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# Asymmetric epoxidation of styrene and chromenes catalysed by chiral (salen)Mn(III) complexes with a pyrrolidine backbone

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**Abstract**

A series of chiral (pyrrolidine salen)Mn(III) complexes were synthesized from $N_{aza}$-substituted (*R*,*R*)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)-3,4-diaminopyrrolidine salen ligands. High yields and comparable enantioselectivity relative to Jacobsen's catalyst were achieved in asymmetric epoxidation of styrene and chromenes using NaClO/PPNO and *m*-CPBA/NMO as the oxidant systems. Complexes **1**–**3**, featuring a tertiary amine unit, displayed higher activity than complex **4**, bearing an amide unit and Jacobsen's catalyst in the NaClO/PPNO aqueous/organic biphasic system. The influence of $CH_3I$ on epoxidation of 6-nitro-2,2-dimethylchromene catalysed by **1**–**4** in the biphasic medium was studied to explore the catalysts with built-in phase-transfer capability. The alkenes' access pathway is discussed on the basis of the steric effect of the $N_{aza}$-substituent in the pyrrolidine backbone of complexes **1**–**3** on the enantioselectivity of epoxidation.


*Keywords:* Asymmetric epoxidation; Enantioselectivity; Pyrrolidine; (Salen)Mn(III) complex; Unfunctionalized alkenes

## 1. Introduction

Catalytic asymmetric epoxidation of alkenes is a powerful method for the synthesis of various chiral organic compounds. During last two decades, various transition metal catalysts have been reported for the highly enantioselective epoxidation of alkenes [1]. In recent years, asymmetric epoxidation catalysed by efficient organocatalysts, including chiral ketones and iminium salts [2–5], has also attracted intense interest. Among several catalytic procedures to optically active epoxides, the asymmetric epoxidation of unfunctionalized alkenes catalysed by chiral (salen)Mn(III) complexes, initially developed by Jacobsen [6] and Katsuki [7], is considered one of the most effective methods discovered in the last 20 years [8,9]. The classic (salen)Mn(III) catalysts display high enantioselectivity for the asymmetric epoxidation of *Z*- and tri-substituted prochiral alkenes, and the chiral (salen)Mn(III) complex known as "Jacobsen's catalyst" (Scheme 1) has proven to be an efficient and practical catalyst for asymmetric epoxidation of various *Z*-alkenes with enantiomeric excesses generally >90% [10].

Although the chiral (salen)Mn(III) complexes derived from *trans*-1,2-diphenylethylenediamine and *trans*-1,2-diaminocyclohexane have been extensively investigated, to the best of our knowledge there are only two reports concerning asymmetric epoxidation of unfunctionalized alkenes catalysed by the chiral (salen)Mn(III) complexes derived from *trans*-3,4-diaminopyrrolidine [11,12]. The advantages of the chiral salen ligand with a pyrrolidine backbone are that different groups and fragments can be readily tethered to the backbone of the ligand through the N atom of pyrrolidine and that a tertiary amine unit of the pyrrolidine salen ligand may impart a built-in phase-transfer capability to the catalyst. For example, the chiral (pyrrolidine salen)Mn(III) catalyst is covalently attached to either the polymer support or silica gel via the N atom of the pyrrolidine moiety [11,12], and such heterogeneous catalysts are recyclable in asymmetric epoxidation of alkenes. Pyrrolidine salen ligands also have been used as a building block to construct photosensitizer–catalyst binuclear Ru(II)Mn(III) and Re(I)Mn(III) complexes as catalyst candidates for photoinduced asymmetric oxidation of organic substrates, in which the

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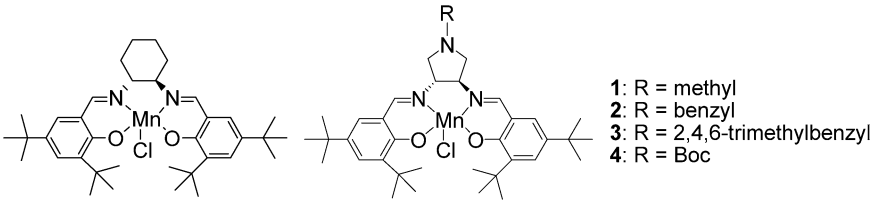



Scheme 1. Jacobsen's catalyst (left) and (pyrrolidine salen)Mn(III) complexes (right).

