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Enantioselective hydrolytic kinetic resolution of epoxides catalyzed by chiral Co(III) salen complexes immobilized in the membrane reactor

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The supported ZSM-5 film was synthesized hydrothermally on the porous supports such as Anodisc and alumina tube. The enantioselective hydrolytic resolution of racemic epoxides was performed in the ZSM-5/Anodisc membrane reactor containing chiral salen complexes. The chiral (Co-salen)$^+$PF$_6^-$ and (Co-salen)$^+$BF$_4^-$ complexes immobilized on the membrane showed a very high enantioselectivity and recyclability in the hydrolysis of epichlorohydrine, 1,2-epoxybutane, 1,2-epoxyhexane and styrene oxide. It was easy to separate the products, and the catalysts could be recycled without observable loss in activity and enantioselectivity using the batch-type and continuous-type membrane reactor. The obtained epoxide product remained in the organic phase and the hydrophilic water-soluble diols diffused into the aqueous phase through the ZSM-5 film layer.

KEY WORDS: enantioselectivity; immobilization; ZSM-5/Anodisc membrane reactor; chiral salen complexes; racemic epoxides.

1. Introduction

The syntheses of optically pure chemicals have gained significant potential over recent years. The heterogeneous chiral catalysts offer practical advantages of the facile separation from reactants and products, as well as recovery and reuse. Attaching the chiral ligands covalently via a suitable functional linker or tether to the support is by far the most important, because the optical purity of the product can vary with the length and the flexibility of the spacer and the pore size affects the enantioselectivity [1–4]. Several immobilization strategies have been shown to give stable and active heterogeneous catalysts. It has been well known that the chiral salen complexes of Co(III) are very enantioselective for the asymmetric hydrolysis (HKR) of terminal epoxides to obtain the optically pure epoxides and diols [5–10]. Epichlorohydrine (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 are extremely versatile synthetic intermediates. These recently developed chiral salen–based catalysts are appealing candidates for covalent attachment of homogeneous salen ligands to the solid supports, and for the development of new methods for the recycling of chiral catalysts. On the basis of these facts, our attention was directed to the development of optically active catalysts desirable for repeated use without any treatment after HKR reaction.

In recent years, the dramatic development of membranes has drawn much attention in view of promising applications as a separation membrane and catalytic reactor. The zeolite has been used as a component in the composite membranes, and zeolite membranes have been synthesized by *in situ* hydrothermal synthesis on the flat surfaces of supports. Especially, there is strong interest in zeolite membranes due to the molecular sieving properties and the mechanical and structural stability. The unsupported self-standing films of zeolite have been obtained by traditional wet hydrothermal synthesis [11–14] and by solid-state transformation [15]. Sano *et al.* have prepared the pure film of ZSM-5 zeolite by controlling the composition ratio of the synthesis mixture without stirring [11,12]. The supported zeolitic films have been widely and deeply investigated. The catalytic membrane system represents one of the most promising areas for the development of membrane catalysis [16]. It allows separation of the reagents with markedly different polarities without the need for a mutual solvent and to increase the conversion of the reactant. In order to obtain high productivity, a thin mesoporous membrane with a high catalyst volume fraction has to be applied.

The catalytic reactors installed with inorganic membranes can increase the reaction conversion beyond the chemical equilibrium. Besides gas separation, zeolite membranes have been applied for the optical resolution of racemic lactic acid [17]. The combination of enantioselective hydrolytic resolution reactions, mentioned above, with membrane processes can provide alternatives to separations and to chemical conversions that are troublesome or impossible using classical methods

Here, in this study, the chiral Co(III) salens immobilized on ZSM-5/Anodisc membrane were applied as catalysts in the hydrolytic kinetic resolution of terminal

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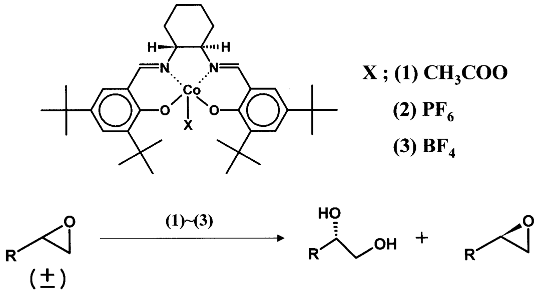

