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Synthesis and activity of macrocyclized chiral Mn(III)–Schiff-base epoxidation catalysts

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Abstract

A series of chiral macrocyclic Mn(III)Salen complexes has been prepared with two salicylidene moieties linked in their 3 and 3′ positions by aliphatic polyether bridges of variable lengths or by a more rigid aromatic junction arm. X-ray structures of ligand precursors and of complex **8** have been performed. All complexes have been used in the asymmetric epoxidation of 1,2-dihydronaphthalene with NaOCl as oxygen atom donor and exhibited modest enantiomeric excesses. Complex **10** was selected to be tested with two *cis*-disubstituted olefins and several oxidants, namely NaOCl, PhIO and *n*-Bu_4NHSO_5. 2,2′-Dimethylchromene oxide was obtained from 2,2′-dimethylchromene with ee values of 56% and 74% when using **10** and NaOCl and PhIO, respectively.

Keywords: Schiff bases; Macrocyclic ligands; Manganese; Asymmetric catalysis; Epoxidation

1. Introduction

Optically active epoxides are key intermediates in organic chemistry because they can undergo stereospecific ring-opening reactions, giving rise to a wide variety of biologically and pharmaceutically important compounds [1,2]. There continues to be great interest in the development of catalysts for asymmetric alkene epoxidation, the most notable successes being the systems of Sharpless, Jacobsen and Katsuki [3–5]. In particular, the chiral manganese Salen complexes developed by Jacobsen (e.g., Fig. 1) [6] and co-workers and Katsuki and co-workers at about the same time were the first catalysts able to perform the asymmetric epoxidation of unfunctionalized alkenes in high enantiomeric excess [7,8]. The capacity of achiral manganese Schiff base complexes to catalyze the epoxidation of olefins with aqueous NaOCl as oxygen atom donor has been initially demonstrated in our group in the early 80 s [9,10].

Various strategies involving a wide range of chiral homogeneous [11,12] and supported [2,13] manganese Salen complexes and different oxidants, the most common being iodosylbenzene [7,14] and sodium hypochlorite [15], have been developed in order to improve the enantioselectivity of the reactions. The design of new ligands still remains important because their structural and electronic properties strongly influence the conformations of the corresponding complexes, which play a crucial role in their catalytic activities [16].

In the present work, we describe the syntheses of a series of macrocyclic chiral Mn(III)–Salen complexes, where the two salicylidene moieties are linked through their 3 and 3′ positions by aliphatic polyether or benzylic diether bridges. Such a strategy has not been previously reported for chiral manganese Schiff base

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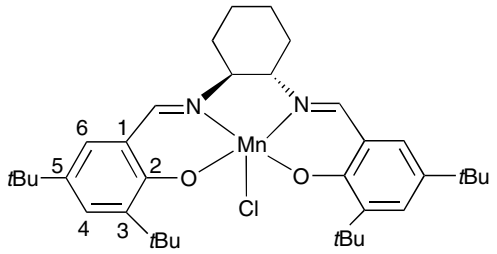


Fig. 1. The Jacobsen's catalyst (**12**).

catalysts. The well known optically active 1,2-diaminocyclohexane or 1,2-diphenylethylene diamine and the bulky *t*-butyl substituents at the 5 and 5′ positions were kept as constants in the design of these catalysts. All the three junction arms used are symmetrical so that the ligands of the corresponding Mn(III) complexes retain the crucial C_2 symmetry. The catalytic activity of these new chiral complexes was assayed in the asymmetric epoxidation of *cis*-disubstitued olefins with several oxygen atom donors.

