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ARTICLE

A Poly(hydroxyethyl methacrylate)-Immobilized Chiral Manganese(III)salen Catalyst for Asymmetric Epoxidation of α-Methylstyrene

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Abstract: Phenylalaninol was introduced in the C5 and C5′ position of a chiral Mn(III)salenCl compound, and the catalyst was then immobilized on poly(hydroxyethyl methacrylate) (pHEMA) by axial coordination. The catalytic system, with (*R*,*R*)(*R*,*R*)pHEMA-immobilized Mn(III)salenCl as catalyst and [bmim]PF_6 as reaction medium, gave excellent catalytic activity and enantioselectivity with 80%–91% ee values and 84%–92% yields for the asymmetric epoxidation of α-methylstyrene. The catalyst can be reused several times without significant loss of catalytic activity. This was due to a chiral synergy between the chiral carbons of the amino alcohol and the chiral carbons of (*R*,*R*)-diaminocyclohexane.

Key words: poly(hydroxyethyl methacrylate); immobilized Mn(III)salen; asymmetric epoxidation; α-methylstyrene; ionic liquid

Metal catalyzed oxidation of organic substrates is of immense importance for chemical and biochemical syntheses. Schiff-base compounds which mimics cytochrome P-450 [1,2] have been developed as catalysts for various asymmetric reactions [3–7]. Various researchers have studied these chiral Mn(III)salen species from the aspects of the design and synthesis of salen ligands and the investigation of steric and electronic effects of the catalyst structure on stereoselectivity and the mechanism of the asymmetric induction [8]. Many epoxides have been successful reacted due to the remarkable stereoselective activity of the chiral diamine of the Jacobsen-like catalyst, but the oxidation catalyzed by a chiral amino alcohol accompanying the chiral diamine of Jacobsen-like derivatives has appeared only recently [9,10]. In our study, we have incorporated chiral phenylalaninol into a Mn(III)salen compound as a homogeneous catalyst.

While a homogeneous catalyst often gives the best enantioselectivity, a heterogeneous catalyst offers the advantages of simplified product purification and recycling of the catalyst. To allow recovery for reuse, a number of supports with high molecular weights have been synthesized and studied [11,12]. Among the many solid supports, a polymer to support the active species has the advantages of ease of handling, recovery, separation, and recycling [13,14]. Our group has used poly(hydroxyethyl methacrylate) (pHEMA) as the solid carrier because it contains abundant hydroxyls, which are highly polar and active. The salen monomer was incorporated onto pHEMA by a coordinate bond similar to that reported in the literature from other methods including non-covalent immobilization, inorganic graft, and copolymerization [15].

The solid-immobilized catalyst can suffer some loss from some catalyst leached from the solid carrier in the catalytic cycle. In order to prevent the small loss of catalyst, an ionic liquid ([bmim]PF_6) as a 'liquid carrier' was used as the reaction medium. The catalytic system, which was the Mn(III)salen compound grafted onto pHEMA by coordinate bonds and then dispersed into the ionic liquid, effectively prevented catalyst loss. To make up for the lower activity of the supported catalyst as compared with the homogeneous catalyst, a chiral amino alcohol (phenylalaninol) was introduced into the Mn(III)salen compound to increase the enantioselective epoxidation of α-methylstyrene. The synergy between the chiral carbon of the amino alcohol present in the C5 and C5′ positions and the chiral carbon of diaminocyclohexane was investigated.

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1 Experimental

(*R*,*R*)-1,2-diaminocyclohexane, 3-*tert*-butyl-2-hydroxybenzaldehyde, and tin(IV)tetrachloride was obtained from Alfa Aesar Chemical Co. Paraformaldehyde, manganese acetate, and 2-amino-3-phenyl-1-propanol were laboratory grade reagents from local suppliers. All other chemicals were reagent grade and used as received.