chiral (pyrrolidine salen)Mn(III) moiety is covalently linked by a carboxamide linkage to Ru(II) and Re(I) fragments [13,14]. In view of the reactivity of the backbone in the pyrrolidine salen ligand and the potential application of chiral (pyrrolidine salen)Mn(III) complexes in epoxidation, it is of interest to study their catalytic properties in asymmetric epoxidation of unfunctionalized alkenes. Recently, we prepared a series of chiral (pyrrolidine salen)Mn(III) complexes **1**–**4** derived from (*R*,*R*)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)-3,4-diaminopyrrolidine salen ligands with $CH_3$, Bn, 2,4,6-trimethylbenzyl and a Boc group bonded to the N atom of the ligand backbone (Scheme 1). The pyrrolidine moieties of complexes **1**–**3** are cyclic tertiary amines, and complex **4** has an amide functionality in its pyrrolidine fragment. The immediate goals of present study were to explore (1) the catalytic properties of **1**–**4** with NaClO and *m*-CPBA as oxidants using styrene and chromenes as model substrates; (2) the influence of $CH_3I$ on the catalytic activity and enantioselectivity of complexes **1**–**3** with NaClO as oxidant under a biphasic reaction condition, to probe the built-in phase-transfer capability of the ammonium salts of **1**–**3** in asymmetric epoxidation of alkenes; and (3) the steric effects of the backbone R groups in (pyrrolidine salen)Mn(III) complexes **1**–**4** on enantioselectivity, to gain insight into the alkenes' access pathway.

## 2. Experimental

### 2.1. Material

α-2-Chloroisodurene, 4-phenylpyridine *N*-oxide (PPNO), and *N*-methylmorpholine *N*-oxide (NMO) were purchased from Acros, Aldrich, and Alfa Aesar, respectively. Other commercially available chemicals were laboratory-grade reagents from local suppliers. Styrene was passed through a pad of neutral alumina before use. 6-Nitro-2,2-dimethylchromene and 6-cyano-2,2-dimethylchromene were synthesized as described previously [15]. Chiral ligand (3*R*,4*R*)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)-3,4-diaminopyrrolidine (hereinafter referred to as pyrrolidine salen ligand) was prepared as described previously [13,16,17]. All solvents used were purified by standard procedures.

### 2.2. Methods

All IR spectra were recorded from KBr pellets using a JASCO FT/IR 430 spectrophotometer. $^1$H NMR spectra were obtained on a Varian INOVA 400NMR apparatus with TMS as an internal standard. 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. Elemental analyses were performed on a THERMOQUEST-FLASH EA 1112 elemental analyzer. The ee values of styrene oxide and the epoxides of substituted 2,2-dimethylchromenes were determined by gas chromatography (using an HP 6890 gas chromatograph) using chiral capillary columns (Chiraldex GTA, 30 m × 250 μm i.d. and HP 19091G-B233, 30 m × 251 μm × 0.25 μm).

### 2.3. Synthesis of $N_{aza}$-substituted pyrrolidine salen ligands

#### 2.3.1. Synthesis of (3*R*,4*R*)-*N*-methylpyrrolidine salen ligand (**5**) and (3*R*,4*R*)-*N*-(2,4,6-trimethylbenzyl)pyrrolidine salen ligand (**7**)

A solution of pyrrolidine salen ligand (0.533 g, 1 mmol), triethylamine (278 μL, 2 mmol), iodomethane (75 μL, 1.2 mmol), or α-2-chloroisodurene (0.168 g, 1 mmol) in ethanol was stirred at room temperature for 48 h and then concentrated under vacuum. The residue was purified by silica gel column chromatography to give the desired chiral ligands:

**5**: Yield 55% (0.30 g). Anal. calcd for $C_{35}H_{53}N_3O_2$: C, 76.74; H, 9.75; N, 7.67. Found: C, 76.50; H, 9.69; N, 7.50%. IR (KBr): ν 2957, 2869, 1626, 1596, 1469, 1440 cm$^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$): δ 1.27 (s, 18H, *tert*-Bu), 1.45 (s, 18H, *tert*-Bu), 2.46 (s, 3H, $NCH_3$), 2.92 (dd, 2H, $CH_2$ of pyrrolidine), 3.10 (dd, 2H, $CH_2$ of pyrrolidine), 3.98 (dd, 2H, CH of pyrrolidine), 7.05 (d, 2H, Ar), 7.38 (d, 2H, Ar), 8.30 (s, 2H, N=CH), 13.44 ppm (s, 2H, OH). $[\alpha]_{589}^{27} = -378$ ($c = 0.02$, $CH_2Cl_2$).

**7**: Yield 91% (0.60 g). Anal. calcd for $C_{44}H_{63}N_3O_2$: C, 79.35; H, 9.53; N, 6.31. Found: C, 79.39; H, 9.56; N, 6.40%. IR (KBr): ν 2957, 2868, 1628, 1595, 1468, 1440 cm$^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$): δ 1.27 (s, 18H, *tert*-Bu), 1.45 (s, 18H, *tert*-Bu), 2.26 (s, 3H, $CH_3$ of 2,4,6-Bn), 2.42 (s, 6H, $CH_3$ of 2,4,6-Bn), 2.89 (dd, 2H, $CH_2$ of pyrrolidine), 3.12 (dd, 2H, $CH_2$ of pyrrolidine), 3.69 (dd, 2H, $CH_2$ of 2,4,6-Bn), 3.92 (dd, 2H, CH of pyrrolidine), 6.85 (s, 2H, CH of 2,4,6-Bn), 7.01 (d, 2H, Ar), 7.37 (d, 2H, Ar), 8.27 (s, 2H, N=CH), 13.55 ppm (s, 2H, OH). $[\alpha]_{589}^{27} = -251$ ($c = 0.02$, $CH_2Cl_2$).

