

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Abstract—A new type of chiral cobalt salen complexes bearing BF_3 Lewis acid proved to be reactive and enantioselective in the hydrolytic resolution of terminal epoxides. The polymer type salen catalysts also showed a high enantioselectivity in the same reaction.

It has been found that the hydrolytic kinetic resolution (HKR) catalyzed by chiral cobalt(III) salen complexes is a simple and effective method for the preparation of optically active epoxides.[1–4] Especially, chiral Co(III)–OAc salen complex is very enantioselective for the hydrolytic kinetic resolution (HKR) of racemic epoxides such as (±)-1,2-epoxybutane (EB), 1,2-epoxypropane (EP), styrene oxide (SO), and (±)-epichlorohydrine (ECH) with water.[2–4] Whereas, the reduced (salen) Co(III)–OAc complex must be regenerated in air after separation of products and this type of catalyst has the drawback of racemization in HKR of epichlorohydrine or epibromohydrine.

We have synthesized new chiral salen Co(III) complexes bearing fluoride compounds as a counter-anion, and applied as catalysts in the HKR of terminal epoxides.[5] Especially, Co(III)–(PF_6), and (BF_4) salen complexes showed the very high catalytic activities and these catalysts could be recycled without observable loss in activity and racemization by simple distillation of products.

Cooperative bimetallic catalysis for the asymmetric HKR of epoxides has been documented in recent papers.[6–8] Therefore, in such mechanistic context, complexes having multiple metal centers can provide improved reactivity relative to monometallic catalysts. Linking the salen catalysts as dimers or to polymeric or to dendrimeric frameworks leads to catalytic systems with similar enantioselectivity and substantially enhanced reactivity relative to monomeric salen.

Herein, we report the synthesis of new chiral salens having BF_3 ligand, and demonstrate that these catalysts exhibit enhanced catalytic activity in the HKR of terminal epoxides as a dimeric or polymeric structure. The general procedure for the HKR of epoxides follows the method as shown in the reported papers.[3,5] The ee% values were determined by capillary GC using a chiral column (CHIRALDEXTM (D-TM), gamma-cyclodextrin trifluoro-acetyl, $40\,m \times 0.25\,mm$ i.d. (Astec)).

We tried to improve the activity of the catalyst by changing the source of ligand instead of BF_4. The compounds of $BF_3{\cdot}2H_2O$ and BF_3·ethyletherate were used as sources of ligand in preparing the salen complexes. For the synthesis of chiral salen catalyst (2), the chiral salen (*R*,*R*)-(−)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexane diamino cobalt(II) (1) was oxidized under air for 4h in the presence of methylene chloride (MC) and $BF_3{\cdot}2H_2O$ (Co(II) salen (1): $BF_3{\cdot}2H_2O$ mole ratio = 1:1) at room temperature. The mixture was concentrated to dryness. When $BF_3{\cdot}2H_2O$ was used as a source of ligand, the salen catalyst gave a relatively low activity as can be seen in Figure 1.

Keywords: Chiral cobalt salen; Lewis acid; BF_3; Resolution; Epoxide.

* Corresponding author. Tel.: +82 32 860 7472; fax: +82 32 872 0959; e-mail: kimgj@inha.ac.kr

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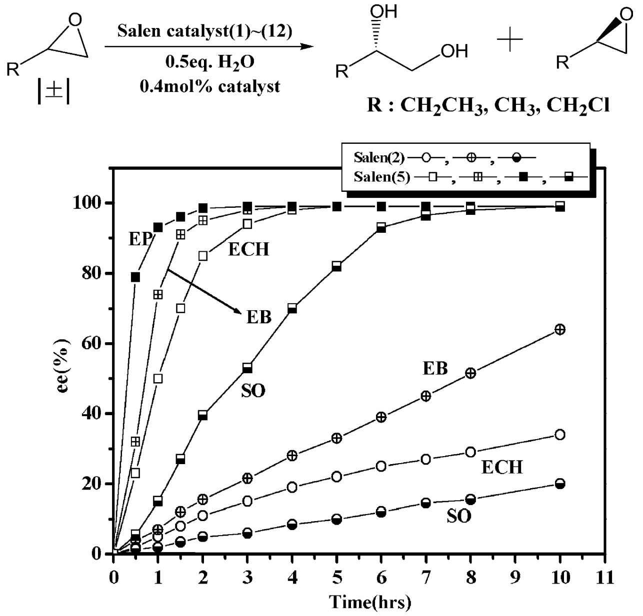