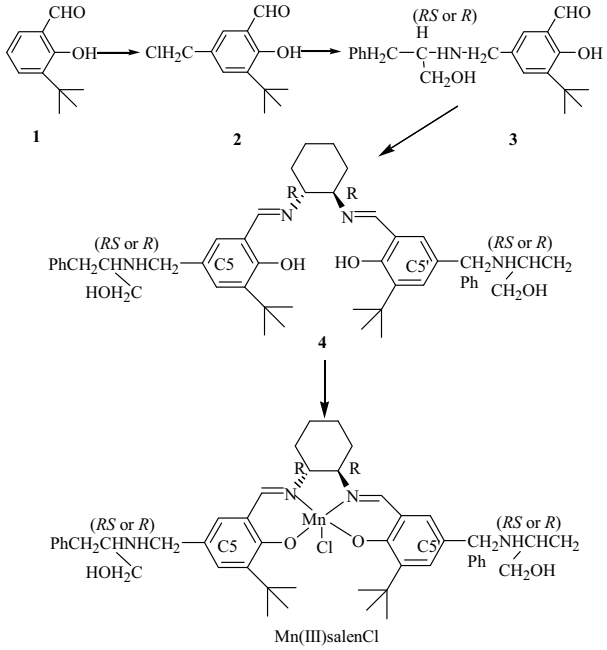
UV-Vis and Fourier transform infrared (FT-IR) spectra, respectively, were recorded from 200 to 800 nm on a UV-3310 spectrophotometer and from 400 to 4000 cm^{-1} on a Nicolet AVATAR 330 FT-IR spectrometer (using KBr pellets). The high performance liquid chromatography (HPLC) analysis was carried out on a Shimadzu instrument (system controller: LC-10AT VP; UV-Vis detector: SPD-10A VP) and the chiral stationary phase column was Daicel Chiralcel OD-H manufactured by Daicel Chemical Industries Ltd. ^{1}H NMR spectra were obtained on a Bruker MSL300 spectrometer operating at 400 MHz.

1.1 Catalyst preparation

The chiral Mn(III)salenCl catalyst 1 and 2 were obtained by the synthesis sequence given in Scheme 1. A mixture of 3-*tert*-butyl-2-hydroxybenzaldehyde (**1**, 17.98 mmol), paraformaldehyde (39.39 mmol), and tetrabutylammonium bromide (1.72 mmol) in 12 ml of concentrated hydrochloric acid was stirred vigorously at 40 °C for 72 h [16]. The reaction mixture was repeatedly extracted with ethyl acetate (15 ml × 5) and the organic phase was washed with 5% $NaHCO_3$ (10 ml × 5) and brine (10 ml × 2), then dried by $MgSO_4$. The solvent was removed by vacuum and 3-*tert*-butyl-5-chloromethyl-2-hydroxybenzaldehyde (**2**) was isolated as a yellow crystalline solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.33 (s, 9H), 4.62 (s, 2H), 7.41 (s, 1H), 7.43 (s, 1H), 10.24 (s, 1H). ^{13}C NMR ($CDCl_3$, 400 MHz): δ 30.5, 31.9, 46.9, 128, 129, 130, 133, 138,157, 192.

3-*tert*-Butyl-5-chloromethyl-2-hydroxybenzaldehyde (16 mmol), 2-amino-3-phenyl-1-propanol (16 mmol), and triethylamine (16 mmol) in 100 ml of toluene was stirred under refluxing for 8 h. The reaction mixture was allowed to cool down to room temperature and then it was poured into water (100 ml). The solution was extracted with dichloromethane (15 ml × 5). The organic layer was washed with brine (10 ml × 2), dried by $MgSO_4$, and concentrated and purified by column chromatography (SiO_2, petroleum/acetic ether = 5/1, v/v) to generate a dark yellow oily compound **3** of 3-*tert*-butyl-2-hydroxy-5-((1-hydroxy-3-phenylpropan-2-ylamino)methyl)benz aldehyde. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.33 (s, 9H), 2.66 (d, 2H), 3.10 (m, 1H), 3.59 (m, 2H), 3.82 (s, 2H), 7.08–7.24 (m, 7H), 10.24 (s, 1H). ^{13}C NMR ($CDCl_3$, 400 MHz): δ 30.5, 31.9, 52.9, 58.1, 66.3, 126–128, 133, 138, 156, 192.

(*R*,*R*)-1,2-diaminocyclohexane (6 mmol) and K_2CO_3 (12.3 mmol) in ethanol were stirred. The resulting mixture was heated to reflux (75–80 °C) and a solution of compound **3** (12 mmol) in ethanol was added in a steady stream. The yellow solution was refluxed for 8 h with stirring. The reaction mixture was cooled to room temperature and collected by vacuum filtration. The crude solid was redissolved in dichloromethane (50 ml) and washed with deionized water (15 ml × 2) and brine (10 ml × 2). After drying over $MgSO_4$, the solvent was concentrated and purified by column chromatography (SiO_2, petroleum/acetic ether = 1/5, v/v) to generate a dark yellow oily chiral compound **4**. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.33 (s, 8H), 1.39–1.88 (m, 8H), 2.66 (d, 2H), 3.05 (m, 2H), 3.10 (m, 2H), 3.59 (m, 4H), 3.82 (s, 4H), 6.95–7.21 (m, 14H). 8.18 (s, 2H). ^{13}C NMR ($CDCl_3$, 400 MHz): δ 23, 25, 30.5, 31.9, 40, 52.9, 58.1, 60, 66.3, 126–128, 136, 138, 156, 161.