#### 2.3.2. Synthesis of (3*R*,4*R*)-*N*-benzylpyrrolidine salen ligand (**6**)

The experimental procedure for the synthesis of **6** was carried out as described previously [12,18] with minor modifications:

**6**: Yield 58% (3.61 g). Anal. calcd for $C_{41}H_{57}N_3O_2$: C, 78.93; H, 9.21; N, 6.73. Found: C, 79.01; H, 9.21; N, 6.76%. IR (KBr): $\nu$ 2957, 2868, 1626, 1595, 1468, 1441 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 1.26 (s, 18H, *tert*-Bu), 1.45 (s, 18H, *tert*-Bu), 2.96 (dd, 2H, $CH_2$ of pyrrolidine), 3.15 (dd, 2H, $CH_2$ of pyrrolidine), 3.76 (s, 2H, $CH_2$ of Bn), 3.98 (dd, 2H, CH of pyrrolidine), 7.03 (d, 2H, Ar), 7.29–7.41 (m, 7H, CH of Ar and CH of Bn), 8.28 (s, 2H, N=CH), 13.49 ppm (s, 2H, OH). $[\alpha]_{589}^{27} = -298$ ($c = 0.02$, $CH_2Cl_2$).

#### 2.3.3. Synthesis of (3*R*,4*R*)-*N*-Boc-pyrrolidine salen ligand (*8*)

A solution of Boc-anhydride (0.218 g, 1 mmol) in ethanol (5 mL) was added dropwise to the solution of pyrrolidine salen ligand (0.533 g, 1 mmol) in ethanol (15 mL). The mixture was stirred at room temperature for 4 h and then concentrated under vacuum. The residue was purified by silica gel column chromatography to give the desired chiral ligand:

**8**: Yield 95% (0.60 g). Anal. calcd for $C_{39}H_{59}N_3O_4$: C, 73.89; H, 9.38; N, 6.63. Found: C, 74.25; H, 9.47; N, 6.58%. IR (KBr): $\nu$ 2960, 2875, 1624, 1594, 1474, 1440 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 1.26 (s, 18H, *tert*-Bu), 1.43 (s, 18H, *tert*-Bu), 1.50 (s, 9H, $CH_3$ of Boc), 3.59 (dd, 2H, $CH_2$ of pyrrolidine), 3.88–3.98 (m, 4H, $CH_2$, and CH of pyrrolidine), 7.04 (s, 2H, Ar), 7.38 (s, 2H, Ar), 8.37 (s, 2H, N=CH), 13.11 ppm (s, 2H, OH). $[\alpha]_{589}^{27} = -238$ ($c = 0.02$, $CH_2Cl_2$).

### 2.4. Synthesis of (pyrrolidine salen)Mn(III) complexes

(Pyrrolidine salen)Mn(III) complexes were prepared as described previously [12], with some modifications:

**1**: Yield 73%. Anal. calcd for $C_{35}H_{51}ClMnN_3O_2 \cdot H_2O$: C, 64.26; H, 8.17; N, 6.42. Found: C, 63.91; H, 8.07; N, 6.26%. IR (KBr): $\nu$ 2958, 2869, 1622, 1535, 1464, 1435 $cm^{-1}$. HR-ESI-MS: $m/z$ calcd for $[M–Cl]^+$: 600.3362, found: 600.3373 (100%).

**2**: Yield 82%. Anal. calcd for $C_{41}H_{55}ClMnN_3O_2 \cdot 0.5H_2O$: C, 68.27; H, 7.83; N, 5.83. Found: C, 68.26; H, 7.94; N, 5.78%. IR (KBr): $\nu$ 2957, 2868, 1620, 1534, 1463, 1433 $cm^{-1}$. HR-ESI-MS: $m/z$ calcd for $[M–Cl]^+$: 676.3675, found: 676.3667 (100%).

**3**: Yield 79%. Anal. calcd for $C_{44}H_{61}ClMnN_3O_2 \cdot 0.5H_2O$: C, 69.23; H, 8.19; N, 5.50. Found: C, 69.22; H, 8.17; N, 5.38%. IR (KBr): $\nu$ 2957, 2868, 1625, 1534, 1463, 1434 $cm^{-1}$. HR-ESI-MS: $m/z$ calcd for $[M–Cl]^+$: 718.4144, found: 718.4155 (100%).

**4**: Yield 86%. Anal. calcd for $C_{39}H_{57}ClMnN_3O_4$: C, 64.85; H, 7.95; N, 5.82. Found: C, 64.69; H, 8.08; N, 5.67%; IR (KBr): $\nu$ 2958, 2870, 1624, 1534, 1463, 1433 $cm^{-1}$. ESI-MS: $m/z$ calcd for $[M–Cl]^+$: 686.4, found: 686.3 (100%).

