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Synthesis of polymeric salen complexes and application in the enantioselective hydrolytic kinetic resolution of epoxides as catalysts

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Abstract

The polymeric (salen) Co(III) catalysts containing various counter anions have been synthesized, and the asymmetric catalytic activities of these newly synthesized polymer-type salen complexes were investigated in the HKR of terminal epoxides. The polymeric chiral salen Co(III) complexes catalyze the hydrolysis of epichlorohydrine, 1,2-epoxybutane, 1,2-epoxyhexane and epoxystyrene with very high enantioselectivities under mild conditions. The catalysts could be recovered and reused several times without further treatment after reaction, showing no loss of activity and enantioselectivity.

Keywords: Polymeric chiral salen; Hydrolysis; Epichlorohydrine; Hydrolytic resolution

1. Introduction

It has been found that several systems based on chiral chromium- and cobalt-salen complexes are very efficient for the highly enantioselective reaction of nucleophiles with epoxides [1–4]. Especially, chiral Co(III) salen complexes are very selective for the asymmetric hydrolysis of terminal epoxides [2–4]. These recently developed salen-based catalysts are appealing candidates for covalent attachment of homogeneous chiral salen ligands to the polymer and inorganic supports, and the corresponding immobilized salen derivatives were shown to be efficient for the hydrolytic kinetic resolution (HKR) of terminal epoxides [5–9]. The heterogeneous catalysts offer practical advantages of the facile separation from reactants and products, as well as recovery and reuse. But some disadvantages can be expected in heterogeneous catalysis in terms of reaction rates and enantioselectivity. The mechanistic study for HKR of epoxides, reported by Annis and Jacobson [9], indicates that the epoxide ring opening reactions proceed through the mechanism involving cooperative interaction between salen catalyst units, so enforcement of a high local concentration of catalyst by attachment to a high-loading support is beneficial to the reactivity. It has been found that there is no observable reaction at lower catalyst concentrations on the silica-support surface. Especially, chiral Co(III)-OAc salen complex is very enantioselective for the HKR of racemic epoxides such as (±)styrene oxide and (±)epichlorohydrine (ECH) with water [3,4,10–14]. ECH is one of the attractive substrates for HKR because the racemates are available inexpensively and the chiral three carbon building blocks derived from that compound is extremely versatile synthetic intermediates. The separation of diol products from unreacted epoxide is easy due to large boiling point difference of the products.