2. Experimental

2.1. General

^{1}H NMR and ^{13}C NMR spectra were run on a Bruker AM 250 with chloroform as internal reference. Mass spectrometry analyses were performed on a Nermag R1010 (EI in MeOH) or a Perkin–Elmer SCIEX Api 365 (ES in MeOH) spectrophotometer. UV–visible spectra were obtained on a Hewlett–Packard 8452A diode array spectrophotometer. IR spectra were recorded on a Perkin–Elmer GX 2000 spectrophotometer. Optical rotations were measured with a Perkin–Elmer 241 polarimeter. Gas chromatography (GC) analyses were performed on a Hewlett–Packard HP4890A chromatograph equipped with a flame ionization detector and a Supelco cyclodextrin-β capillary column (betadex 120, 30 m × 0.25 mm, 0.25 μm film) and coupled to a Hewlett–Packard HP3395 integrator. The injector temperature was 240 °C and the column temperature 140 °C, with a column pressure of 10 psi. 1,4-Dibromobenzene was used as internal standard for the GC analyses. Di- and tri-ethylene glycol were di-tosylated according literature procedure [17]. Potassium monopersulfate, the triple salt $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$ was a gift from Interox (Curox®). Tetrabutylammomium hydrogenpersulfate, n-Bu_4NHSO_5 [18] and iodosylbenzene, PhIO [19] were prepared according literature procedures. The epoxides were identified by comparison of GC data with those obtained by reaction of the corresponding olefin with *m*-chloroperbenzoic acid. Other commercially available reagents and solvents were purchased from standard chemical suppliers and used without further purification.

2.2. Preparations

2.2.1. 2,3-Dihydroxy-5-tert-butylbenzaldehyde (*1*)

To a mixture of 4-*tert*-butylcatechol (15 g, 1.15 mmol) in 45 cm^3 methanol and NaOH (46 g, 1.15 mmol) in 40 cm^3 water was added dropwise 100 cm^3 chloroform (1.25 mmol) under vigorous mechanical stirring and over a period of 1 h 30. The reaction mixture is very exothermic and the temperature has to be kept at 30 °C with a cold water bath. After complete addition of chloroform, the resulting slurry solution was stirred for 2 h at room temperature and then acidified at pH 5–6 with 6 M HCl. The crude product was extracted with CH_2Cl_2 (2 × 100 cm^3), washed with 100 cm^3 brine and dried over Na_2SO_4. After evaporation of the solvent, the dark brown oil was purified by two consecutive column chromatographies (silicagel, hexane/ethyl acetate (90/10) as eluent) and finally recrystallized in hot hexane, affording 1.36 g of pale yellow crystals (8%) suitable for X-ray analysis. Calc. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 68.18; H, 7.16%. δ_H (250 MHz, $CDCl_3$) 1.30 (9H, s, *t*-Bu), 5.58 (1H, s, OH), 7.11 (1H, d, *J* 2.2 Hz, ArH), 7.26 (1H, d, *J* 2.2 Hz, ArH), 9.87 (1H, s, CHO), 10.90 (1H, s, OH). δ_c (63 MHz, $CDCl_3$) 31.19, 34.25, 119.84, 119.93, 120.56, 143.69, 144.28, 146.16, 197.06. *m/z* (EI) 194 (M, 37), 179 (M − CH_3, 100).

2.2.2. 3,3′-(3-Oxapentane-1,5-diyldioxy)bis(2-hydroxy-5-tert-butylbenzaldehyde) (*2*)

To a suspension of sodium hydride (previously dried 1 h under vacuum, 908 mg of a 60% suspension in mineral oil, 22.7 mmol) in 8 cm^3 dry DMSO under a nitrogen atmosphere, a solution of **1** (2 g, 10.3 mmol) in 8 cm^3 dry DMSO was added over a period of 1 h 30 under vigorous stirring. The temperature was kept below 25 °C with a cold water bath. After stirring for 1 h, diethylene glycol ditosylate (2.13 g, 5.15 mmol) was added in one portion. The reaction mixture was stirred for 48 h and then acidified at pH 1 with 25 cm^3 6 M HCl. The crude product was extracted with CH_2Cl_2 (3 × 100 cm^3), washed with 100 cm^3 brine and dried over Na_2SO_4. After evaporation of the solvent, the resulting oil was dissolved in Et_2O (20 cm^3) and precipitated with 80 cm^3 hexane (1.2 g, 51%). Calc. for $C_{26}H_{34}O_7 \cdot H_2O$: C, 65.48; H, 7.83. Found: C, 65.53; H, 7.61%. δ_H (250 MHz, $CDCl_3$) 1.29 ppm (18H, s, *t*-Bu), 3.98 (4H, m, OCH_2), 4.27 (4H, m, OCH_2), 7.17 (2H, d, *J* 2.2 Hz, ArH), 7.25 (2H, d, *J* 2.2 Hz, ArH), 9.90 (2H, s, CHO), 10.78 (2H, s, OH). δ_c (63 MHz, $CDCl_3$) 31.20, 34.0, 69.50, 70.06, 119.83, 120.49, 121.49, 142.92, 146.88, 150.14, 196.46. *m/z* (EI) 458 (M, 100). Suitable crystals were obtained for X-ray analysis.

