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Asymmetric epoxidation of chromenes catalyzed by chiral pyrrolidine SalenMn(III) complexes with an anchored functional group

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Chiral pyrrolidine SalenMn(III) complexes with an anchored functional group at the N_{aza}-substituent in the pyrrolidine backbone were synthesized, and used as catalysts for asymmetric epoxidation of substituted chromenes. The complex 1 with an anchored imidazole as acceptor could effectively catalyze epoxidation of substituted chromenes in the absence of expensive additive 4-phenyl pyridine *N*-oxide (PPNO) by the coordination of the anchored organic base to the central manganese ion. Complexes 2 and 3 with a quaternary ammonium salt unit at the N_{aza}-substituent in the pyrrolidine backbone displayed higher activities than Jacobsen catalyst and the analogous complex 4 without anchored functional group in the aforementioned reaction.

Keywords: pyrrolidine SalenMn(III) complexes; asymmetric epoxidation; chromene; enantioselectivity

Introduction

Chiral epoxides are versatile intermediates for the synthesis of many biologically active compounds.[1] During last two decades, various catalysts have been developed for the preparation of chiral epoxides.[2] Among several catalytic systems, the asymmetric epoxidation of unfunctionalized alkenes were catalyzed successfully by chiral SalenMn(III) complexes derived from *trans*-1,2-diaminocyclohexane, independently reported by the groups of Jacobsen and co-workers[3–5] and Katsuki and co-workers.[6,7] In particular, Jacobsen and co-workers developed an efficient two-phase system, with an aqueous phase containing NaClO and an organic phase composed of a solution of substrates and Jacobsen catalyst or its analogues (Scheme 1),[5] which exhibited excellent activities and enantioselectivities for libraries of substrates, but the epoxidation procedure generally required a long reaction time. Usually, the organic co-catalysts are added to the aforementioned catalytic system to improve both catalyst activity and product enantioselectivity. It was reported that the use of 4-phenyl pyridine *N*-oxide (PPNO),[8] 4-phenylpropyl pyridine *N*-oxide (PPPNO),[9] methylmorphline-*N*-oxide (NMO)[10] and imidazole compounds,[11] etc., not only stabilize the catalytically active intermediate species Mn(V)-oxo, but also act as phase-transfer reagents in transporting HOCl from aqueous to organic phase.[12,13] Also, quaternary ammonium salts[14] and carboxylate salts[15] are perfect co-catalysts for this reaction. Recently, an enhanced reaction rate was observed in the epoxidation of unfunctionalized alkenes catalyzed by the chiral SalenMn(III) complexes with intramolecular phase-transfer capability.[16,17]

Herein, we report a catalytic system based on the chiral pyrrolidine SalenMn(III) complexes with an anchored functional group for the asymmetric epoxidation of substituted chromenes (Scheme 1). The pyrrolidine SalenMn(III) complex **1** bearing an imidazole group at the N_{aza}-substituent in the pyrrolidine backbone, linked by a 1,10-dibromodecane bridge, showed high activity and enantioselectivity in the absence of any cocatalyst, while chiral pyrrolidine SalenMn(III) complexes **2** and **3**, with an anchored internal quaternary ammonium salt, displayed significantly higher activities than the complex **4** with a *N*-benzoyl group as well as Jacobsen catalyst for asymmetric epoxidation of substituted chromenes with NaClO/PPNO as oxidant system in the aqueous–organic biphasic medium. The enhancement of reaction rate is attributed to the phase transfer capability of the intramolecular quaternary ammonium salt unit of the SalenMn(III) catalyst.

Experimental

Materials and instruments

N-Methylimidazole was purchased from Aldrich and distilled over sodium metal prior to use. 1,10-dibromodecane, 4-(*N*,*N*-dimethylamino) pyridine (DMAP), 4-phenylpyridine *N*-oxide (PPNO) were purchased from Aldrich without further purification. Other commercially available chemicals were laboratory-grade reagents from local suppliers. 6-Nitro-2,2-dimethylchromene and 6-cyano-2,2-dimethylchromene were synthesized as described previously.[18] Chiral ligand (3*R*,4*R*)-*N*,*N*′-bis(3,5-di-tertbutylsalicylidene)-3,4-diaminopyrrolidine (hereinafter referred to as pyrrolidine salen ligand) was prepared as described