Scheme 1. The structure of catalysts and hydrolytic kinetic resolution system.

epoxides. Therefore, Co(III) salen complexes have resulted in a very high diol yield and ee% and the biphasic organic/aqueous membrane reactor is maintained to separate the product as a optically pure isomer. To the best of our knowledge, the work reported here is the new route to synthesize the optically pure epoxides using a membrane reactor. No attempt has been made to hydrolyze the racemic epoxides to diols enantioselectively using an immobilized chiral salen complex in the inorganic membrane.

2. Experimental

2.1. Preparation of catalysts

For this study, the conventional Jacobson's catalyst was prepared according to the procedure reported in the literature [5–9]. The compound of (1*R*,2*R*)-(−)-*N,N′*-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexane diaminocobalt(II) (Aldrich Chemical Co. Inc) was treated with a dehydrated acetic acid in toluene at room temperature under air for 2 h.

We have also synthesized (salen) Co catalysts containing different count-anions and these newly synthesized chiral salen Co(III) complexes (**2**, **3**) have been applied as catalysts to investigate the effect of catalyst structure on the enantioselectivity in the HKR of terminal epoxides. For the synthesis of catalysts (**2**) or (**3**), the chiral salen (1*R*,2*R*)-(−)-*N,N′*-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediamino cobalt(II) was treated with ferrocenium hexafluorophosphate or ferrocenium tetrafluoroborate in acetonitrile solvent under air respectively. The mixtures were concentrated to dryness and washed with hexane to remove the side product, ferrocene. These catalysts will be denoted as Co(III)-(PF_6) and Co(III)-(BF_4).

2.2. Membrane reactor

The supported ZSM-5 film was synthesized hydrothermally on the porous support (Anodisc 47; Whatman Co., pore size) from the reaction mixture of SiO_2-$0.13Na_2O$-$52H_2O$-0.12 TPAOH composition at 170 °C in an autoclave. The ZSM-5 crystals grown on the porous matrix were very closely bound together.

The method for impregnation of the homogeneous complex at the interface between macroporous matrix (Anodisc 47) and ZSM-5 film layer is shown in figure 1. The salen Co(III) complexes were loaded into the macropore of Anodisc 47 by impregnation under vacuum. The salen catalyst must exist near the interface of ZSM-5 film to contact with both biphasic reactants such as epoxides and water.

Figure 2 shows the configuration of a membrane reactor system. The chiral salen Co(III) complexes were used as catalysts in a biphasic membrane reactor, wherein the two phases exist separately. One reaction vessel separated by the membrane was filled with water and the other with racemic epoxide in the presence of dichloromethane as shown in figure 2.

The surface of Anodisc layer, on which the chiral salen was immobilized, was contacted with water and the other side (ZSM-5 layer) was wetted by the organic phase such as reactants (epoxide) and solvents. The actual Jacobsen's catalyst having *tert*-butyl groups cannot diffuse into the pore channel of ZSM-5 crystals. Furthermore, because the chiral salen catalyst is insoluble in water, the loading of chiral salen was maintained in the membrane layer without extraction during the reaction.

As a result, this membrane reactor combines the chemical reaction with the continuous extraction of products at the same time. The obtained epoxide product remained in the organic phase and the hydrophilic water-soluble diols could diffuse into the aqueous phase