### 2.5. General procedure for asymmetric epoxidation of styrene and chromenes

#### 2.5.1. Using NaClO as oxidant [19]

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 salen)Mn(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 portionwise. 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.

#### 2.5.2. Using m-CPBA as oxidant [20]

A solution of alkene (0.4 mmol), NMO (270 mg, 2 mmol), *o*-dichlorobenzene (internal standard, 56 μL, 0.5 mmol), and (pyrrolidine salen)Mn(III) complex (0.008 mmol) in $CH_2Cl_2$ (2 mL) was cooled to the desired temperature. Solid *m*-CPBA (138 mg, 0.8 mmol) was added in four portions over 2 min. The reaction mixture was stirred for 1 h, after which NaOH (4 mL, 1.0 M) was added. The mixture was treated by the aforementioned procedure to get the corresponding epoxide.

#### 2.5.3. Using $CH_3I$ as additive

A solution of alkene (0.4 mmol), PPNO (13.7 mg, 0.08 mmol), *o*-dichlorobenzene (internal standard, 56 μL, 0.5 mmol), $CH_3I$, and (pyrrolidine salen)Mn(III) complex (0.008 mmol) in $CH_2Cl_2$ (1 mL) was stirred for 1 h and then cooled to 0 °C. The further reaction and the purification of epoxides were done as described in Section 2.5.1.

## 3. Results and discussion

### 3.1. Asymmetric epoxidation of styrene and chromenes catalysed by *1*–*4*

The catalytic activity and selectivity of complexes **1**–**4** were explored for the asymmetric epoxidation of styrene, 6-nitro-2,2-dimethylchromene and 6-cyano-2,2-dimethylchromene using NaClO/PPNO or *m*-CPBA/NMO as an oxidant system. Jacobsen's catalyst was also examined for comparison purposes. The results are summarized in Table 1. All reactions proceeded smoothly, and complexes **1**–**4** gave high yields of the epoxides at 2 mol% catalyst loading with both NaClO/PPNO and *m*-CPBA/NMO as oxidant systems. In the NaClO aqueous/organic biphasic system without additive PPNO, complex **2** took 16 h to epoxidize styrene, and the ee obtained (25%) was relatively low (entry 5 vs. entry 2), indicating that PPNO as an axial ligand has a pronounced effect on both the activity and the enantioselectivity of the asymmetric epoxidation reaction, as has been reported for other chiral (salen)Mn(III)

Table 1
Asymmetric epoxidation of styrene, 6-nitro-2,2-dimethylchromene and 6-cyano-2,2-dimethylchromene catalysed by complexes **1**–**4** with NaClO/PPNO[a] and *m*-CPBA/NMO[b] as oxidant systems

| Entry | Substrate[c] | Catalyst | Oxidant system | Time (h) | Yield (%)[d] | ee (%)[e] | Configuration |
|---|---|---|---|---|---|---|---|
| 1 | **A** | **1** | NaClO/PPNO | 0.5 | 100 | 37 | *R* |
| 2 | | **2** | NaClO/PPNO | 0.5 | 100 | 38 | *R* |
| 3 | | **3** | NaClO/PPNO | 0.5 | 100 | 39 | *R* |
| 4 | | **4** | NaClO/PPNO | 2 | 94 | 37 | *R* |
| 5 | | **2** | NaClO | 16 | 51 | 25 | *R* |
| 6 | | **1** | *m*-CPBA/NMO | 10 min | 100 | 39 | *R* |
| 7 | | **2** | *m*-CPBA/NMO | 10 min | 100 | 40 | *R* |
| 8 | | **3** | *m*-CPBA/NMO | 10 min | 100 | 44 | *R* |
| 9 | | **4** | *m*-CPBA/NMO | 10 min | 99 | 41 | *R* |
| 10 | | **2** | *m*-CPBA | 1.5 | 90 | 0 | *R* |
| 11[f] | | **2** | *m*-CPBA/NMO | 15 min | 100 | 50 | *R* |
| 12 | **B** | Jacobsen's catalyst | NaClO/PPNO | 8 | 92 | 90 | 3*R*, 4*R* |
| 13 | | **1** | NaClO/PPNO | 5 | 92 | 86 | 3*R*, 4*R* |
| 14 | | **2** | NaClO/PPNO | 6 | 93 | 88 | 3*R*, 4*R* |
| 15 | | **3** | NaClO/PPNO | 6 | 91 | 89 | 3*R*, 4*R* |
| 16 | | **4** | NaClO/PPNO | 8 | 86 | 91 | 3*R*, 4*R* |
| 17 | | **1** | *m*-CPBA/NMO | 1 | 94 | 91 | 3*R*, 4*R* |
| 18 | | **2** | *m*-CPBA/NMO | 1 | 92 | 91 | 3*R*, 4*R* |
| 19 | | **3** | *m*-CPBA/NMO | 1 | 99 | 93 | 3*R*, 4*R* |
| 20 | | **4** | *m*-CPBA/NMO | 1 | 99 | 94 | 3*R*, 4*R* |
| 21 | **C** | Jacobsen's catalyst | NaClO/PPNO | 7 | 96 | 93 | 3*R*, 4*R* |
| 22 | | **1** | NaClO/PPNO | 4 | 95 | 89 | 3*R*, 4*R* |
| 23 | | **2** | NaClO/PPNO | 4.5 | 92 | 89 | 3*R*, 4*R* |
| 24 | | **3** | NaClO/PPNO | 6 | 93 | 91 | 3*R*, 4*R* |
| 25 | | **4** | NaClO/PPNO | 8 | 86 | 93 | 3*R*, 4*R* |
| 26 | | **1** | *m*-CPBA/NMO | 1 | 99 | 91 | 3*R*, 4*R* |
| 27 | | **2** | *m*-CPBA/NMO | 1 | 97 | 92 | 3*R*, 4*R* |
| 28 | | **3** | *m*-CPBA/NMO | 1 | 97 | 96 | 3*R*, 4*R* |
| 29 | | **4** | *m*-CPBA/NMO | 1 | 98 | 95 | 3*R*, 4*R* |