*2.2.3. 3,3′-(3,6-Dioxaoctane-1,8-diyldioxy)bis(2-hydroxy-5-tert- butylbenzaldehyde) (**3**)*

The compound **3** was synthesized by using the same procedure as for **2**, from sodium hydride (480 mg of a 60% suspension in mineral oil, 11.86 mmol) in 4 cm^3 dry DMSO, **1** (1 g, 5.15 mmol) in 4 cm^3 dry DMSO and triethylene glycol ditosylate (1.18 g, 5.15 mmol). The crude product was dissolved in 10 cm^3 diethyl ether and precipitated with hexane (100 cm^3). The resulting yellow oil was recrystallized in hot cyclohexane, affording **3** as white crystals suitable for X-ray analysis (400 mg, 31%). Calc. for $C_{28}H_{38}O_8$: C, 66.85; H, 7.56. Found: C, 66.52; H, 7.14%. δ_H (250 MHz, $CDCl_3$) 1.29 ppm (18H, s, *t*-Bu), 3.77 (4H, s, OCH_2), 3.89 (4H, m, OCH_2), 4.29 (4H, m, OCH_2), 7.17 (2H, d, *J* 2.2 Hz, ArH), 7.24 (2H, d, *J* 2.2 Hz, ArH), 9.92 (2H, s, CHO), 10.69 (2H, s, OH). δ_c (63 MHz, $CDCl_3$) 31.16, 34.25, 69.10, 69.28, 70.66, 119.19, 119.86, 120.90, 142.66, 146.82, 149.98, 196.03. *m/z* (DCI/NH_3) 520 ($M + NH_4^+$, 100). Suitable crystals were obtained for X-ray analysis.

*2.2.4. 1,3-Benzenedimethanol-di-p-tosylate (**4**)*

In a solution of 15 cm^3 H_2O and 3 g NaOH (75.2 mmol), 4 g (29 mmol) of 1,3-benzenedimethanol were dissolved. Over a period of 20 min, tosyl chloride (12.16 g, 63.9 mmol) in 25 cm^3 THF was added dropwise and the resulting solution stirred overnight. The reaction mixture was extracted with 100 cm^3 toluene, washed with 100 cm^3 H_2O, 100 cm^3 of a saturated $NaHCO_3$ aqueous solution and dried over Na_2SO_4. The crude product was dissolved in 10 cm^3 CH_2Cl_2 and precipitated with hexane (100 cm^3). The white precipitate was filtered off and dried under vacuum (4.5 g, 35%). Calc. for $C_{22}H_{22}O_6S_2 \cdot 0.5$ H_2O: C, 58.02; H, 5.27. Found: C, 58.41; H, 5.02%. δ_H (250 MHz, $CDCl_3$) 2.44 ppm (6H, s, CH_3), 4.98 (4H, s, CH_2), 7.09 (1H, s, ArH), 7.18–7.28 (3H, m, ArH), 7.30 (4H, d, *J* 8.7 Hz, TsH), 7.77 (4H, d, *J* 8.4 Hz, TsH). *m/z* (ES) 469 ($M + Na^+$, 100).