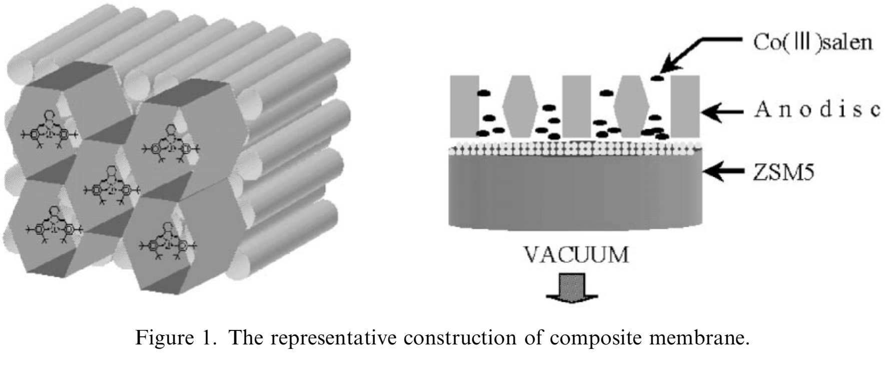

Figure 1. The representative construction of composite membrane.

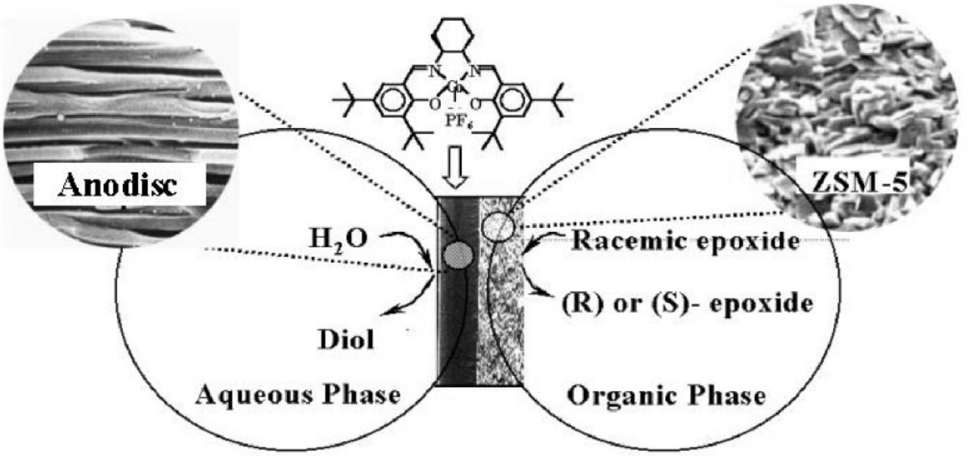

Figure 2. ZSM-5/Anodisc membrane system used in the enantioselective HKR of racemic epoxides.

across the ZSM-5 film layer. The asymmetric hydrolysis of epoxides with water was performed over the chiral Co(III) salen catalysts deposited on the membrane at room temperature.

The synthesized ZSM-5 materials were characterized by TEM and XRD. The ee% values were determined by capillary GC using a chiral column (Chiral DEX-TM, Gamma-cyclodextrin trifluoroacetyl, 40 m × 0.25 mm i.d. (Alltec)).

3. Results and discussion

Figure 3 shows the X-ray diffraction pattern of ZSM-5 film grown on the substrate. As shown in figure 3, the diffraction pattern of hydrothermally synthesized ZSM-5 film is essentially same as that of powder ZSM-5 crystal. Other crystalline phases were not observed in the X-ray diffractogram of calcined products. Kiyozumi *et al.* [13] have studied the synthesis of oriented ZSM-5 zeolite film on mercury surface. They reported that the strong (0*k*0) and (*h*00) diffraction lines were always recognized in the X-ray pattern of mercury side film, indicating that the crystals are oriented. However, the X-ray diffraction pattern shown in figure 3 indicates that the zeolitic film is not oriented but intergrown.

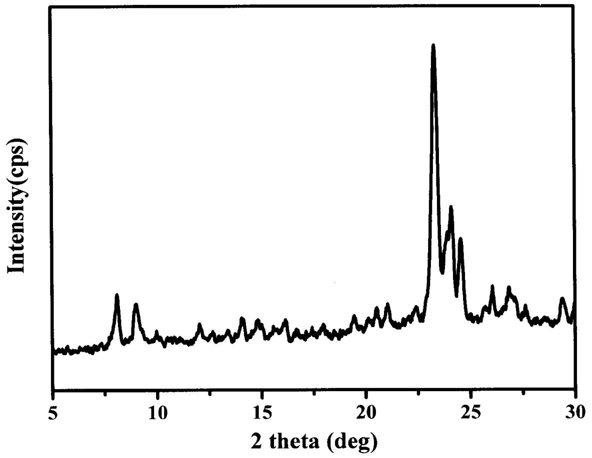

Figure 3. X-ray diffraction pattern of the ZSM-5 membrane.