[a] Reactions were carried out at 0 °C in $CH_2Cl_2$ (1 mL) 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] Reactions were carried out at 0 °C in $CH_2Cl_2$ (2 ml) with *m*-CPBA (0.8 mmol) and NMO (2 mmol). Other conditions are the same as aforementioned.
[c] **A** = styrene, **B** = 6-nitro-2,2-dimethylchromene, **C** = 6-cyano-2,2-dimethylchromene.
[d] GC conversions (entries 1–11) or isolated yields (entries 12–29).
[e] Determined by GC with chiral capillary columns (Chiraldex GTA, 30 m × 250 μm (i.d.) for entries 1–11 and HP19091G-B233, 30 m × 251 μm × 0.25 μm for entries 12–29).
[f] The reaction was carried out at −78 °C.

catalysts [21,22]. In the absence of the additive NMO, the activity of **2** apparently decreased, and the enantioselectivity was completely lost for epoxidation of styrene with *m*-CPBA as an oxidant (entry 10 vs. entry 7) [20]. In general, the epoxidation reaction in the *m*-CPBA/NMO system was much faster than that in the NaClO/PPNO biphasic system and afforded higher ee values. For example, complex **3** gave 96% ee for the epoxidation of 6-cyano-2,2-dimethylchromene in the *m*-CPBA/NMO system within 1 h (entry 28), whereas the same reaction in the NaClO/PPNO system was completed in 6 h with 91% ee (entry 24). In the case of styrene, enantiomeric excess values (37–44%, entries 1–4 and 6–9) were not encouraging. When the reaction temperature was lowered from 0 to −78 °C, the enantioselectivity of **2** in the *m*-CPBA/NMO system was improved from 40% ee to 50% ee (entry 7 vs. entry 11). Complexes **1**–**4** afforded 86–94% and 89–96% ee (entries 13–20 and 22–29) for asymmetric epoxidation of 6-nitro-2,2-dimethylchromene and 6-cyano-2,2-dimethylchromene, respectively.

As shown in Table 1, the overall reaction rates of asymmetric epoxidation of substituted chromenes in the NaClO/PPNO aqueous/organic biphasic system by complexes **1**–**3** bearing a tertiary amine unit are considerably faster than those of their analogous Jacobsen's catalyst (Fig. 1), with comparable yields and slightly lower ee's (entries 12–15 and 21–24). In contrast, the (pyrrolidine salen)Mn(III) complex **4** bearing an amide unit showed somewhat lower activity than Jacobsen's catalyst for the same reaction, with a lower yield and a similar ee (entries 16 vs. 12 and 25 vs. 21). The enhanced activities of complexes **1**–**3** might be attributed to the presence of a tertiary amine unit in the pyrrolidine moiety, imparting the built-in phase-transfer capability to the catalyst [23,24]. The lower yield of **4** is presumably caused by decomposition of **4** with an amide bond in the basic aqueous/organic medium.

### 3.2. The effect of $CH_3I$ on asymmetric epoxidation of 6-nitro-2,2-dimethylchromene

The epoxidation of chromenes catalysed by chiral (salen) Mn(III) complexes with NaClO as an oxidant under biphasic reaction conditions generally requires a long reaction time even in

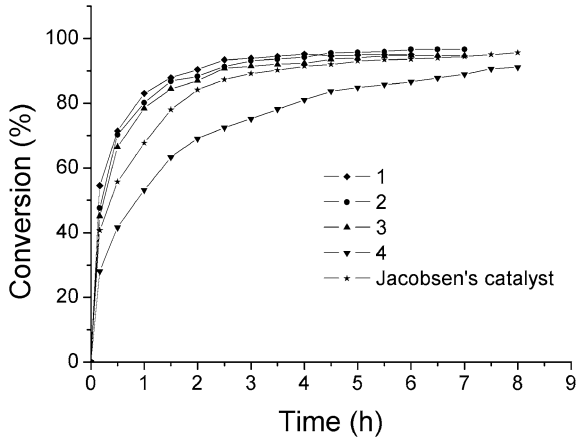



Fig. 1. The conversion versus reaction time plot for epoxidation of 6-nitro-2,2-dimethylchromene catalysed by **1**–**4** and Jacobsen's catalyst with NaClO/PPNO as oxidant system at 0 °C.