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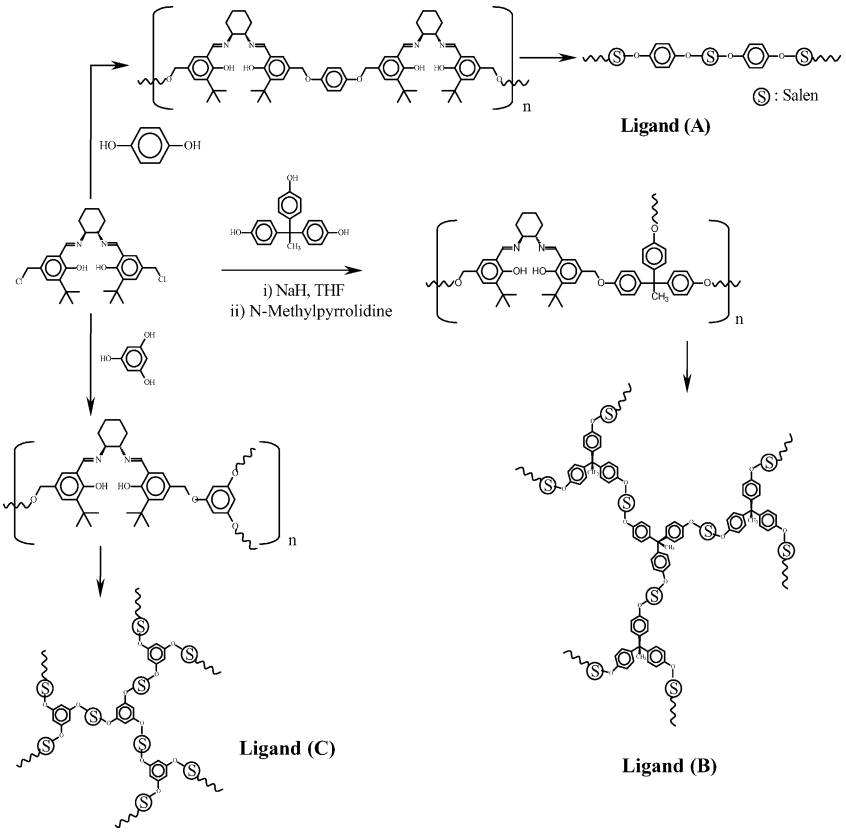
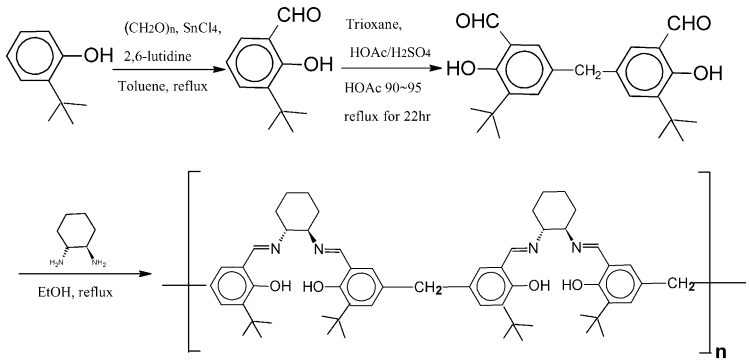
Whereas, the well-known (salen) Co(III)-OAc complex must be regenerated by treatment with acetic acid in air after reaction and separation of products [3]. Furthermore, this type catalyst has the drawback of the racemization in HKR of ECH and it may stand as a critical issue. Based on these data, our attention was directed to the development of optically active catalysts desirable for repeated use without any treatment after HKR reaction, and the racemization of optically pure epoxide has been completely overcome by using the new catalysts bearing less coordinating counterions. Furthermore, it appeared to us that it would be interesting to polymerize the chiral salen units as tetradendate ligands and to compare the catalytic abilities for the HKR of terminal epoxides into optically pure epoxide. The polymeric chiral salen can offer the practical advantage in the separation of products. Only a few studies concerning the synthesis of polymeric chiral salens and their catalytic properties have been published in the open literature. Yao and co-workers have recently reported the synthesis of polymeric salen and application in the asymmetric HKR [10] and in the epoxidation [11] as a catalyst. Here in this study, we have synthesized different two kinds of counter anion-containing polymeric (salen) Co catalysts and the asymmetric catalytic activities of these newly synthesized polymer-type chiral salen Co(III) complexes have been investigated in the HKR of some terminal epoxides.

2. Experimental

The synthetic sequences to obtain the various chiral polymeric salens are shown in Schemes 1 and 2. First, the optically pure salen ligand, bearing chloromethyl groups, was submitted to polymerization with hydroquinone, 1,3,5-trihydroxybenzene



Scheme 1.



Ligand (D)

Scheme 2.

and 1,1,1-tris(4-hydroxy phenyl)ethane in the presence of *N*-methylpyrrolidine. The chloromethylated salen and dry *N*-methylpyrrolidine were added to the sodium phenoxide derivatives in THF. Then, it was stirred at room temperature for 5 h and heated to reflux for 72 h under nitrogen. The solvent was evaporated under vacuum and the residue was dissolved in CH_2Cl_2. The organic phase was washed with water and dried. The average molecular weight of product was about 6000. The molecular weight was determined by GCP (Waters 410 T50). This polymeric chiral salen is formed as a linear chain and is soluble in THF and CH_2Cl_2. We anticipated that by introduction of 1,1,1-tris(4-hydroxy phenyl)ethane (or 1,3,5-trihydroxybenzene) portion into the salen polymer the solubility in normal solvents could be minimized and the branched polymer salen could be obtained. The branched–type polymer salens were obtained by using the mixture of hydroquinone and 1,1,1-tris(4-hydroxy phenyl)ethane. It is noteworthy that this method can lead to the synthesis of the family of chiral salen dendrimers, which exhibit the tree-like structure. Second, the polymeric salen ligand was synthesized by using dimeric dialdehyde derivative, which was reported by Jacobs and co-workers [15]. 3-*tert*-Butyl-2-hydroxybenzaldehyde was converted to 3-*tert*-butyl-5-chloromethyl-2-hydroxybenzaldehyde by the chloromethylation method [5]. The 3-*tert*-butylsalicylaldehyde (5 g, 28.1 mmol) and trioxane (0.8 g, 8.85 mmol) in 20 ml of glacial acetic acid were heated to a temperature of 90–95 °C under nitrogen atmosphere. The concentrated sulfuric acid and glacial acetic acid(1:45) was added to the mixture dropwise. Subsequently, the reaction mixture was poured into 200 ml of ice-water and allowed to stand overnight. The precipitated solid was filtered and extracted twice with *n*-hexane (2× 5 ml). Recrystallization from 7.5 ml acetone gave the pure dialdehyde.