Figure 4 shows the SEM images of purely siliceous ZSM-5 grown on the surface of porous support. The zeolite crystals in the film were obtained as the intergrown aggregates as can be seen in figure 4(c). The chiral salen Co(III) complexes (@15 Å) did not diffuse into the pore of ZSM-5 membranes, indicating that the zeolite film has grown without pinholes in the layer. The surfaces of porous substrates were fully covered with ZSM-5 crystals as the crystallization time was prolonged (figure 4(f)).

The trends in the reactivity and enantioselectivity of (salen) Co(III) complexes were examined first for the hydrolytic resolution of epoxides in the batch-type reactor. Epichlorohydrine, 1,2-epoxybutane and styrene oxide of racemic form were hydrolyzed efficiently over Co(III)-OAc-type chiral salen catalysts (**1**) at 20 with a very high enantioselectivity of up to 98 ee%. The well-known chiral Co(III) salen catalyst, active for HKR, has OAc group, which was weakly attached to a cobalt. After HKR reaction, –OAc group became dissociated, and then the catalyst showed no activities when they were reused under the same reaction conditions without regeneration treatment. However, Co(III)-(PF_6) and (BF_4) salen complexes (**2**, **3**) showed the superior catalytic activities to those obtained by the conventional chiral (salen)Co(III)-(OAc) catalyst (**1**). It is noteworthy that the salen Co(III)-(PF_6) catalyst (**2**) could be recycled without observable loss in activity, and it was reused for further catalytic reactions. Use of Co(III)-(PF_6) and (BF_4) type salen catalysts avoided the necessity of further treatment after separation of products.

These catalysts were selected for use as catalysts in the membrane reactor system. The optically pure epoxides could be obtained enantioselectively in the ZSM-5/Anodisc membrane reactor containing chiral salen complexes as can be seen in figure 2. The results obtained in the asymmetric HKR are summarized in