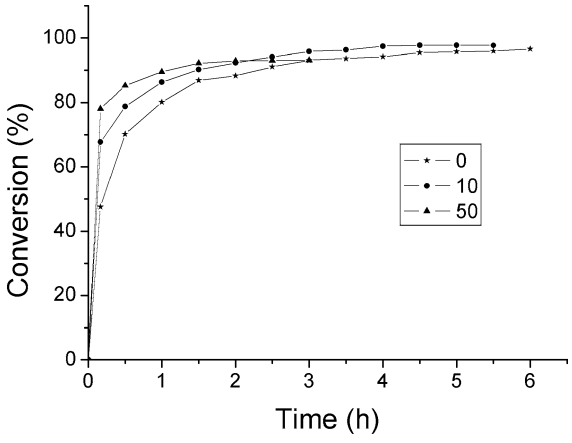



Fig. 2. The conversion versus reaction time plot for epoxidation of 6-nitro-2,2-dimethylchromene catalysed by **2** in the presence of 0, 10 and 50 equiv of $CH_3I$ with NaClO/PPNO as oxidant system at 0 °C.

Table 2
Asymmetric epoxidation of 6-nitro-2,2-dimethylchromene catalysed by **1**–**4** with NaClO/PPNO[a] at 0 °C

| Entry | Catalyst | $CH_3I$[b] | Time (h) | Yield[c] (%) | ee[d] (%) | Configuration |
|---|---|---|---|---|---|---|
| 30 (vs. 13)[e] | **1** | 50 | 1 (5) | 80 (92) | 70 (86) | 3*R*, 4*R* |
| 31 (vs. 14) | **2** | 2 | 5 (6) | 92 (93) | 88 (88) | 3*R*, 4*R* |
| 32 | **2** | 10 | 4.5 | 90 | 86 | 3*R*, 4*R* |
| 33 | **2** | 50 | 2 | 84 | 83 | 3*R*, 4*R* |
| 34 (vs. 15) | **3** | 50 | 2 (6) | 90 (91) | 88 (89) | 3*R*, 4*R* |
| 35 (vs. 16) | **4** | 50 | 8 (8) | 87 (86) | 91 (91) | 3*R*, 4*R* |
| 36 | **4** | 100 | 8 | 86 | 91 | 3*R*, 4*R* |

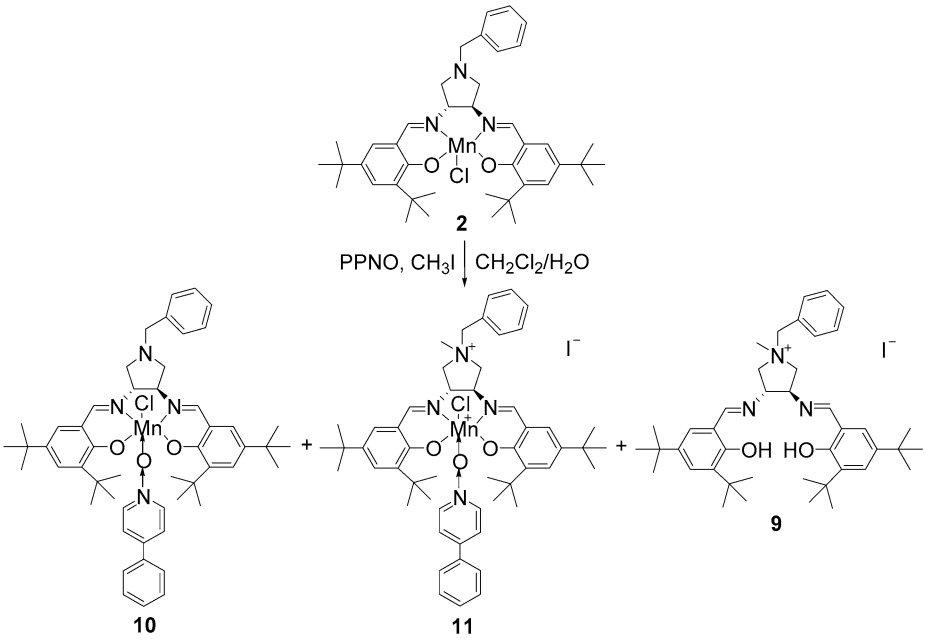
[a] Reactions were carried out in $CH_2Cl_2$ (1 mL) with alkene (0.4 mmol), PPNO (0.08 mmol), *o*-dichlorobenzene (internal standard, 0.5 mmol), $CH_3I$, catalyst (0.008 mmol, 2 mol%) and NaClO aqueous solution (pH, 11.3, 0.8 mmol).
[b] Based on the mol of catalyst.
[c] Isolated yield.
[d] Determined by GC with a chiral capillary column (HP 19091G-B233, 30 m × 251 μm × 0.25 μm).
[e] The data in the parentheses are obtained from the same reaction in the absence of $CH_3I$.