Figure 1. The catalytic activities of cobalt salen complexes (2) and (5) in the asymmetric HKR of terminal epoxides. 0.4mol% catalyst, reaction at rt (EP: epoxy propane, EB: epoxy butane, ECH: epichlorohydrine, SO: styrene oxide).

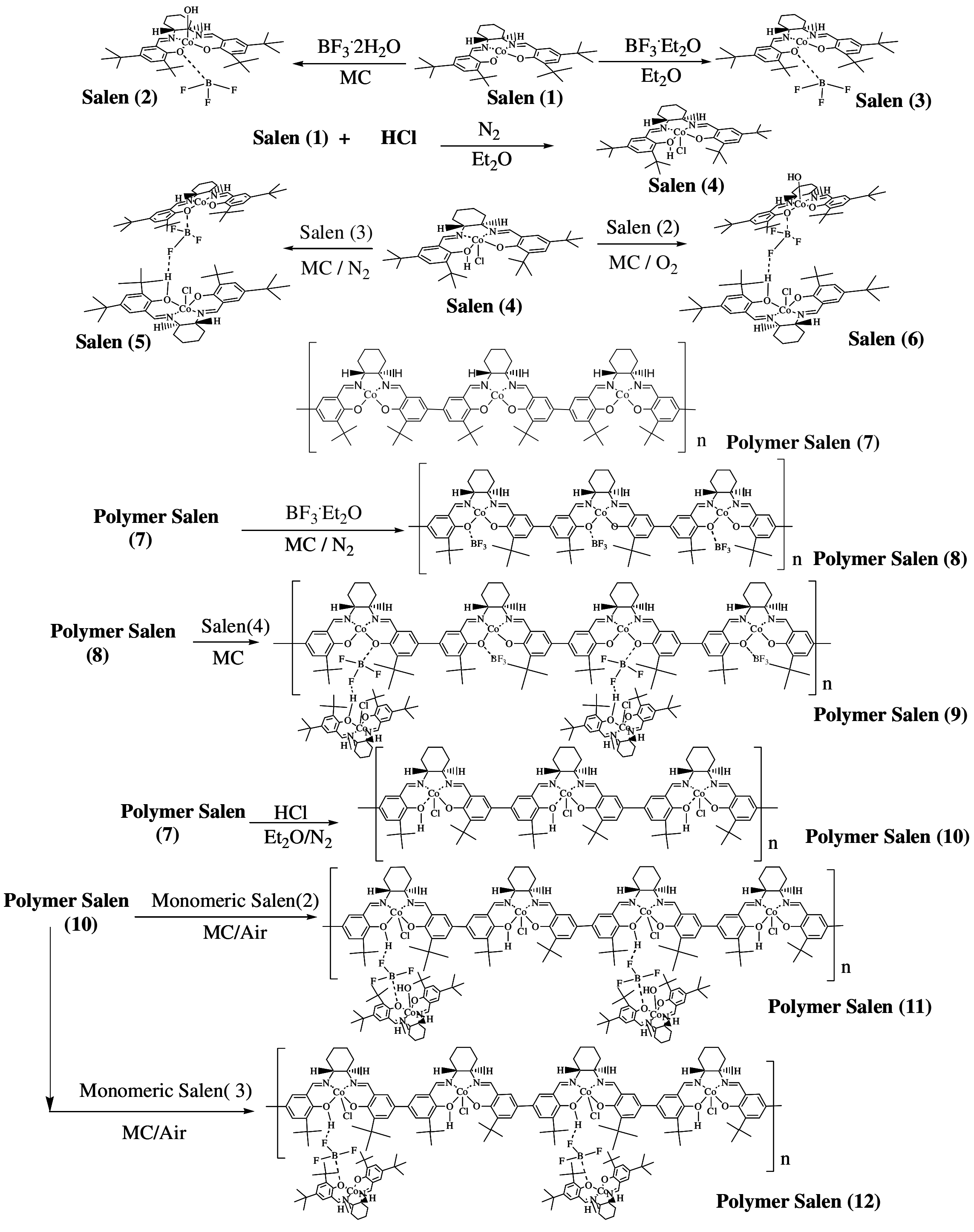
It is known that $BF_3{\cdot}2H_2O$ compounds exist as $BF_3OH^{(-)}$ anion and $H_3O^{(+)}$ in the solution. The Co(II) salen was oxidized to Co(III) species under the aerobic conditions in the presence of BF_3OH anions, when the Co(II) salen (1) was treated with $BF_3{\cdot}2H_2O$ in the mole ratio of 1:1. The oxidation of cobalt species was confirmed by ESCA analysis, showing the peak at the binding energy of 780nm due to Co(III) (e.g., Co(II) at 783nm). For the salen catalyst (2), the characteristic absorption band of Co(II) salen(1) at 430nm disappeared and a new band at 380nm was investigated on the UV–vis spectra. Furthermore, this salen complex (2) showed the absorption peaks for hydroxyl group over $3600\,cm^{-1}$ on the IR spectra. Thus, these results have led to a proposed structure of salen Co–OH complex (2) containing BF_3 unit linked to the oxygen of salens.[9] It has been reported that the metal atoms of Lewis acids such as AlH_3 and Al(*i*-Bu)$_3$ form bonding with two phenolic oxygens of cobalt-salen.[10] On the basis of their discussions, a possible structure for Lewis acid BF_3 including salen catalyst (2) is depicted in Scheme 1.