The polymeric salen ligand (D) was readily synthesized by the reaction of 10 mmol dimeric dialdehyde derivatives with 10 mmol of (1*S*, 2*S*)-(+)-1,2-diaminocyclohexane (or (1*R*, 2*R*)-(−)-1,2-diaminocyclohexane) in boiling ethanol solution. While the reaction was performed, precipitates were formed in the reaction solution. After reaction for 2 h, the precipitated solid was filtered and extracted twice with *n*-hexane and methanol. This product was dark brownish solid and was not dissolved in any solvent.

The Co(II)-type polymeric salen ligands were obtained by the reaction between the salen ligands and hydrous cobalt (II) acetate in a boiling ethanol**.** The Co(III)-type polymeric salen ligands were prepared by following the same procedure described in the literature [6–8]. The polymeric salen ligands containing cobalt in the structure were filtered and rinsed sequentially with water, methanol, CH_2Cl_2, THF, methanol and CH_2Cl_2, and then dried in vacuo to yield the product as a dark brown powder. For the synthesis of chiral Co(III) salen polymer catalysts, the Co(II) polymer salen was treated with ferrocenium hexafluorophosphate or ferrocenium tetrafluoroborate in acetonitrile under air, respectively. The mixtures were washed with hexane to remove the side product, ferrocene. These catalysts will be denoted as Co(III)-(PF_6) and

Co(III)-(BF_4). They were used as catalysts in the HKR of epoxides such as (±)ECH, 1,2-epoxybutane and 1,2-epoxyhexane to evaluate catalytic activities.

The general procedure for the HKR of epoxides follows the method as shown in the reported papers [3]. The conversion and ee% values were determined by capillary GC using chiral columns (CHIRALDEXTM(D-TM), Gamma-cyclodextrin trifluoroacetyl, 40 m × 0.25 mm i.d.; CHIRALDEX B-DM, beta cyclodextrin, 20 m × 0.32 mm i.d., Alltech).

3. Results and discussion

As expected, the final powder chelates containing Co metal were insoluble for organic solvents such as toluene, alcohol, and THF, and they were stable without extraction during an asymmetric HKR reaction. And the salen chelates having a low molecular weight were washed out with solvents repeatedly, and the yield of polymeric salen ligand (A) obtained as a powder was relatively low (60%). After incorporation of cobalt ions into the polymeric salen ligand (B), the resultant solid was washed repeatedly by the sequence as mentioned above, affording the powder chelates in 75% yield. The subsequent reaction of aldehyde with an amine group in the diaminocyclohexane produces a IR peak at 1640 cm^{-1} corresponding to the imine stretching vibration. The polymeric salen ligand showed this strong imine peak on the IR spectra. The

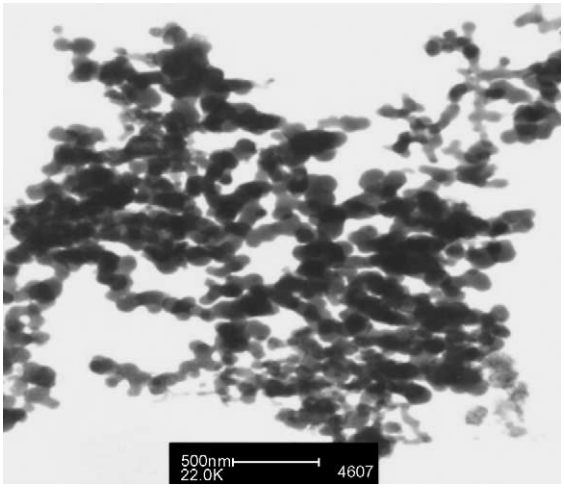
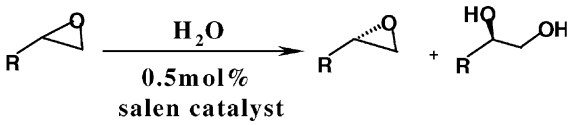