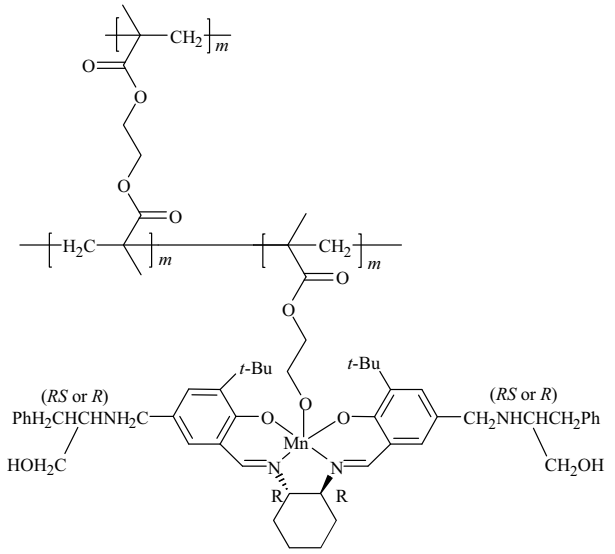
Catalyst 1 = (*R*,*R*)(*RS*,*RS*)Mn(III)salenCl

Catalyst 2 = (*R*,*R*)(*R*,*R*)Mn(III)salenCl

Scheme 1. Route for the preparation of the chiral Mn(III)salenCl compound.

Under vigorous stirring, 15 ml of ethanol containing 8 mmol of manganese acetate was added dropwise to 15 ml of ethanol solution containing 4 mmol of chiral compound **4** under nitrogen protection. The mixture was refluxed for 5 h, then 10 ml of ethanol containing 24 mmol of lithium chloride was added to the mixture under stirring for 3 h. After the reaction was over, the crude product was collected by filtration, redissolved in dichloromethane (50 ml), and washed with distilled water (15 ml × 2) and brine (10 ml × 2). After the solvent was concentrated, chiral Mn(III)salenCl was obtained and dried under vacuum. FT-IR (KBr, cm^{-1}): ν 3520, 3120, 3040, 2610, 1612, 1540, 1490, 1280, 1175, 990, 460, 310.

The pHEMA-immobilized Mn(III)salenCl compound (Scheme 2) was prepared as follows. pHEMA powder (1.10 g) was refluxed in an aqueous solution of sodium hydroxide (100



Catalyst 3 = (*R*,*R*)(*RS*,*RS*)pHEMA-immobilized Mn(III)salenCl

Catalyst 4 = (*R*,*R*)(*R*,*R*)pHEMA-immobilized Mn(III)salenCl

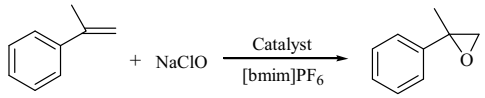
Scheme 2. Route for preparation of the chiral pHEMA-immobilized Mn(III)salen compound.

ml, 13.3 mmol/g) for 3 h. The solid was filtrated and washed with distilled water until pH 7, and dried at 120 °C in an oven. A white powder was obtained under vacuum, which was designated as Na(pHEMA).

A mixture of Mn(III)salenCl (1.0 mmol) and Na(pHEMA) (2.0 g) was added into ethanol (60 ml) and stirred for 8 h under refluxing. The suspension was then filtrated, washed thoroughly with ethanol and CH_2Cl_2 to produce pHEMA-immobilized Mn(III)salenCl as small yellow powder particles. The CH_2Cl_2 filtrate was examined by FT-IR until there was no Mn(III)salenCl (with CH_2Cl_2 as reference) peak. FT-IR (KBr, cm^{-1}): *ν* 3520, 3120, 3040, 2610, 1728, 1725, 1627, 1540, 1490, 1280, 1175, 990, 471, 310.