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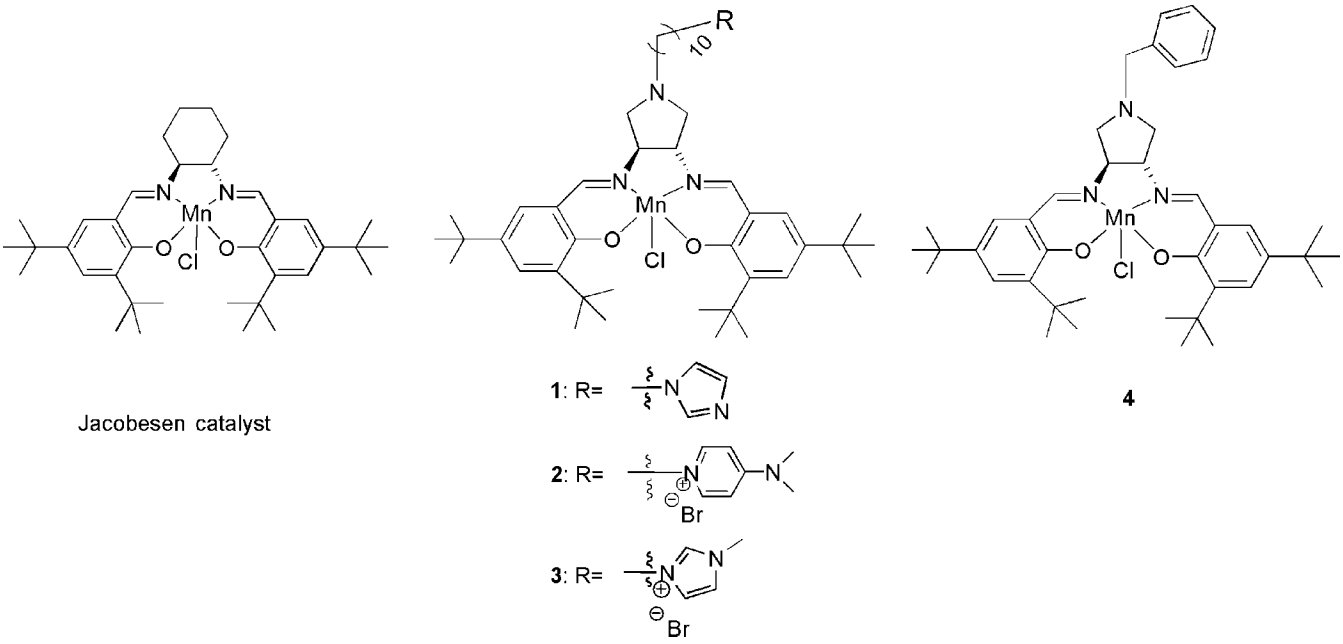


Scheme 1. Jacobsen catalyst (left) and pyrrolidine SalenMn(III) complexes (right).

previously.[19–21] All solvents used were purified by standard procedures.

^{1}H and ^{13}C NMR spectra were recorded on Varian INOVA-400 MHz type (^{1}H, 400 MHz) and Bruker 500 MHz type (^{13}C, 125 MHz) spectrometers, respectively. Their peak freguencies were referenced vs internal standard (TMS) shifts at 0 ppm for ^{1}H NMR and against the solvent, chloroform-*d* at 77.0 ppm for ^{13}C NMR, respectively. Mass spectra were performed by electrospray ionization (ESI) on an HP1100 MSD instrument and by HR-ESI-MS on an HPLC-Q-TOF MS (Micromass) mass spectrometer. Optical rotations at 589 nm were measured with a Jasco P-1010 digital polarimeter. The ee values of the epoxides of substituted 2,2-dimethylchromenes were determined by gas chromatography on a 6890N gas chromatograph (Agilent Co.) using a chiral capillary column (HP 19091G-B233, 30 m × 251 μm × 0.25 μm).

Synthesis of N_{aza}-substituted pyrrolidine salen ligands (Scheme 2)