the presence of PPNO or PPPNO (4-(3-phenylpropyl)pyridine-*N*-oxide) [25–27]. Reportedly the activity can be enhanced in the two-phase reaction medium using (salen)Mn(III) catalysts with built-in phase-transfer capability [23,24], constructed by introducing the tertiary amine unit(s) to the salen ligand.

To investigate the influence of the quaternary ammonium unit formed in the molecule of the catalyst, we studied the effect of $CH_3I$ on epoxidation of 6-nitro-2,2-dimethylchromene. The catalytic results are summarized in Table 2. The epoxidation of 6-nitro-2,2-dimethylchromene by **1**–**3** bearing a tertiary amine moiety in the absence of $CH_3I$ took 5–6 h to the end of the reaction (entries 13–15 in Table 1), whereas in the presence of 50 equiv of $CH_3I$ versus the catalyst, epoxidation was completed within 1–2 h (entries 30, 33, and 34 in Table 2). An increase in the amount of added $CH_3I$ from 2 to 50 equiv had an apparent positive effect on the overall reaction rate with complexes **1** and **2** (entries 30–33, Fig. 2), but at the same time brought about considerable decreases in yields and enantioselectivity. The epoxidation of 6-nitro-2,2-dimethylchromene by complex **3** in the presence of 50 equiv of $CH_3I$ versus **3** was completed within 2 h, 4 h shorter than the reaction time needed for the same reaction in the absence of $CH_3I$, with no decrease in yield and ee value (entry 34). As for complex **4**, featuring an amide unit in the salen ligand, the addition of $CH_3I$, even to 100 equiv versus **4**, produced no observable effect on the overall reaction rate, the yield, and the ee value in the epoxidation of 6-nitro-2,2-dimethylchromene (entries 35 and 36). According to the catalytic results, the significant enhancement of the overall reaction rate for the epoxidation of 6-nitro-2,2-dimethylchromene by **1**–**3** is attributed to the formation of the quaternary ammonium unit in the salen ligand of intermediate **11** (Scheme 2),which has a built-in phase-transfer capability and may facilitate the reaction in a biphasic medium. The decomposition of the catalyst during the reaction from loss of the central metal causes the decreased yield and enantioselectivity. To determine the Mn(III) species formed in the presence of PPNO and $CH_3I$, the mixture of complex **2**, 10 equiv of PPNO, and 10 equiv of $CH_3I$ was stirred for 1 h in the $CH_2Cl_2/H_2O$ (10/1, v/v) two-phase medium, and the solution was characterized by ESI-MS (Fig. 3). As shown in the MS spectrum, there are two manganese-containing species: a PPNO axially-coordinated Mn(III) complex **10** ($[M–Cl]^+$, found: $m/z$ = 847.5, calcd: 847.4) and a quaternary ammonium intermediate **11** ($[M–Cl–I]^{2+}$, found: $m/z = 431.4$, calcd: 431.2). An ammonium salt **9** ($[M–I]^+$, found: $m/z = 638.5$, calcd: 638.5) of the pyrrolidine salen ligand, formed by dissociation of the Mn(III) ion in the catalyst (Scheme 2), is also detected in the solution. Research on the catalysts with built-in phase-transfer capability is currently underway in our laboratory.

### *3.3. The steric effect of the backbone R group on enantioselectivity and the proposed side-on approach pathway*

Soon after the discovery of asymmetric epoxidation catalysed by chiral (salen)Mn(III) complexes, side-on approach models were developed to explain the enantioselectivities of products. In general, there are three possible side-on approach




Scheme 2.

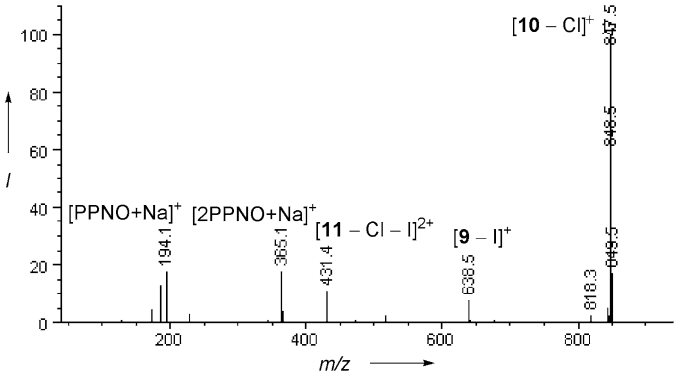
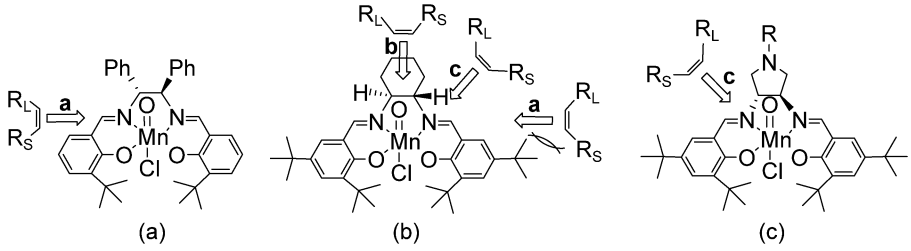