*2.2.5. 3,3′-(1,3-Benzenediyldioxy)bis(2-hydroxy-5-tert-butylbenzaldehyde) (**5**)*

The compound **5** was synthesized by using the same procedure as for **2**, from sodium hydride (440 mg of a 60% suspension in mineral oil, 10.67 mmol) in 6 cm^3 dry DMSO, **1** (900 mg, 4.64 mmol) in 6 cm^3 dry DMSO and **4** (1.04 g, 2.32 mmol). The reaction was monitored by ^1H NMR, showing that starting 2,3-dihydroxy-5-*tert*-butylbenzaldehyde was still present. Two subsequent portions of **4** (100 mg, 2.2 mmol) were thus added at $t = 12$ and 24 h. The crude product was purified by column chromatography (silicagel, hexane/ethyl acetate (90/10) as eluent) and recrystallization in hot cyclohexane, affording 151 mg of a white solid (13%). Calc. for $C_{30}H_{34}O_6 \cdot 0.1H_2O$: C, 73.18; H, 6.89. Found: C, 72.97; H, 6.51%. δ_H (250 MHz, $CDCl_3$) 1.24 ppm (18H, s, *t*-Bu), 5.18 (4H, s, CH_2), 7.15 (2H, d, *J* 2.1 Hz, ArH), 7.19 (2H, d, *J* 2.1 Hz, ArH), 7.39 (3H, m, ArH), 7.57 (1H s, ArH), 9.89 (2H, s, CHO), 10.93 (2H, s, OH). δ_c (63 MHz, $CDCl_3$) 31.16, 34.20, 71.54, 120.06, 120.43, 121.65, 126.80, 127.35, 128.88, 137.18, 142.72, 146.54, 150.26, 196.84. *m/z* (ES) 491.1 ($M + H^+$), 513.3 ($M + Na^+$), 529.3 ($M + K^+$).

*2.2.6. Mn^{III}–Salen complex **6***

The compound **2** (400 mg, 0.87 mmol) was dissolved in 120 cm^3 EtOH under a nitrogen atmosphere. To the resulting solution was added successively (1*S*,2*S*)-(+)-1,2-diaminocyclohexane (100 mg, 0.87 mmol) and manganese (II) diacetate tetrahydrate (214 mg, 0.87 mmol). After stirring overnight, dioxygen was bubbled through the solution for 4 h. The reaction mixture was concentrated to 20 cm^3, treated with 20 cm^3 brine and extracted with 2×50 cm^3 CH_2Cl_2. The organic layer was washed with 100 cm^3 H_2O and dried over Na_2SO_4. After evaporation of the solvent and drying under vacuum, 404 mg (74%) of complex **6** was obtained as a dark brown microcrystalline solid. Calc. for $C_{32}H_{42}N_2O_5ClMn \cdot 2$-$H_2O$: C, 58.14; H, 7.01; N, 4.24; Cl, 5.36; Mn, 8.31. Found: C, 57.93; H, 7.29; N, 4.39; Cl, 5.60; Mn, 8.14%. *m/z* (ES) 589.2 (M − Cl). ν_{max}/cm^{-1} 1616 (C=N). λ_{max}/nm (MeOH) 278 ($\varepsilon/dm^3\,mol^{-1}\,cm^{-1}$ 16 110), 326 (13 110), 414 (5910). α (589 nm, 20 °C, 0.048 g dm^{-3} in MeOH, 10 cm path) = +0.0242°.

*2.2.7. Mn^{III}–Salen complex **7***

The complex **7** was synthesized as described above, starting from **2** (320 mg, 0.70 mmol) in 100 cm^3 EtOH, (1*R*,2*R*)-(+)-1,2-diaminocyclohexane (75 mg, 0.70 mmol) and $Mn(OAc)_2 \cdot 4H_2O$ (171 mg, 0.70 mmol). Yield: 360 mg, 82% as a dark brown microcrystalline solid. Calc. for $C_{32}H_{42}N_2O_5ClMn \cdot 1H_2O$: C, 59.77; H, 6.90; N, 4.36; Cl, 5.52; Mn, 8.55. Found: C, 60.06; H, 6.85; N, 4.00; Cl, 5.40; Mn, 8.58%. *m/z* (ES) 589.3 (M − Cl), 1213.6 ($Mn_2^{III}Salen_2Cl$). ν_{max}/cm^{-1} 1616 (C=N). λ_{max}/nm (MeOH) 278 ($\varepsilon/dm^3\,mol^{-1}\,cm^{-1}$ 16 110), 322 (13 570), 412 (5500). α (589 nm, 20 °C, 0.044 g dm^{-3} in MeOH, 10 cm path) = −0.0218°.