Fig. 1. The TEM image of polymeric Co(III) salen catalyst (D).

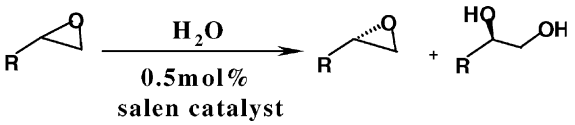
Table 1
Enantioselective hydrolysis of terminal epoxides to diols on the polymeric chiral Co(III)-(PF_6)-type salen catalysts[a]



Entry	Substrate	Ligand	Time (h)	Yield of epoxide (%)	ee% of epoxide	Yield of diol (%)	ee% of diol
1	ECH	A	9	42	99	45	98
2	ECH	B	9	40	99	44	98
3	ECH	C	9	41	99	46	97
4	ECH	D	9	43	99	45	98
5	SO	A	45	32	98	41	96
6	SO	B	45	23	98	45	96
7	SO	C	45	21	97	45	94
8	SO	D	45	30	98	44	97
9	EB	A	5	43	98	47	98
10	EB	B	5	46	99	47	98
11	EB	C	5	45	99	48	97
12	EB	D	5	46	98	45	98
13	HB	A	9	42	98	84	97
14	HB	B	9	36	98	47	97
15	HB	C	9	38	98	47	96
16	HB	D	9	42	99	45	98

[a] ECH, epichlorohydrine; SO, styrene oxide; EB, 1,2-epoxybutane; HB, 1,2-epoxyhexane. Catalyst: Co(III)-(PF_6)-type polymeric salen. Epoxide: 10 mmol, water: 5.5 mmol, chiral salen catalyst: 0.5 mol% and reaction temperature: 20 °C.

Table 2
Enantioselective hydrolysis of terminal epoxides to diols on the polymeric chiral Co(III)-(BF4)-type salen catalysts[a]



Entry	Substrate	Catalyst	Time (h)	Yield of epoxide (%)	ee% of epoxide	Yield of diol (%)	ee% of diol
1	ECH	A	12	46	99	46	98
2	ECH	B	12	44	99	44	97
3	ECH	D	12	44	99	46	97
4	SO	A	48	43	99	47	98
5	SO	B	48	44	98	48	98
6	SO	D	48	44	98	47	98
7	EB	A	6	42	97	45	96
8	EB	B	6	44	98	44	97
9	EB	D	6	42	98	47	98
10	HO	A	11	45	98	47	98
11	HO	B	11	45	99	48	97
12	HO	D	11	43	98	47	98

[a] ECH, epichlorohydrine; SO, styrene oxide; EB, 1,2-epoxybutane; HB, 1,2-epoxyhexane. Catalyst: Co(III)-(BF_4)-type polymeric salen catalysts. Epoxide: 10 mmol, water: 0.55 mmol, chiral salen catalyst: 0.5 mol% and reaction temperature: 20 °C.

IR spectrum for polymer salen was same as that for the homogeneous monomeric salen.

Fig. 1 shows a TEM image of polymeric Co(III) salen catalyst (D). The aggregated form was found in the photograph. The average molecular weight of this sample was about 10,000. This means about 10 salen units are connected together. As a result, the chains of polymeric salen may be permitted to rotate freely and the spherical structure would be formed in dried state in the absence of solvents as can be seen in Fig. 1.

The trends in the activity and enantioselectivity of the synthesized Co(III)-(PF_6)-type salen polymers were examined for the asymmetric HKR of terminal epoxides. This reaction was also carried out with the homogeneous salen catalysts having the same structure as polymeric salens. Table 1 shows the results obtained using the Co(III)-(PF_6)-type polymeric salen as a catalyst. The asymmetric HKR of terminal epoxides were also performed using the Co(III)-(BF_4)-type polymeric salens and the results are summarized in Table 2.