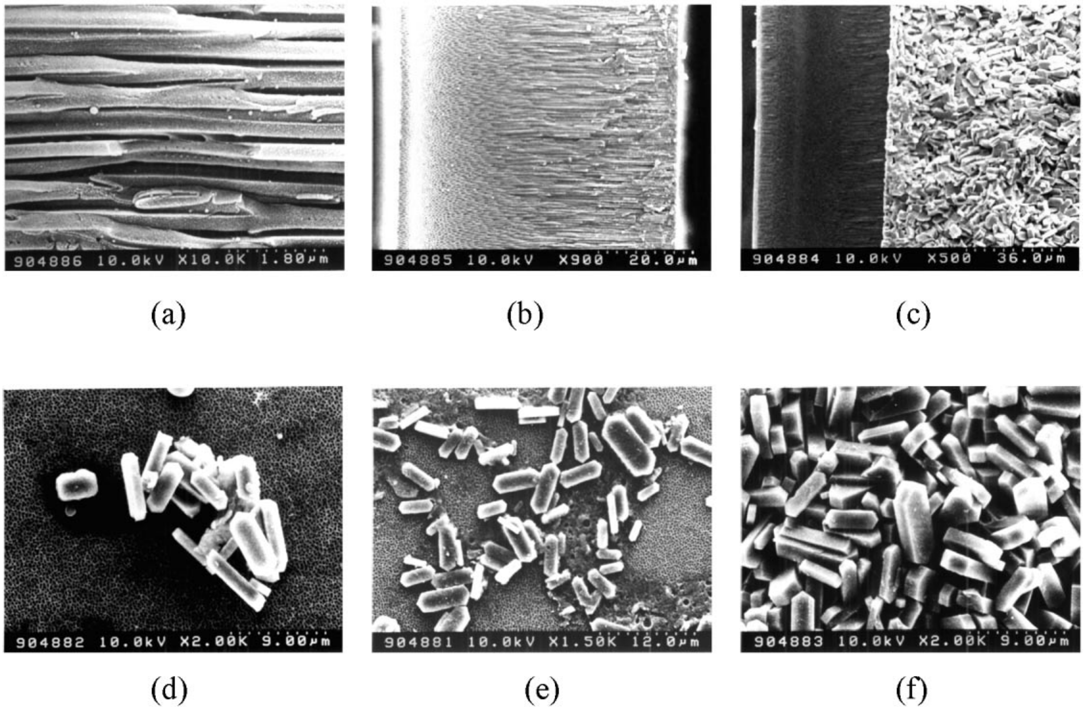

Figure 4. SEM images of ZSM-5 crystal film grown on the Anodisc support. (a) Enlargement of (b), (b) cross-section of Anodisc 47, (c) cross-section of ZSM-5 crystal grown on Anodisc, and ZSM-5 crystallized with different reaction time; (d) 7 h, (e) 16 h, (f) 48 h.

figure 5. As shown in figure 5, the ee% of epoxides increased linearly as the conversion of the reactant increased in the membrane reactor system. The conversions and enantioselectivities have increased with the prolonged reaction time. The turnover rate became slow with increased reaction time, indicating the reduced diffusive transport of the substrate with the increasing product concentration. These phenomena are also shown for the reaction performed in the batch-type reactor. The reaction using the ZSM-5/Co(III) salen membrane reactor gave almost the same selectivity as compared to homogeneous salen catalysts used in the batch-type reactor, when the hydrolysis reaction had been terminated. By using the immobilized chiral salen membrane catalysts, the product separation became easier and the catalyst could be recycled without observable loss in activity. When the organic-phase feed stream containing a reactant epoxide was contacted with the catalyst at the interface of membrane, the epoxide remained in an organic phase and the converted hydrophilic diol diffused into the aqueous phase on the other side. After using Co(III)-(PF_6) complex (**2**) immobilized on ZSM-5/Anodisc membrane, the resultant solutions exhibited no color and Co(III) salen complex was not detected both in the aqueous and organic solution. This means that Co(III) salen complexes immobilized on the membrane exist in the pore system without any extraction during the reaction. The catalyst in membrane could be recycled many times by filling the reactants in the separated reactor. The catalytic activity and selectivity of Co(salen) complexes

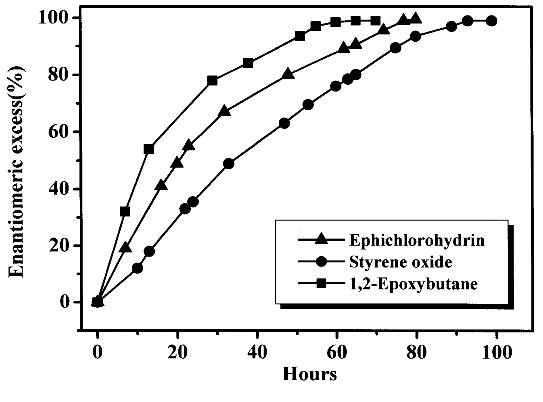

Figure 5. Enantioselectivities of Co(salen) complex (**2**) for the HKR using different racemic epoxides.

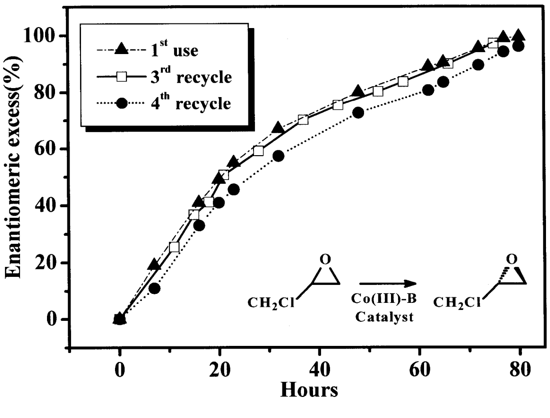

Figure 6. Enantioselectivities and recycle ability of Co(salen) complex (**2**) investigated in the batch-type membrane system.