*2.2.8. Mn^{III}–Salen complex **8***

The complex **8** was obtained as described for complex **6** from **2** (320 mg, 0.70 mmol) in 100 cm^3 EtOH, (1*S*,2*S*)-(−)-1,2-diphenylethylenediamine (148 mg, 0.70 mmol) and $Mn(OAc)_2 \cdot 4H_2O$ (171 mg, 0.70 mmol). Yield: 450 mg, 89% as a dark brown microcrystalline solid. Calc. for $C_{40}H_{44}N_2O_5ClMn \cdot 2H_2O$: C, 63.28; H, 6.37; N, 3.69; Cl, 4.68; Mn, 7.24. Found: C, 63.35; H, 6.26; N, 3.40; Cl, 4.78; Mn, 7.54%. *m/z* (ES) 687.3 (M - Cl). ν_{max}/cm^{-1} 1616 (C=N). λ_{max}/nm (MeOH) 276 ($\varepsilon/dm^3\,mol^{-1}\,cm^{-1}$ 32 500), 330 (21 000), 422 (8360). α (589 nm, 20 °C, 0.049 g dm^{-3} in MeOH, 10 cm path) = +0.0212°.

2.2.9. Mn^{III}–Salen complex **9**

The complex **9** was obtained as described for complex **8** on the same scale, starting from (1*R*,2*R*)-(+)-1,2-diphenylethylenediamine. Yield: 450 mg, 89% as a dark brown microcrystalline solid. Calc. for $C_{40}H_{44}N_2O_5ClMn \cdot 2H_2O$: C, 63.28; H, 6.37; N, 3.69; Cl, 4.68; Mn, 7.24. Found: C, 63.61; H, 6.34; N, 3.46; Cl, 4.59; Mn, 7.01%. *m/z* (ES) 687.3 (M − Cl). ν_{max}/cm^{-1} 1616 (C═N). λ_{max}/nm (MeOH) 276 ($\varepsilon/dm^3\,mol^{-1}\,cm^{-1}$ 32600), 328 (22600), 426 (8732). α (589 nm, 20 °C, 0.049 g dm^{-3} in MeOH, 10 cm path) = −0.0217°.

2.2.10. Mn^{III}–Salen complex **10**

The complex **10** was synthesized as described above, starting from **3** (400 mg, 0.80 mmol) in 80 cm^3 EtOH, (1*S*,2*S*)-(+)-1,2-diaminocyclohexane (91 mg, 0.80 mmol) and $Mn(OAc)_2 \cdot 4H_2O$ (195 mg, 0.70 mmol). Yield: 365 mg, 69% as a dark brown microcrystalline solid. Calc. for $C_{34}H_{46}N_2O_6ClMn \cdot CH_2Cl_2$: C, 55.70; H, 6.37; N, 3.71; Cl, 4.70; Mn, 7.29. Found: C, 55.65; H, 6.56; N, 3.65; Cl, 4.68; Mn, 7.49%. *m/z* (ES) 633.4 (M − Cl), 656.4 (Mn^{II}Salen + Na), 672.2 (Mn^{II}Salen + K). ν_{max}/cm^{-1} 1621 (C═N). λ_{max}/nm (MeOH) 274 ($\varepsilon/dm^3\,mol^{-1}\,cm^{-1}$ 10770), 324 (8983), 412 (3760). α (589 nm, 20 °C, 0.049 g dm^{-3} in MeOH, 10 cm path) = +0.0213°.