Synthesis of salen ligand ***L₀***

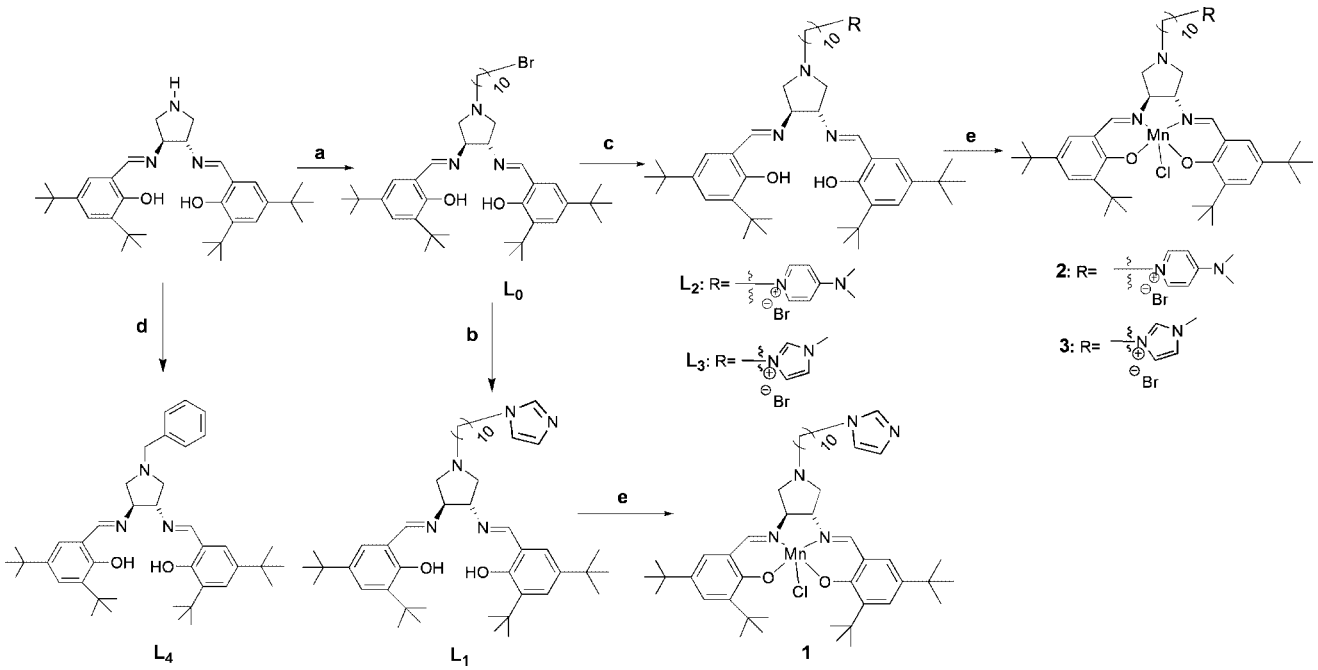
A solution of pyrrolidine salen ligand (0.501 g, 0.94 mmol) in dry toluene (10 ml) was added dropwise to the solution of 1,10-dibromodecane (0.339 g, 1.13 mmol) and dry triethylamine (0.52 ml, 3.76 mmol) in dry toluene (5 ml). The mixture was stirred at 70 °C for 36 h in dark and then concentrated under vacuum. The residue was purified by chromatography on a silica gel column (ethyl acetate–petroleum ether, 1 : 19) to give the desired ligand **L_0**. Yield 56% (0.40 g). $[\alpha]_{589}^{25} = -269^\circ$ ($c = 0.30$, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.52 (s, 2H, OH), 8.30 (s, 2H, N=CH), 7.38 (s, 2H, CH of Ar), 7.04 (s, 2H, CH of Ar), 3.96 (m, 2H, CH of pyrrolidine), 3.41 (m, 2H, CH_2 of decane), 3.09 (m, 2H, CH_2 of pyrrolidine), 2.93 (m, 2H, CH_2 of pyrrolidine), 2.50 (m, 2H, CH_2 of decane), 1.82 (m, 2H, CH_2 of decane), 1.42 (s, 18H, ^{t}Bu), 1.30 (m, 14H, CH_2 of decane), 1.26 (s, 18H, ^{t}Bu); MS (ESI): *m/z* calcd for $[C_{44}H_{70}BrN_3O_2 + H]^+ = 752.5$, found 752.5.