Both the Co(III)-(PF_6)- and Co(III)-(BF_4)-type polymeric salen showed excellent enantioselectivities with the substrates such as epichlorohydrine, styrene oxide, epoxybutane and epoxyhexane. The reaction using the Co(III)-(PF_6) (or Co(III)-(BF_4))-type poly-

Table 3
The activity of various catalyst as number of reaction

Catalyst	Reaction time (h)	No. of reaction	ee% of epoxide	ee% of diol
(Co-Salen)OAc	4	1	>99.8	>99.8
	8	2	17	>99.8
Co(III)-(A)	4	1	>99.8	>99.8
	6	2	>99.8	>99.8
	8	3	>99.8	>99.8
	12	4	>99.8	>98.5
	20	6	>99.6	>96.2
Co(III)-(B)	4	1	>99.8	>99.8
	6	2	>99.8	>99.8
	8	3	>99.8	>99.8
	12	4	>99.8	>98.5
	20	5	>99.5	>96.2
Co(III)-(C)	4	1	>99.8	>99.8
	6	2	>99.8	>99.8
	8	3	>99.8	>99.7
	12	4	>99.7	>98.5
	20	6	>99.5	>96.2
Co(III)-(D)	4	1	>99.8	>99.8
	6	2	>99.8	>99.8
	8	3	>99.8	>99.6
	12	4	>99.6	>97.8
	20	6	>98.4	>95.8

meric salen exhibited the almost same enantioselectivity as monomeric salen catalysts. The results of monomeric salen catalysts are shown in Table 3.

Epichlorohydrine and epoxystyrene gave very high yield and ee% of optically pure epoxide over chiral Co(III)-(PF_6) (or Co(III)-(BF_4))-type polymeric salen as catalysts. Use of polymer-type salen avoided the necessity of catalyst separation by distillation. It is so easy to isolate the Co(III)-(PF_6) (or Co(III)-(BF_4))-type polymeric salen from the product mixture containing epoxides and diols, because of its low solubility in *n*-hexane. The polymeric salen powder as well as low molecular oligomer salen could be recovered after extraction of the product without distillation. The catalyst was recoverable by simple filtration and *n*-hexane rinse, and the diol product