2.2.11. Mn^{III}–Salen complex **11**

The complex **11** was synthesized as described above, starting from **5** (65 mg, 0.13 mmol) in 20 cm^3 EtOH, (1*S*,2*S*)-(+)-1,2-diaminocyclohexane (15 mg, 0.13 mmol) and $Mn(OAc)_2 \cdot 4H_2O$ (33 mg, 0.13 mmol). Yield: 40 mg, 47% as a dark brown powder. Calc. for $C_{36}H_{42}N_2O_4ClMn$: C, 65.80; H, 6.44; N, 4.26; Cl, 4.50; Mn, 8.36. Found: C, 65.75; H, 6.49; N, 3.96; Cl, 4.21; Mn, 8.56. *m/z* (ES) 621.4 (M − Cl), 679.6 (Mn^{II}Salen + Na). ν_{max}/cm^{-1} 1615 (C═N). λ_{max}/nm (MeOH) 276 ($\varepsilon/dm^3\,mol^{-1}\,cm^{-1}$ 11370), 318 (8763), 408 (3653). α (589 nm, 20 °C, 0.049 g dm^{-3} in MeOH, 10 cm path) = +0.099°.

2.3. Catalytic epoxidation procedures

2.3.1. With sodium hypochlorite as oxidant

A typical reaction mixture contained 1,2-dihydronaphthalene (14 μL, 0.1 mmol) and 1,4-dibromobenzene (23.6 mg, 0.1 mmol) in 0.5 cm^3 CH_2Cl_2, 5 μmol of the appropriate catalyst (0.5 cm^3 of a 10 mM CH_2Cl_2 stock solution; catalyst/substrate ratio = 5%) and 4-phenylpyridine *N*-oxide (4.3 mg, 25 μmol) when precised. After stirring at room temperature or 0 °C for 10 min, 0.2 mmol NaOCl (0.4 cm^3 of a 0.5 M solution in 0.16 cm^3 of a 0.05 M aqueous Na_2HPO_4 solution; 2 eq. of oxidant with respect to the substrate) was added. After vigorous stirring for 2 h, the reaction was diluted with water (2 cm^3) and CH_2Cl_2 (2 cm^3). The layers were separated, the organic phase dried over Na_2SO_4, concentrated to 1 cm^3 and analyzed by GC as described in general remarks above.

2.3.2. With iodosylbenzene as oxidant

The reaction mixture was prepared according to the procedure described above. After stirring at room temperature or 0 °C for 10 min, PhIO (44 mg, 0.2 mmol, 2 eq. of oxidant with respect to the substrate), MeOH (0.225 cm^3) and H_2O (0.025 cm^3) were added. After stirring for 2 h, the reaction mixture was diluted with CH_2Cl_2 (2 cm^3) and filtered on celite. The filtrate was worked up as described above and analyzed by GC.

2.3.3. With n-tetrabutylammonium hydrogensulfate as oxidant

The reaction mixture was prepared according to the procedure described above but the substrate and catalyst were dissolved in CH_3CN (total volume 1 cm^3) instead of CH_2Cl_2. After stirring at 0 °C for 10 min, *n*-Bu_4NHSO_5 (71 mg, 0.2 mmol, 2 eq. of oxidant with respect to the substrate) was added. After stirring for 30 min, the reaction was quenched by adding an excess of sodium dithionite, diluted with CH_3CN (2 cm^3) and filtered on celite. The filtrate was worked up as previously and analyzed by GC.