1.2 Enantioselective epoxidation of unfunctionalized α-methylstyrene

The enantioselective epoxidation of α-methylstyrene (Scheme 3) was performed by the following procedure. First, 2 mmol of α-methylstyrene and 0.4 mmol of axial base NH_4OAc were added to 4 ml of [bmim]PF_6 containing 0.2 mmol of catalyst (10 mol% based on the mol of the α-methylstyrene) under stirring at 0 °C. A solution of Na_2HPO_4 (0.05 mol/L) was added to a pre-cooled solution of aqueous NaClO (0.58 mol/L) as an oxidant. The pH value of this mixed solution was accurately adjusted to 11.3 by the slow addition of HCl (1 mol/L) or NaOH (1 mol/L). After the reaction, 20 ml of *n*-hexane was directly added to the reaction mixture. The *n*-hexane phase was separated and concentrated under reduced pressure, then the residue was purified by column chromatography (SiO_2, petroleum ether/CH_2Cl_2 = 2/1, v/v) to obtain the epoxides. The ionic liquid containing the catalyst was separated for recycling. The



Scheme 3. Enantioselective epoxidation of α-methylstyrene in [bmim]PF_6.

reaction products were analyzed by HPLC using UV-detection at wavelength 254 nm; eluent agent: *n*-hexane/*i*-PrOH = 99/1, v/v; flow rate: 0.8 ml/min; column pressure: 2.0–3.0 MPa; column temperature: 25 °C.

2 Results and discussion

2.1 FT-IR spectra

The FT-IR spectrum of Na(pHEMA) in Fig. 1 showed one peak characteristic of the alcoholic group at 3475 cm^{-1} (stretching C–O). Ester groups were identified by the peaks at 1728 cm^{-1} (C=O stretching) and 1175 cm^{-1} (C–O stretching). The other peaks were C–C and C–H vibrations of $–CH_3$ and $–CH_2$ groups. The peak at 519 cm^{-1} of pHEMA-immobilized Mn(III)salen was due to the Mn–N bond. The FT-IR spectrum of pHEMA-immobilized Mn(III)salen also showed an absorption band at 1578 cm^{-1}, which was assigned to the C=N vibrations of the imines present in the Mn(III)salenCl compound. This proved that the Mn(III)salenCl was successfully immobilized onto the Na(pHEMA) [17].

2.2 UV-Vis spectra

The UV-Vis spectra of neat chiral Mn(III)salenCl and pHEMA-immobilized Mn(III)salenCl **a**re shown in Fig. 2. The peak at 433 nm was assigned to charge-transfer transitions between the metal and ligand. The peak at 508 nm was assigned to the *d*-*d* transitions in the Mn(III)salenCl compound [18]. pHEMA-immobilized Mn(III)salenCl, in which the pHEMA was attached by the direct axial coordination of the metal center, exhibited a red shift in the wavelength ranges

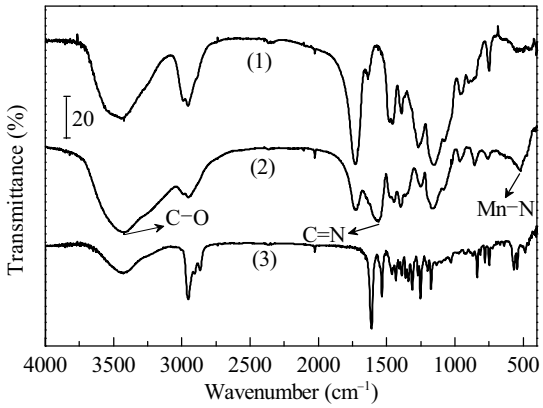


Fig. 1. FT-IR spectra of different compounds. (1) Na(pHEMA); (2) pHEMA-immobilized Mn(III)salenCl; (3) Mn(III)salenCl.

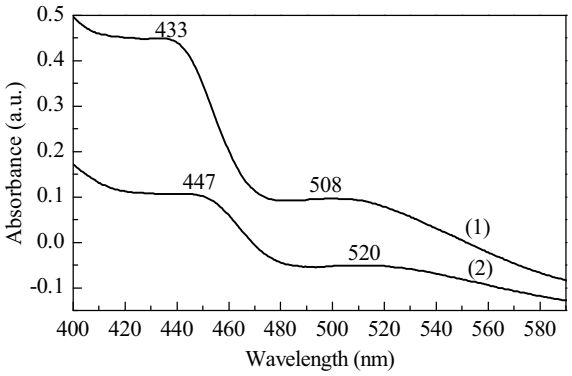


Fig. 2. UV-Vis spectra of Mn(III)salenCl (1) and pHEMA-immobilized Mn(III)salenCl (2).

from 433 to 447 nm and from 508 to 520 nm, which were due to the strong coordination between the metal center and the hydroxy group of the pHEMA. These findings proved that the Mn(III)salenCl was bonded onto the pHEMA compound.