To investigate the effect of BF_3 source on the catalytic activity, $BF_3{\cdot}Et_2O$ was chosen and used to prepare the cobalt salen complexes. When the Co(II) salen (1) was treated with $BF_3{\cdot}Et_2O$ (mole ratio = 1:1) in MC under nitrogen, the oxidation state of cobalt was found to be +2 by ESCA analysis. For this salen (3), the new strong absorption peak at 280nm was found on the UV–vis spectra, which was not shown for the salen complexes such as Co–OAc, Co–PF_6 and Co–BF_4. By using the chiral salen catalyst (3), only the moderate reactivity was obtained as can be seen in Figure 2. As mentioned above, the boron of Lewis acid BF_3 can be combined with two phenolic oxygens of salen molecule.[9] It is well known that cobalt(III) species are real active sites for the ring opening reactions.[11] However, the chiral Co(II) salen catalyst (3) containing BF_3 ligand exhibited the catalytic activity in HKR of epoxides under strictly anaerobic conditions.

The chiral salen complex (4) has been obtained by the treatment between Co(II) salen (1) and HCl (1:1 mole ratio) in ethylether under a nitrogen atmosphere. In this case, cobalt species in the salen complex were maintained as +2 oxidation state. The HCl-containing Co(II) salen (4) as well as salen (1) itself had no catalytic activity in HKR of epoxides. It has been investigated that the Co(II) salen can be anchored on the solid acids such as H^+-type MCM-41 and aluminosilicates. Because the oxygens of salen molecule are connected to two ionizable protons before complexation with cobalt ion, it is supposed that the proton of HCl would be coordinated to one oxygen, generating the hydroxyl group, and the chlorine to cobalt(II) cation by the treatment of salen (1) with HCl. By treating the salen catalyst (3) with equivalent HCl-containing Co(II) salen (4) in MC under nitrogen atmosphere, the catalytic activity has improved remarkably. Additionally, when the chiral salen complex (2) was reacted with the equivalent HCl-containing Co(II) salen (4) under the same conditions as above, this salen complex (6) afforded not only remarkably enhanced reactivity but also high enantioselectivity, showing the similar activity as compared to the catalyst (5). For the catalysts (6), co-presence of Co(III) and Co(II) species was confirmed by UV and ESCA analyses. The crystal structure of salen (5) is the same as that of salen (6), but it is different from that of salen (3 or 4). This means that salen catalyst (5 or 6) is not only the physical mixture of salen (4) and (2 or 3), but also shows the different structure from salen (2) and (3). The shift of F-NMR peaks for salen (5) and (6) was found after treatment between salen (4) and (2,3).