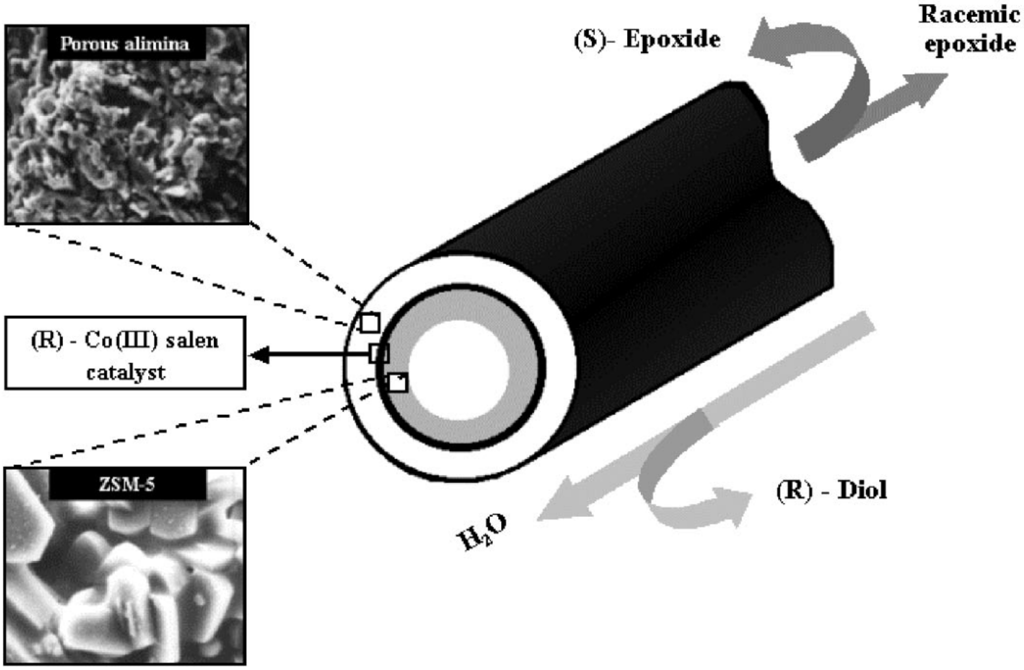

Figure 7. Schematic of continuous flow-type ZSM-5/alumina membrane reactor system for the enantioselective HKR of epoxides.

(**2** and **3**) had not changed more or less after reusing four times, as shown in figure 6. Co(III)-(PF_6) complex (**2**) in the membrane had exhibited high optical purity of product (up to 99.8 ee%) during the repeated reuse in the hydrolysis reaction, but prolonged reaction time was needed as the number of recycle was increased. However, Co(III)-(OAc) complex (**1**) must be regenerated with acetic acid under air for reuse as a catalyst. This is due to the reduction of Co(III) to Co(II).

The catalytic activity of $(\text{Co-salen})^+PF_6^-$ complex was also investigated in the continuous-type membrane reactor system for the kinetic resolution of epoxides. The general procedure of asymmetric hydrolysis using a continuous-type reactor is same as the batch-type reactor system. The continuous-type reactor system used in this study is shown in figure 7. The organic and the aqueous phases were separately circulated in the two circuits following the criteria that the organic phase, containing the substrate epoxide, was circulated along the side of the ZSM-5 layer. Because the $(\text{Co-salen})^+PF_6^-$ complex is insoluble in water, the salen catalyst is entrapped at the interface between the microporous ZSM-5 layer through which the salen cannot pass and the macroporous layer of alumina as shown in figure 7. The salen catalyst was treated to exist near the interface of ZSM-5 film and porous alumina by vacuum for easy contact with both biphasic reactants. The hydrophilic product diol diffused into the aqueous phase through the macropore, whereas the unreacted optically pure epoxide remained in the organic phase. A countercurrent flow was chosen for the circulation of the two separated phases.