Table 1 summarizes the catalytic performance of the pHEMA-immobilized Mn(III)salenCl and Mn(III)salenCl in the enantioselective epoxidation of unfunctionalized α-methylstyrene. In the chiral induction, the first cycle results of catalyst 1 for asymmetric epoxidation of α-methylstyrene in pure [bmim]PF_6 gave the ee value of 80% and yield of 85%. However, in the third recycle, the ee value decreased to 56%. Chiral (*R*)-phenylalaninol was added in the C5 and C5′ position of catalyst 1 and (*R*,*R*)(*R*,*R*) Mn(III)salenCl named catalyst 2 was obtained. Compared with catalyst 1, the catalytic performance of catalyst 2 was better, with the yield increased from 85% to 90% and ee value increased from 80% to 93% in cycle 1. Overall, the change from the racemic phenylalaninol of catalyst 1 to (*R*)-phenylalaninol of catalyst 2 gave increases in the yield and ee value of the epoxide. However, the ee values for epoxidation catalyzed by catalyst 2 reduced rapidly from 93% to 64% over three recycles. *n*-Hexane as an extractant was detected by FT-IR. FT-IR spectra of the extraction solvent in the second and third recycles showed the characteristic absorption peak of the Mn(III)salenCl catalyst. This proved that the process had the problem of the loss of Mn(III)salenCl catalyst from the ionic liquid in the recycling, which resulted in the low ee values and yields of α-methylstyrene epoxide after the ionic liquid [bmim]PF_6 containing Mn(III)salenCl catalyst was recycled only three times.

Table 1 Epoxidation of α-methylstyrene catalyzed by Mn(III)salenCl and pHEMA-immobilized Mn(III)salenCl with ionic liquid [bmim]PF_6 as reaction medium

Catalyst	ee[a]/yield[b] (%)				
	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5
Catalyst 1	80/85	72/72	56/50	—	—
Catalyst 2	93/90	85/78	64/61	—	—
Catalyst 3	79/86	76/84	74/83	72/81	70/79
Catalyst 4	91/92	89/90	87/89	83/87	80/84

Reaction conditions: α-methylstyrene 2 mmol, catalyst 0.2 mmol (10 mol%), NaClO 5.8 mmol, NH_4OAc 0.4 mmol (20 mol%).

[a]Determined by HPLC over a chiral OD-H column.

[b]Yield of the isolated epoxide.

In order to reduce catalyst loss, the Mn(III)salenCl catalyst was immobilized on the pHEMA by coordinate bonds, and then dispersed in the ionic liquid. This catalytic system, named as a double-immobilized system, effectively prevented catalyst loss. The catalytic performance of the heterogeneous catalyst was compared with the corresponding ee values of the homogeneous catalyst (catalyst 1 vs catalyst 3, catalyst 2 vs catalyst 4). In the five recycles, the ee values were only slightly degraded (70% < ee < 79% by catalyst 3, 80% < ee < 91% by catalyst 4). This showed that the recycle ability of the double-immobilized system was improved and catalytic activity was well maintained.

With respect to increasing the ee value, it was evident that the catalytic performance of catalyst 4 was improved as compared to catalyst 3, with the yield increased from 86% to 92% and ee value increased from 79% to 91% in cycle 1. Meanwhile, the ee value still reached 80% in the fifth recycle. The increase in activity and selectivity was attributed to the chiral synergy between the chiral carbons of (*R*)-phenylalaninol and the chiral carbons of (*R*,*R*)-diamino-cyclohexane. The experimental data showed that the catalytic system with (*R*,*R*)(*R*,*R*)-pHEMA-immobilized Mn(III)salenCl as catalyst and [bmim]PF_6 as reaction medium for the asymmetric epoxidation of α-methylstyrene exhibited excellent catalytic activity and enantioselectivity with 91%–80% ee values and 92%–84% yields, and the catalyst can be reused several times without significant loss of catalytic activity.

3 Conclusions

A pHEMA-immobilized Mn(III)salenCl catalyst in the ionic liquid [bmim]PF_6 for the asymmetric epoxidation of α-methylstyrene exhibited excellent catalytic activity and enantioselectivity with 91%–80% ee values and 92%–84% yields. The polymer-immobilized Mn(III)salenCl catalyst can be easily recycled by simply filtration and was relatively stable in activity and enantioselectivity after three recycles. Catalyst 2 and 4 containing four chiral carbons as compared to the catalyst 1 and 3 gave better yields and ee values of epoxides. This was possibly due to the chiral synergy between the chiral carbons of amino alcohol and the chiral carbons of (*R*,*R*)-diamino-cyclohexane.

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