2.4. X-ray crystallography

Crystal data for **1**, **2**, **3** and **8**: ***1***: $C_{11}H_{14}O_3$, M = 194.22, triclinic, $P\bar{1}$, a = 6.370(2) Å, b = 10.280(4) Å, c = 17.372(6) Å, α = 72.844(7)°, β = 86.901(8)°, γ = 77.167(7)°, V = 1059.8(7) $Å^3$, Z = 4, T = 173(2) K, μ = 0.088 mm^{-1}, 4602 reflections (2947 independent, R_{int} = 0.0283), largest electron density residue: 0.227 e $Å^{-3}$, R_1 (for $I > 2\sigma(I)$) = 0.0590 and wR_2 = 0.1773 (all data) with $R_1 = \sum|F_o| - |F_c|/\sum|F_o|$ and $wR_2 = (\sum w(F_o^2 - F_c)^2)^2/\sum wF_o^2)^2)^{0.5}$. ***2***: $C_{26}H_{34}O_7$, M = 458.53, triclinic, $P\bar{1}$, a = 8.404(9) Å, b = 10.174(11) Å, c = 16.657(18) Å, α = 99.22(3)°, β = 94.98(2)°, γ = 113.36(2)°, V = 1273(2) $Å^3$, Z = 2, T = 193(2) K, μ = 0.086 mm^{-1}, 3835 reflections (3065 independent, R_{int} = 0.0388), largest electron density residue: 0.220 e $Å^{-3}$, R_1 (for $I > 2\sigma(I)$) = 0.0569 and wR_2 = 0.1613 (all data). ***3***: $C_{28}H_{40}O_9$, M = 520.60, monoclinic, *C2/c*, a = 20.69(2) Å, b = 16.72(2) Å, c = 9.05(1) Å, β = 114.16(2)°, V = 2856(6) $Å^3$, Z = 4, T = 193(2) K, μ = 0.090 mm^{-1}, 4520 reflections (1377 independent, R_{int} = 0.4036), largest electron density residue: 0.216 e $Å^{-3}$, R_1 (for $I > 2\sigma(I)$) = 0.1447 and wR_2 = 0.4632 (all data). Very small weak diffracting crystals and highly disorder problems are the reasons for the high R values and a data/parameter ratio of 6.62. ***8***: $C_{43}H_{50}ClMnN_2O_6$, M = 781.24, triclinic, *P1*, a = 12.261(3) Å, b = 13.190(3) Å, c = 14.265(3) Å, α =

87.453(4)°, $\beta = 64.721(4)°$, $\gamma = 72.381(4)°$, $V = 1978.5(7)$ Å^3, $Z = 2$, $T = 193(2)$ K, $\mu = 0.451$ mm^{-1}, 11 958 reflections (9153 independent, $R_{int} = 0.1004$), largest electron density residue: 0.576 e Å^{-3}, R_1 (for $I > 2\sigma(I)$) = 0.0728 and $wR_2 = 0.1786$ (all data). ***8*** forms very thin and weak diffracting plates which explains the *R* values. The absolute structure parameter refines to a value of −0.05(5).

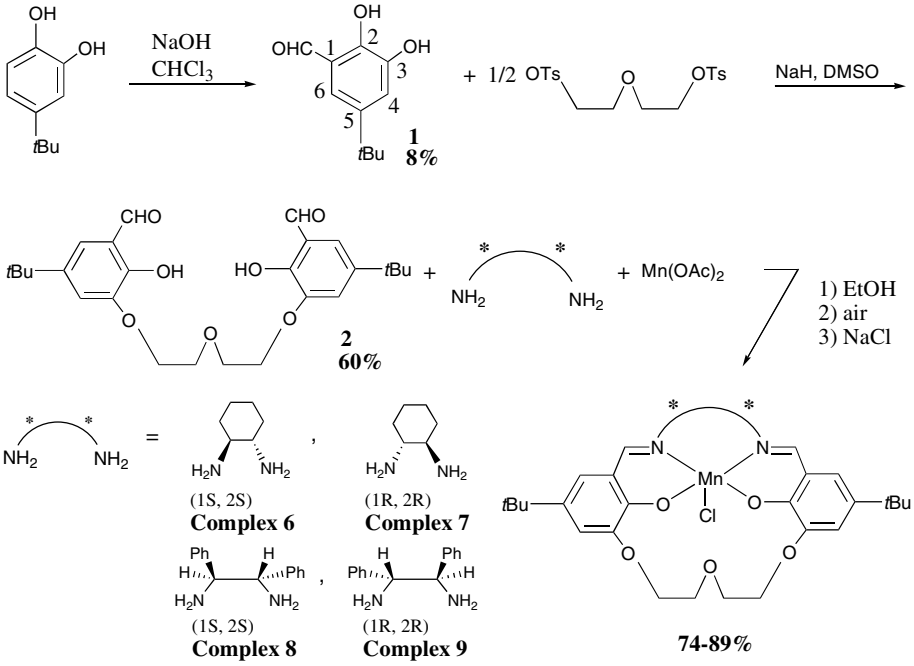
Data for all structures were collected at low temperatures using an oil-coated shock-cooled crystal on a Bruker-AXS CCD 1000 diffractometer with Mo Kα radiation ($\lambda = 0.71073$ Å). The structures were solved by direct methods (SHELXS-97) [20] and all non-hydrogen atoms were refined anisotropically using the least-squares method on F^2 [21]. CCDC 219914 (***1***), 219915 (***2***), 219916 (***3***) and 219917 (***8***) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