Fig. 3. ESI-MS spectrum of the solution obtained from the reaction of **2**, 10 equiv of PPNO and 10 equiv of $CH_3I$ in the $CH_2Cl_2/H_2O$ (10/1, v/v) two phase medium.

pathways for alkenes to access the oxo(salen)Mn(V) active center (Scheme 3). Jacobsen, assuming a planar structure of the salen ligand in an oxo(salen)Mn(V) catalyst [6,9], proposed that the molecule of alkene approaches the oxo(salen)Mn(V) center along either pathway **a**, favored by *trans*-1,2-diphenylethylene-derived catalysts (Scheme 3a), or pathway **b**, favored by *trans*-1,2-diaminocyclohexane-derived catalysts because of the presence of bulky *tert*-butyl groups at the C5 and C5′ positions of the salen ligand (Scheme 3b). Katsuki put forward two plausible pathways: pathway **c**, along the direction of the N–Mn bond due to the steric and $\pi$-electronic repulsions between the benzene ring of the salen ligand and the substituent on the alkene [28,29], and pathway **a**, based on a nonplanar oxo(salen)Mn(V) catalyst (Scheme 3b) [10,22,30,31]. However, the structure of the active catalyst and the actual pathway of alkene's access to the oxo(salen)Mn(V) center are not completely clear.

We prepared (pyrrolidine salen)Mn(III) complexes **1**–**3** with different backbone R groups in an attempt to gain insight into the steric effect of the R group on the enantioselectivity of alkene epoxidation. An increase in the size of the R group on the N atom of the (pyrrolidine salen)Mn(III) complex, from methyl (**1**) and benzyl (**2**) to 2,4,6,-trimethylbenzyl (**3**), led to a slight but observable increase in the enantioselectivity of the catalysts for asymmetric epoxidation of styrene and chromenes (entries 1–3, 6–8, 13–15, 17–19, 22–24, and 26–28). A similar tendency was also observed in the epoxidation of 6-nitro-2,2-dimethylchromene catalysed by complexes **1**–**3** in the presence of 50 equiv of $CH_3I$ versus catalyst (entries 30, 33, and 34 in Table 2). These results convey some information about the alkenes' access pathway in catalytic asymmetric epoxidation.

Provided that the molecule of alkene approached the (oxo)Mn(V) center along pathway **b**, the steric hindrance on




Scheme 3. Proposed side-on approach pathways for alkenes' access.

the backbone of the catalyst would have a significant negative effect on both epoxidation rate and enantioselectivity. On the other hand, it could be predicted that an increase in the size of the backbone R group should have a negligible effect on epoxidation via pathway **a**. The present catalytic results are in disagreement with either of the side-on approaches **a** or **b** as a major pathway. The catalytic results support side-on approach pathway **c**; that is, alkenes approach the nonplanar oxo(pyrrolidine salen)Mn(V) active site along the direction of the N–Mn bond (Scheme 3c).

## 4. Conclusion

The results of the present work show that $N_{aza}$-substituted chiral (pyrrolidine salen)Mn(III) complexes **1**–**4**, in combination with NaClO/PPNO and *m*-CPBA/NMO as the oxidant systems, are highly active for the asymmetric epoxidation of styrene and substituted chromenes, affording comparable enantioselectivity relative to Jacobsen's catalyst. The higher activity of complexes **1**–**3**, which feature a tertiary amine unit, compared with complex **4** bearing an amide unit and Jacobsen's catalyst, in the NaClO/PPNO aqueous/organic biphasic system is attributed to the built-in biphasic-transfer capability of **1**–**3**. Adding an excess of $CH_3I$ to the biphasic system further quickened the epoxidation reaction of 6-nitro-2,2-dimethylchromene catalysed by **1**–**3**, compromising the yield and enantioselectivity for **1** and **2** without decreasing the yield and ee value for **3**. In contrast, adding a large excess $CH_3I$ had no observable effect on the overall reaction rate, yield, and enantioselectivity for epoxidation of 6-nitro-2,2-dimethylchromene catalysed by complex **4**. An increase in the size of the $N_{aza}$-substituent on the pyrrolidine backbone of complexes **1**–**3** led to a slight increase in enantioselectivity, supporting the side-on approach pathway of alkenes to the nonplanar oxo(pyrrolidine salen)Mn(V) active site along the direction of the N–Mn bond.

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