The terminal epoxides were readily catalyzed by ZSM-5/porous alumina membrane catalyst. The results of epoxide hydrolysis, preformed in the continuous membrane system, are summarized in table 1. It

Table 1
Enantioselective hydrolysis of terminal epoxides to diols by ZSM-5/porous alumina membrane containing the various chiral Co(III) salen catalysts

Entry	Catalyst	Substrate	Time (h)	Epoxide yield (%)	Epoxide (ee%)	Diol (ee%)
1	2	Epichlorohydrin	27	45	99	96
2	3	Epichlorohydrin	27	45	99	96
3	2	Styrene oxide	56	38	98	94
4	3	Styrene oxide	56	38	98	95
5	2	1,2-Epoxyhexane	40	42	98	98
6	3	1,2-Epoxyhexane	40	42	98	98
7	2	α-pinene oxide	48	38	87	82
8	3	α-pinene oxide	48	38	84	70

Note: Catalyst: 2 = $(\text{Co-salen})^+PF_6$, 3 = $(\text{Co-salen})^+BF_4^-$.

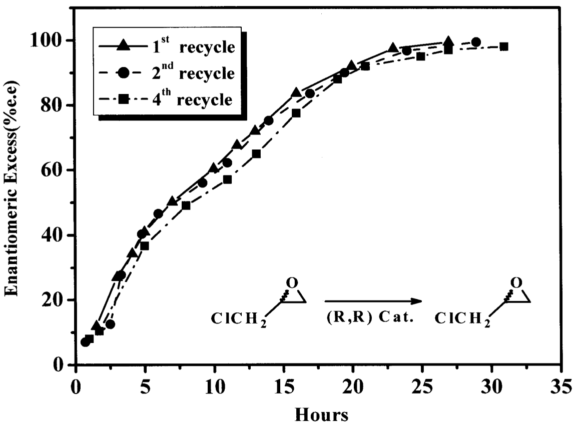

Figure 8. Asymmetric catalytic activity and recycle ability of Co(salen) complex (**2**) obtained in the continuous flow-type membrane system.

was found that the hydrolysis reaction and product separation were carried out simultaneously using the heterogenized salen complexes in the membrane. Epichlorohydrine, styrene oxide, 1,2-epoxyhexane and α-pinene oxide gave a very high yield and ee% of epoxide or diol over the chiral Co(III) salen complex immobilized in the membrane reactor.

The catalytic activity and selectivity of Co(salen) complexes have not changed more or less after reusing four times, as shown in figure 8. It is noteworthy that the chiral Co(III)-(PF_6) salens in the membrane could be recycled without observable loss in activity and it was reused for further catalytic reactions. Use of Co(III)-(PF_6)-type salen catalysts in the membrane system avoided the necessity of further treatment after separation of products. However, the salen Co(III)-(OAc) catalysts must be regenerated with acetic acid in air to enable the repeated use in HKR of ECH. The enantiomeric excess reduced by using the conventional (Co-salen)-OAc catalyst in the second hydrolysis reaction, if not regenerated by HOAc under air.

In conclusion, the asymmetric hydrolysis of the terminal and mesoepoxides to diols using the heterogenized catalysts can be applied with success by using the zeolite membrane reactor. A high enantioselectivity was attainable on the Co(III) salen catalysts. On the basis of asymmetric hydrolytic resolution of various epoxides, the chiral (salen) complexes immobilized on mesoporous material by the present procedure can be applied as an effective heterogenized catalyst for the asymmetric reactions performed in the biphasic organic/aqueous condition. This enantioselective catalytic membrane system adopted in this study may be of interest for the application of new reactions. The catalyst in membrane could be recycled again by filling the reactants in the separated reactor. The catalytic activity and selectivity of Co(salen) complexes have not changed after recycle.

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