Synthesis of salen ligand ***L₁***

NaH (0.108 g, 4.50 mmol) was added slowly in portions to a solution of imidazole (0.102 g, 1.50 mmol) in dry THF (10 ml) and the resulting reaction mixture was stirred under nitrogen for 4 h at room temperature. To the mixture was added pyrrolidine salen ligand **L_0** (1.127 g, 1.50 mmol). The whole mixture was stired at room temperature for 24 h in the dark before concentration under vacuum. The residue was purified by chromatography on a silica gel column eluting with ethyl acetate to give the desired chiral ligand **L_1**. Yield 58% (0.64 g). $[\alpha]_{589}^{25} = -235^\circ$ ($c = 0.35$, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.49 (s, 2H, OH), 8.30 (s, 2H, N=CH), 7.46 (s, 1H, CH of imidazole), 7.38 (s, 2H, CH of Ar), 7.05 (d, 1H, CH of imidazole), 7.04 (s, 2H, CH of Ar), 6.90 (d, 1H, CH of imidazole), 3.96 (m, 2H, CH of pyrrolidine), 3.92 (m, 2H, CH_2 of decane), 3.11 (m, 2H, CH_2 of pyrrolidine), 2.91 (m, 2H, CH_2 of pyrrolidine), 2.50 (m, 2H, CH_2 of decane), 1.85 (m, 2H, CH_2 of decane), 1.45 (s, 18H, ^{t}Bu), 1.29 (m, 14H, CH_2 of decane), 1.27 (s, 18H, ^{t}Bu); ^{13}C NMR: ($CDCl_3$) 166.5, 157.9, 140.3, 137.7, 136.6, 129.4, 127.2, 126.3, 118.8, 117.6, 60.7, 57.0, 46.5, 35.0, 34.1, 31.4, 29.3, 29.1, 28.7, 28.5, 28.1, 27.5, 26.6; HRMS (ESI): *m/z* calcd for $[C_{47}H_{73}N_5O_2 + H]^+ = 740.5764$, found 740.5738; $[C_{47}H_{73}N_5O_2 + 2H]^{2+}/2 = 370.7882$, found 370.7844.

Synthesis of salen ligand ***L₂***

KI (0.005 g, 0.03 mmol) was added to the solution of pyrrolidine salen ligand L_1 (0.225 g, 0.30 mmol) and 4-(*N*,*N*-dimethylamino) pyridine (DMAP) (0.055 g, 0.45 mmol) in dry CH_3CN (15 ml), the resulting reaction mixture was heated to reflux for 24 h in dark. The mixture was poured into H_2O (10 ml) and was extracted with CH_2Cl_2 (3 × 5 ml), followed by drying with anhydrous sodium sulfate. After filtration to remove solid impurities and drying agent, solvent was removed *in vacuo*, the residue was purified by chromatography on a silica gel column (dichloromethane–ethanol, 10 : 1) to give the desired ligand **L_2**. Yield 64% (0.16 g). $[\alpha]_{589}^{26} = -186^\circ$ ($c = 0.30$, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.70 (s, 2H, OH), 8.44 (d, 2H, CH of DMAP),



Scheme 2. Reagents and conditions: (a) pyrrolidine salen ligand, 1,10-dibromodecane, dry Et_3N, dry toluene, N_2, 70 °C, 36 h; (b) (1) NaH, imidazole, dry THF, N_2, r.t., 4 h, (2) L_1, r.t., 24 h; (c) KI, L_1, DMAP (or *N*-MeIm), dry CH_3CN, N_2, reflux, 24 h; (d) Et_3N, benzyl chloride, EtOH, r.t., 48 h; (e) (1) $Mn(OAc)_2 \cdot 4H_2O$, toluene–ethanol, reflux, 2 h, (2) LiCl, O_2, 3 h.

8.41 (s, 2H, N=CH), 7.38 (s, 2H, CH of Ar), 7.05 (s, 2H, CH of Ar), 6.98 (d, 2H, CH of DMAP), 4.34 (m, 2H, CH of pyrrolidine), 3.98 (m, 2H, CH_2 of pyrrolidine), 3.71 (m, 2H, CH_2 of pyrrolidine), 3.25 (s, 6H, CH_3 of DMAP), 1.94 (m, 2H, CH_2 of decane), 1.42 (s, 18H, ^{t}Bu), 1.32 (m, 18H, CH_2 of decane), 1.24 (s, 18H, ^{t}Bu). ^{13}C NMR: ($CDCl_3$) 169.9, 158.0, 156.4, 142.5, 140.7, 136.9, 128.1, 127.0, 117.5, 108.6, 72.2, 58.4, 57.4, 56.8, 40.8, 35.2, 34.3, 31.5, 30.8, 29.6, 28.5, 26.5, 25.7; MS (ESI): *m/z* calcd for $[C_{51}H_{80}BrN_5O_2 - Br]^+ = 794.6$, found 794.6; $[C_{51}H_{80}BrN_5O_2 - Br + H]^{2+}/2 = 397.8$, found 397.8.