The salen Co(III)–OH complex can serve as both for the nucleophilic and Lewis acidic components. Nielson et al. have reported that HKR reactions carried out under conditions in which both Co–OH and Co–X (X = Cl, OTs, OAc, SbF_6) are present display dramatic increases in activity, compared to the pure Co–OH system.[9] Similarly, in this work, the salen catalyst (6) showed remarkably accelerated reaction rates with a high enantiomeric excess % for epoxides. Especially, the salen catalysts having dimeric structures such as (5), (6) and (9) gave an improved selectivity as compared to salen (3), (4) and (8) in the HKR reaction of styrene oxide. Based on the HKR reaction results and analysis data, we speculated the structure of salens (5 and 6) as a dimeric form. In the case of salen catalyst (5), one Co(II) salen is oxidized to Co(III) by balancing with $OH^{(-)}$ anion and it is linked to the other Co(II) salen through the hydrogen bond between fluoride of BF_3 and the proton binding to Co(II) salen (Scheme 1). For the salen (5), two Co(II) salen complexes may be linked in the similar manner as salen (6).

Consequently, binding the two-salen units appeared to induce a cooperative mechanism, albeit through a far



Scheme 1.

less enantiodiscriminating transition state than that attained with the monomeric catalysts as shown in Scheme 2.

The construction of salen polymers consisting of repeating C_2 symmetric salen units was carried out to investigate whether the additional monomeric salen might link to the polymer backbone. The Co(II)-type polymeric salen (7) was obtained by the reaction between the salen ligands and hydrous cobalt(II) acetate after condensation of dimeric dialdehyde derivative and (*R*,*R*)-diaminocyclo hexane in boiling dioxane.[12,13] However, this polymeric chiral Co(II) salen (7) has no catalytic activity in HKR of epoxides.

The polymer salen catalyst (8) can be obtained by the reaction between the polymeric salen (7) and $BF_3{\cdot}Et_2O$ (mole ratio = 1:1) in MC under anaerobic conditions. This catalyst showed relatively low reactivity in HKR of ECH, EB, and EP. Whereas, after treating the

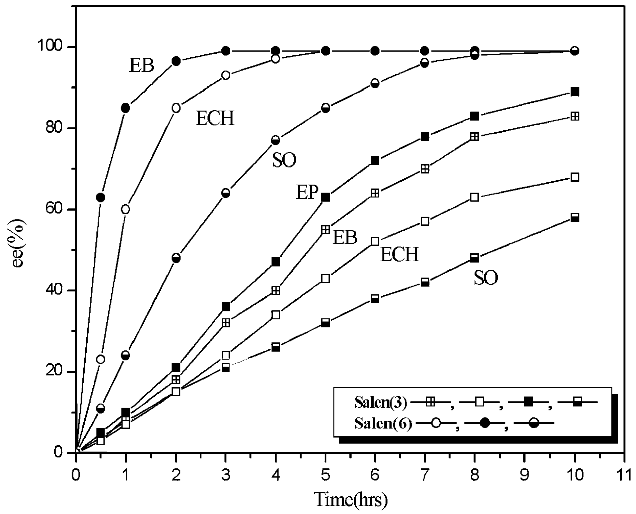


Figure 2. The catalytic activities of cobalt salen complexes (3) and (6) in the asymmetric HKR of terminal epoxides. 0.4mol% catalyst, reaction at rt.