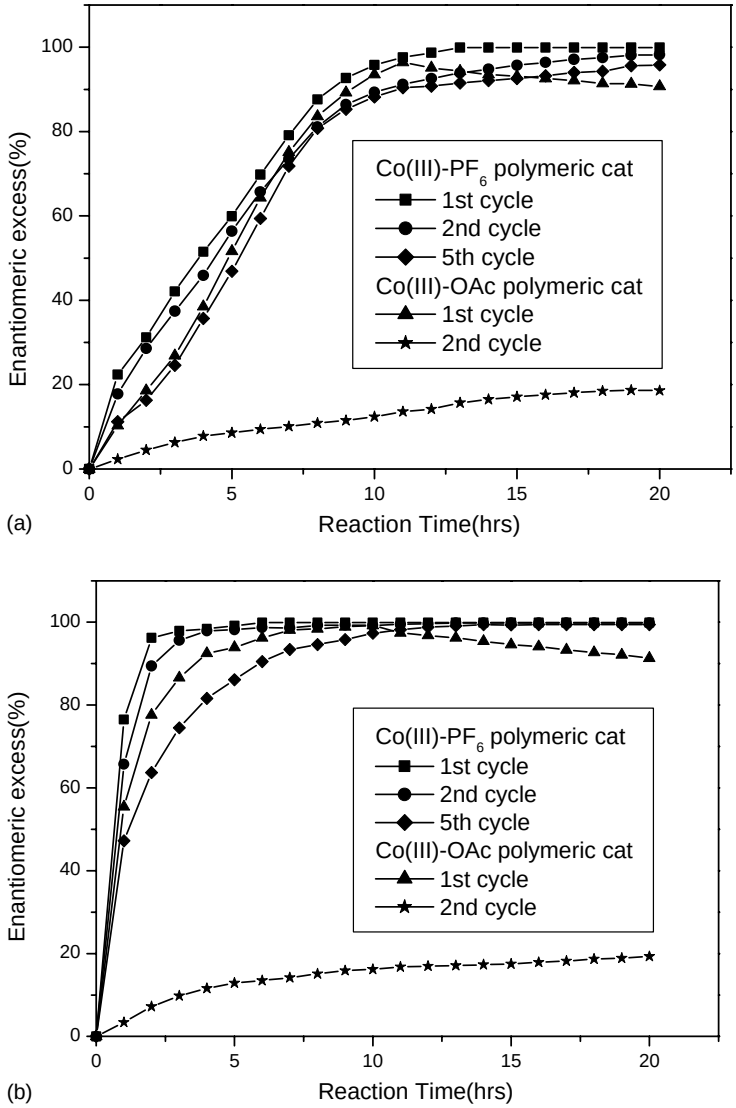


Fig. 2. The catalytic activities and recyclabilities of Co(III)-(PF_6) polymeric salen catalyst (D) and Co(III)-(OAc)-type polymeric salen catalyst (D) in the asymmetric HKR of epoxides: (a) (±)epichlorohydrine and (b) (±)epoxybutane. 0.5 mol% catalyst, reaction at room temperature.

Table 4
Recyclability of chiral Co(III)-(PF_6)-type of polymeric salen catalyst (D) in asymmetric HKR of ECH[a]

	Cycle						
	1	2	3	4	5	6	7
Yield (%)	45	45	45	45	45	45	44
ee% of ECH	99	99	99	99	99	99	99

[a] Catalysts were reused without further treatment after simple filtration of products.

could be removed by washing with water. Whereas, the monomeric salen chelates cannot be isolated by precipitation except distillation. The use of insoluble polymeric salen catalysts could allow the product isolation by simple filtration and solvent removal. After using Co(III)-polymeric salen catalyst, the resultant solution exhibited no color and the catalyst could be recovered by simple filtration. This means that covalently connected Co-polymeric salen ligands are stable during the reaction.

Table 4 summaries the obtained results, when the Co(III)-(PF_6)-type polymeric salen catalyst (D) were recycled as catalysts in the asymmetric HKR of ECH. The series of epichlorohydrine HKR in which the chiral Co(III)-(PF_6) polymeric salen catalyst (D) could be reused for seven times after simple separation of products. These polymeric salen catalyst (D) were reused after simple washing with a CH_2Cl_2 solvent and drying under vacuum at 60 °C. Whereas, as can be seen in Fig. 2, the Co(III)-(OAc)-type polymeric salen catalyst (D) must be regenerated with acetic acid in air after evaporation of products to enable their repeated use in asymmetric HKR of ECH. The enantiomeric excess became reduced to 20% by using the conventional Co(III)-(OAc)-type polymeric salen catalyst (D) in the second hydrolysis reaction, if not regenerated by HOAc in air. This is due to the reduction of Co(III) to Co(II). The chiral Co(III)-(PF_6) polymeric salen catalyst (D) exhibited the same enantioselectivity up to 99% ee through the repeated use for six times in HKR of 1,2-epoxybutane.

The important feature in the HKR of ECH by using Co(III)-(PF_6)-type polymeric salen catalyst (D) is that no racemization is found not only during the distillation but also after attaining the highest ee% value of epoxide. The enantioselectivity of ECH on Co(III)-(PF_6) catalyst has not changed more or less until 48 h, showing up to 99% ee. In contrast, racemization of ECH was observed to take place with Co(III)-(OAc)-type polymeric salen catalyst (D) during the reaction and product distillation as can be seen in Fig. 2. The ee% of product epoxide became decreased slowly via racemization over this –(OAc) containing polymeric salen catalyst.

4. Conclusion

The new Co(III)-(PF_6)- and Co(III)-(BF_4)-type polymeric chiral salen catalysts showed to be effective in the asymmetric HKR of epoxides with promising enantioselectivities. The catalysts could be recovered and reused several times without loss of activity and stereoselectivity. On the basis of asymmetric HKR of various epoxides, the polymeric chiral (salen) complexes obtained by the present procedure can be applied as effective heterogenized catalysts for the asymmetric reactions.

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