Synthesis of salen ligand ***L₃***

It was synthesized as a similar procedure of ligand **L_2**, only with the substitution of *N*-methylimidazole (*N*-MeIm) for DMAP. Yield 56% (0.47 g). $[\alpha]_{589}^{26} = -210^\circ$ ($c = 0.3$, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.08 (s, 2H, OH), 8.37 (s, 2H, N=CH), 7.48 (s, 1H, CH of *N*-MeIm), 7.38 (s, 2H, CH of Ar), 7.36 (d, 1H, CH of *N*-MeIm), 7.05 (s, 2H, CH of Ar), 6.89 (s, 1H, CH of *N*-MeIm), 4.32 (m, 2H, CH of pyrrolidine), 3.71 (m, 3H, CH_3 of *N*-MeIm), 3.38 (m, 2H, CH_2 of pyrrolidine), 3.15 (m, 2H, CH_2 of pyrrolidine), 2.82 (m, 2H, CH_2 of decane), 1.97 (m, 2H, CH_2 of decane), 1.65 (m, 2H, CH_2 of decane),1.45 (s, 18H, ^{t}Bu), 1.32 (m,14H, CH_2 of decane), 1.27 (s, 18H, ^{t}Bu). ^{13}C NMR: ($CDCl_3$) 168.2, 157.9, 140.5, 136.7,137.4, 127.7, 126.7, 123.3, 121.9, 117.4,73.7, 59.0, 58.4, 56.7, 50.3, 37.1, 35.0, 34.1, 33.4, 31.4, 29.4, 28.8, 26.8, 25.9; MS (ESI): *m/z* calcd for $[C_{48}H_{76}BrN_5O_2 - Br]^+ = 754.5$, found 754.5; $[C_{48}H_{76}BrN_5O_2 - Br + H]^{2+}/2 = 377.8$, found 377.8.

Synthesis of salen ligand ***L₄***

The experimental procedure for the synthesis of **L_4** was carried out as described previously[22,23] with minor modification. Yield 58%. $[\alpha]_{589}^{25} = -298^\circ$ ($c = 0.02$, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.51 (s, 2H, OH), 8.28 (s, 2H, N=CH), 7.29–7.41 (m, 7H, CH of Ar and CH of Bn), 7.03 (d, 2H, Ar), 3.76 (s, 2H, CH_2 of Bn), 3.14 (m, 2H, CH_2 of pyrrolidine), 2.95 (m, 2H, CH_2 of pyrrolidine), 1.45 (s, 18H,^{t}Bu), 1.26 (s, 18H, ^{t}Bu). MS (ESI): *m/z* calcd for $[C_{41}H_{57}N_3O_2 + H]^+ = 623.4451$, found 624.4431.

Synthesis of pyrrolidine SalenMn(III) complexes

Complexes **1–4** were prepared according to literature protocols with minor modification.[22,24] The pyrrolidine salen ligand (1 mmol) was dissolved in hot toluene–ethanol (45 ml, 1 : 2, v/v) and solid $Mn(OAc)_2 \cdot 4H_2O$ (0.735 g, 3 mmol) was added in one portion. The solution was heated to reflux for 2 h, then LiCl (0.126 g, 3 mmol) was added and the mixture was further refluxed for 3 h while air was bubbled through the refluxing mixture. The mixture was cooled to room temperature and filtered. The solvent was removed from the filtrate and the residue was extracted with CH_2Cl_2. The organic layer was washed with water and brine and then dried over anhydrous sodium sulfate. The concentrated filtrate was purified by chromatography on a silica gel column using dichloromethane–methanol (10: 1, v/v) as eluent. The desired monomeric or dimeric pyrrolidine SalenMn(III) complex was obtained as a dark brown solid after thorough removal of solvent.

1: Yield 74%. MS (ESI): *m/z* calcd for $[C_{47}H_{71}ClMnN_5O_2 - Cl]^+ = 792.5$, found 792.5; $[C_{47}H_{71}ClMnN_5O_2 - Cl + H]^{2+}/2 = 396.7$, found 396.7; FTIR (in CH_2Cl_2): 2955, 2922, 2850, 1733, 1652, 1458, 1377 cm^{-1}.

2: Yield 60%. HRMS (ESI): *m/z* calcd for $[C_{51}H_{78}BrClMnN_5O_2 - Br - Cl]^{2+}/2 = 423.7766$, found 423.7758; FTIR (in CH_2Cl_2): 2955, 2922, 2850, 1737, 1650, 1573, 1537, 1462, 1377 cm^{-1}.