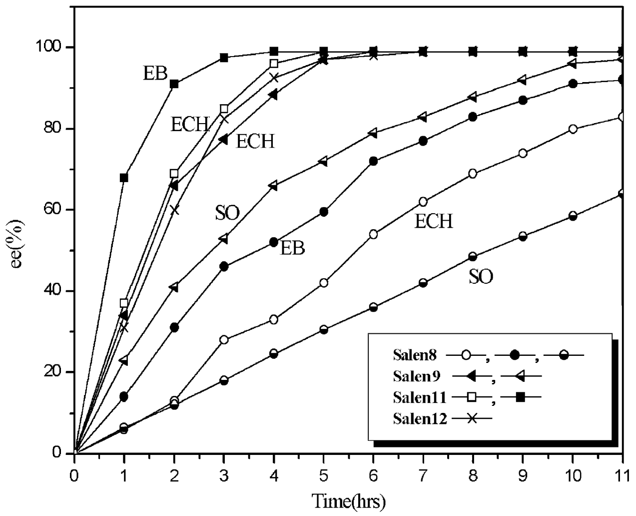
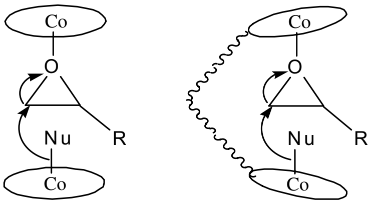


Figure 3. The catalytic activities of cobalt salen complexes (8,9,11) and (12) in the asymmetric HKR of terminal epoxides. 0.4mol% catalyst, reaction at rt.

polymeric salen catalyst (8) with equivalent HCl-containing Co(II) salen (4) in MC under nitrogen atmosphere, the catalytic activity has improved significantly as shown in Figure 3.

In addition, the monomeric Co(III) salen (2) and Co(II) salen (3) were also attached to the polymeric Co(II) salen (10) after washing this polymer salen with dil-HCl, respectively. The attachment of monomeric salen complexes to the polymeric cobalt salen can be confirmed also by the increase of sample weight after sufficient washing and drying. When the polymeric Co(II) salen (10) was treated with the monomeric Co(III) chiral salen (2), the weight of dried powder has increased after washing with MC solvent until the filtrate was transparent, indicating that the monomeric salen compounds are linking on the polymer backbones (increase of 34wt%). The greatly increased activities were investigated on the polymer salen catalyst (11) or (12) after anchoring the monomeric Co(II) salen (2) or (3). Thus, these results strongly support the idea that units of salen complexes are linked together as a dimeric form. This explains why complexes (5, 9, 11 and 12) are better catalysts than the monomeric catalyst (2) or polymeric salen (8) having linear backbones. The polymeric salens (9, 11) lost the activity partially after first reaction by the dissociation of monomeric salens from the polymer backbone, indicating that the band strength between the dimeric two salen unit is not so strong. The activity of polymeric salen catalyst used in the reaction has been recovered by treatment with monomeric salen.



Scheme 2.

In conclusion, the new chiral cobalt salen catalysts have afforded highly valuable terminal epoxides in enantiomerically pure form for HKR of (±)-epoxides with promising reactivity. The cobalt salen complexes containing the electronegative fluoride ions gave a high enantioselectivity for HKR of terminal epoxides even in +2 oxidation state. The results obtained by instrumental analysis and in the catalytic reactions support the idea that the reactive catalysts prepared using BF_3 compounds have a dimeric structure linked by two salen molecules. On the basis of asymmetric HKR of various epoxides, the chiral (salen) complexes obtained by the present procedure can be applied as an effective catalyst for the asymmetric HKR reactions.

Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tetlet.2004.08.067.

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