3: Yield 63%. HRMS (ESI): *m/z* calcd for $[C_{48}H_{74}BrClMnN_5O_2 - Br - Cl]^{2+}/2 = 403.7609$, found 403.7657; FTIR (in CH_2Cl_2): 2955, 2924, 2852, 1633, 1463, 1377, cm^{-1}.

4: Yield 83%. HRMS (ESI): *m/z* calcd for $[C_{41}H_{55}ClMnN_3O_2 - Cl]^+ = 676.3675$, found 676.3674; FTIR (in CH_2Cl_2): 2956, 2925, 1632, 1531, 1459, 1383 cm^{-1}.

General procedure for asymmetric epoxidation of chromenes

To a cooled solution (0 °C) of alkene (0.4 mmol), PPNO (13.7 mg, 0.08 mmol), *o*-dichlorobenzene (internal standard, 56 µl, 0.5 mmol), and pyrrolidine SalenMn(III) complex (0.008 mmol) in CH_2Cl_2 (1 ml), a precooled NaClO aqueous solution (0.8 mmol, pH = 11.3, 0 °C) was added portion wise. The mixture was stirred at 0 °C, and the reaction was monitored by gas chromatography. When the reaction reached a steady conversion, the mixture was diluted with CH_2Cl_2 (3 ml). The phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 ml × 2). The combined organic layers were washed with brine (3 ml × 2) and dried over anhydrous sodium sulfate. The concentrated filtrate was purified by silica gel column chromatography to afford the corresponding epoxide.

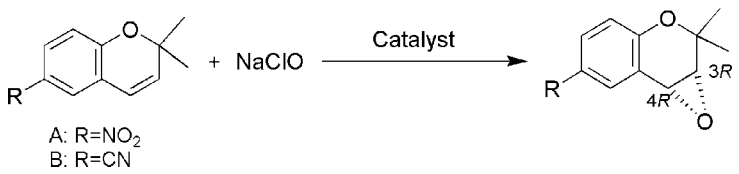
Results and Discussion

Asymmetric epoxidation of substituted chromenes catalyzed by the pyrrolidine SalenMn(III) complex with an anchored imidazole as acceptor

The catalytic activity and enantioselectivity of pyrrolidine SalenMn(III) complex **1** bearing an imidazole group at the N_{aza}-substituent in the pyrrolidine backbone was examined for asymmetric epoxidation of substituted chromenes using NaClO as oxidant in CH_2Cl_2 at 0 °C. 6-Nitro-2,2-dimethylchromene and 6-cyano-2,2-dimethylchromene were selected as model substrates because their corresponding epoxides are useful in the synthesis of selective potassium channel activator drugs.[25] The results are summarized in Table 1. For comparison purpose, Jacobsen catalyst and analogous complex **4** with a *N*-benzyl group at the N_{aza}-substituent in the pyrrolidine backbone were also preformed for this reaction at the same conditions.

In the absence of any co-catalyst, the complex **1** shows higher activity and enantioselectivity than the complex **4** with a *N*-benzyl group at the N_{aza}-substituent in the pyrrolidine backbone or Jacobsen catalyst alone as catalyst for asymmetric epoxidation of substituted chromenes using NaClO as oxidant (Table 1, entries 2, 4, 8, 10 and 12). The addition of PPNO nearly has no effect on catalytic activity, and only results in a slight improvement in enantioselectivity (entries 3 and 9). The results indicate that the imidazole group at the N_{aza}-substituent in the pyrrolidine backbone as an axial ligand has a pronounced effect on both catalytic activity and asymmetric induction. The imidazole group probably not only stabilizes the catalytically active intermediate species Mn(V)-oxo by its coordination to the manganese ion, but also acts as phase-transfer reagent to transport HClO from aqueous to organic phase.[13,26] Berkessel *et al*. have reported biomimetic asymmetric epoxidation using a manganese(Salalen) complex bearing an imidazole substitute at the C7 carbon, wherein the imidazole group was considered to coordinate at the apical position of the complex.[27] The axial coordination of the anchored imidazole group to the metal center was confirmed by ultraviolet–visible light (UV–vis) spectral analysis. In comparison to the UV–vis spectra of the complex **4** in dichloromethane, a red shift at the wavelength from 285 to 335 nm was observed in the spectra of the complex **1**. Recently, excellent enantioselectivity was observed in asymmetric epoxidation of substituted chromenes using aqueous hydrogen peroxide as oxidant, with the use of pentacoordinated Mn–Salen complexes as catalyst.[28] In this system, the role of the anchored imidazole group was considered to regulate the conformation of the manganese(III) complexes and further accelerate the conversion of the hydroperoxo intermediate to the oxo species.

Table 1. Asymmetric epoxidation of substituted chromenes catalyzed by complexes **1** and **4** with NaClO[a] as oxidant



Entry	Substrate[b]	Catalyst	Oxidant system	Yield (%)[c]	ee (%)[d]	Configuration
1	A	Jacobsen catalyst	NaClO/PPNO	92	90	3*R*,4*R*
2		Jacobsen catalyst	NaClO	75	80	3*R*,4*R*
3		**1**	NaClO/PPNO	91	86	3*R*,4*R*
4		**1**	NaClO	90	84	3*R*,4*R*
5		**4**	NaClO/PPNO	74	83	3*R*,4*R*
6		**4**	NaClO	64	79	3*R*,4*R*
7	B	Jacobsen catalyst	NaClO/PPNO	91	91	3*R*,4*R*
8		Jacobsen catalyst	NaClO	71	77	3*R*,4*R*
9		**1**	NaClO/PPNO	89	85	3*R*,4*R*
10		**1**	NaClO	88	82	3*R*,4*R*
11		**4**	NaClO/PPNO	84	87	3*R*,4*R*
12		**4**	NaClO	62	75	3*R*,4*R*

[a] Reactions were carried out at 0 °C in CH_2Cl_2 (1 ml) for 8 h with alkene (0.4 mmol), catalyst (0.008 mmol, 2 mol%), NaClO aqueous solution (pH = 11.3, 0.8 mmol), PPNO (0.08 mmol) and *o*-dichlorobenzene (internal standard, 0.5 mmol).
[b] A = 6-nitro-2,2-dimethylchromene, B = 6-cyano-2,2-dimethylchromene.
[c] Isolated yield.
[d] Determined by GC with chiral capillary columns (HP19091G-B233, 30 m × 251 µm × 0.25 µm).

Asymmetric epoxidation of substituted chromenes catalyzed by the pyrrolidine SalenMn(III) complex with an anchored quaternary ammonium salt as phase transfer reagent

The epoxidation of substituted chromenes catalyzed by chiral SalenMn(III) complexes with NaClO as oxidant under biphasic reaction conditions generally requires a long reaction time even in the presence of an axial ligand.[29,30] As previously reported, the rate can be increased using SalenMn(III) complexes with intramolecular phase-transfer capability by the tertiary amine unit(s) to the salen ligand.[16,17] The SalenMn(III) complexes could effectively increase the overall reaction rate with the addition of 50 equiv. CH_3I.[31] However, there exist at least three manganese-containing species and the crucial intermediate is not clear. More recently, Yin's group reported a series of novel chiral salen Mn(III) complexes functionalized by 1-propylamine-3-methylimidazolium tetrafluoroborate at one side of the 5 position or two sides of the 5,5′-position of the salen ligand, which significantly increased the solubility and thus improved the catalytic activity for enantioselective epoxidation of styrene.[32]

To further study the intramolecular phase transfer capability, the pyrrolidine SalenMn(III) complexes **2** and **3** bearing the quaternary ammonium unit at the N_{aza}-substituent in the pyrrolidine backbone linked by a 1,10-dibromodecane bridge were synthesized and examined for the epoxidation of substituted chromenes in the NaClO–PPNO biphasic system. The results are summarized in Table 2. For comparison, catalytic results of Jacobsen catalyst and the complex **4** were also examined for this reaction at the same conditions.

As shown in Table 2, under the same conditions, the reaction rates with complexes **2** and **3** bearing an internal quaternary ammonium salts as catalyst are significantly increased as compared with that for the complex **4** with a *N*-benzyl group for the epoxidation of substituted chromenes (entries 1, 2 vs 3; 5, 6 vs 7). The time required to the end of the reaction in the complexes **2** and **3** systems was shorter than those of Jacobsen catalyst, with comparable yields and slightly lower ee values (entries 1, 2 vs 4; 5, 6 vs 8). For example, 62 and 92% conversions were obtained within 8 h using complex **4** and the Jacobsen catalyst for the epoxidation of 6-nitro-2,2-dimethylchromene (entries 3 and 4), respectively, whereas complexes **2** and **3** gave more than 91% in 3.5 h under the same conditions (entries 1 and 2).

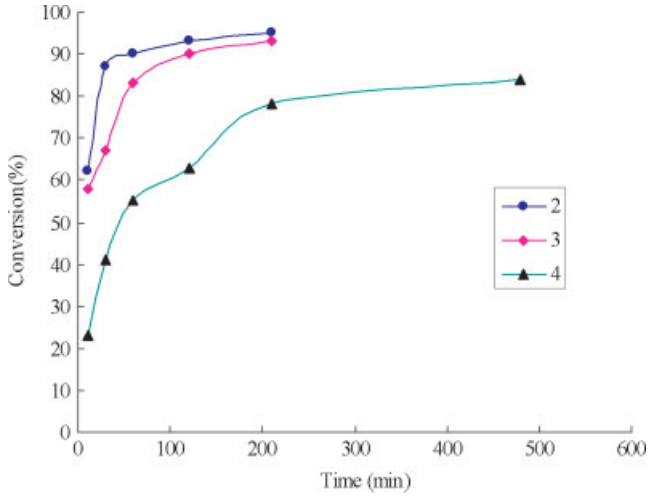


Figure 1. The conversion vs reaction time plot for epoxidation of 6-nitro-2,2-dimethylchromene catalyzed by **2**–**4** with NaClO/PPNO as an oxidant system at 0 °C.

As shown in Fig. 1, the complexes **2** and **3** bearing an internal quaternary ammonium salt exhibit higher activity than the complex **4** for the epoxidation of substituted chromenes, especially in the beginning of the reaction. For example, the complex **4** gave a 15% conversion of 6-nitro-2,2-dimethylchromene in the first 10 min of the reaction (entry 3), while a conversion of up to 52% was obtained for the complex **2** in the same reaction period (entry 1). In order to further evaluate the reaction rate with the complexes **2** and **3** bearing a quaternary ammonium salt unit, the 30 min conversions of substituted chromenes were obtained; complexes **2**–**4** gave 89, 83 and 47% conversions of 6-nitro-2,2-dimethylchromene, respectively (entries 1, 2 and 3).

According to the catalytic results, the significant enhancement of the overall reaction rates for the epoxidation of substituted chromenes by the pyrrolidine SalenMn(III) complexes **2** and **3** are attributed to phase-transfer capability of the quaternary ammonium salt unit at the N_{aza}-substituent in the pyrrolidine backbone.

Table 2. Asymmetric epoxidation substituted chromenes catalyzed by complexes **2**–**4** with NaClO/PPNO as oxidant system[a]

Entry	Substrate[b]	Catalyst	Conversion (%)[c] after 10 (30) min	Time (h)[d] [yield (%)[e]]	ee (%)[f]	Configuration
1	A	**2**	52 (89)	3.5 (92)	84	3*R*,4*R*
2		**3**	42 (83)	3.5 (91)	84	3*R*,4*R*
3		**4**	15 (47)	8.0 (74)	83	3*R*,4*R*
4		Jacobsen catalyst	–	8.0 (92)	90	3*R*,4*R*
5	B	**2**	62 (87)	3.5 (95)	92	3*R*,4*R*
6		**3**	58 (67)	3.5 (93)	88	3*R*,4*R*
7		**4**	23 (41)	8.0 (84)	87	3*R*,4*R*
8		Jacobsen catalyst	–	8.0 (91)	91	3*R*,4*R*

[a] The reaction condition is the same as that in footnote 'a' of Table 1.
[b] A = 6-nitro-2,2-dimethylchromene, B = 6-cyano-2,2-dimethylchromene.
[c] Determined by GC, no detectable amount of by-product was found.
[d] The time needed to the end of the reaction.
[e] Isolated yield.
[f] Determined by GC with chiral capillary columns (HP19091G-B233, 30 m × 251 μm × 0.25 μm).

Conclusion

We have developed a series of novel chiral pyrrolidine SalenMn(III) complexes **1–3** with an anchored functional group such as imidazole or quaternary ammonium salt at the N_{aza}-substituent in the pyrrolidine backbone. Complex **1** with in-built imidazole group could efficiently catalyze the epoxidation of substituted chromenes with NaClO as oxidant in the aqueous–organic biphasic system without the additive expensive hydrophobic PPNO. The comparable activity and ee value were obtained in comparison to Jacobsen catalyst. Complexes **2** and **3**, featuring quaternary ammonium units, exhibited obviously higher activity than the complex **4** with an *N*-benzoyl group, in the asymmetric epoxidation of substituted chromenes with NaClO/PPNO as an oxidant system, due to phase transfer capability of the quaternary ammonium salt unit at the N_{aza}-substituent in the pyrrolidine backbone of the catalyst.

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