3. Results and discussion

3.1. Synthesis and characterization of chiral macrocyclic Mn(III)–Schiff-base complexes

We have selected two aliphatic bridges of variable lengths to investigate the influence of the flexibility in the corresponding Mn(III) complexes. Moreover, a more rigid aromatic linker has been employed, in order to reinforce the steric hindrance on the opposite side of the chiral moiety and thus to favor the approach of the olefin substrate in the vicinity of the diimine for a better stereoinduction.

The synthetic pathway for Mn^{III}–Salen complexes **6–9** including the diethylene glycol junction arm is illustrated in Scheme 1. The first step involved the preparation of 2,3-dihydroxy-5-*tert*-butylbenzaldehyde **1**. Most of the classical methods or modified procedures employed for the formylation of phenols, i.e., Vilsmeier–Haack (dimethylformamide/phosphorous oxychloride) [22], Casiraghi (tin tetra chloride/ paraformaldehyde) [23,24], or Duff reactions (hexanemethylenetetramine/ acetic acid or trifluoroacetic acid) [25,6] were unsuccessful in our case. We have also performed the *O*-protection of 4-*tert*-butylcatechol using several protective groups: di-methylester, di-acetylester, di-*tert*-butylsilylether and di-methyleneacetal. However, the formylation of these *O*-protected catechols by the different above cited procedures has only led to the starting 4-*tert*-butylcatechol. Finally, the Reimer–Tiemann method ($NaOH/CHCl_3$) [26], involving a dichlorocarbene as active species, allowed us to obtain **1** with a yield of 8%. Despite a poor yield, this reaction is easy to carry out, requires inexpensive reagents and **1** can be easily obtained on gram scale. 2,3-Dihydroxy-5-*tert*-butylbenzaldehyde **1** has been isolated as colorless crystals by recrystallization in hexane (X-ray structure analysis see Supplementary Material). The ^{1}H NMR spectrum gives a deshielded chemical shift for one phenolic proton, which is in good agreement with the observation of an intramolecular hydrogen bond between the aldehyde



Scheme 1. Reaction pathways used for the preparation of complexes **6–9**.

oxygen and the neighbouring hydroxy group in the structure. The dialdehyde **2** was prepared according the one-step procedure described in the literature [27], by reaction of **1** with two equivalents of NaH in DMSO to give the dianion, which was treated with 0.5 equivalent of diethylene glycol ditosylate [17]. After acidic work up and purification by chromatography followed by crystallization in hexane, the dialdehyde **2** was obtained as colorless crystals with a yield of 60% (Fig. 2).

The template synthesis of complexes **6**–**9** was realized by mixing the dialdehyde **2**, the desired chiral diamine and manganese(II) acetate in stoichiometric proportions, in ethanol under a nitrogen atmosphere (Scheme 1). After air oxidation and exchange of the axial anionic ligand, compounds **6**–**9** were isolated in good yields (74–89%). The template method is required in the case of short bridges like diethylene glycol. Otherwise, the condensation of the free Schiff base leads to a mixture of mono-, di-, tri- and tetrameric species, decreasing dramatically the yield of the desired ligand.

Complexes **10** and **11** were prepared in a similar manner, starting from triethylene gycol ditosylate [17] or 1,3-benzenedimethanol-di-*p*-tosylate as junction bridge and (1*S*,2*S*)-(+)-1,2-diaminocyclohexane (Scheme 2). The dialdehyde **3** was crystallized in cyclohexane (Fig. 2).

The variable lengths of the aliphatic bridges in the two aldehydes result in different distances between the connecting oxygen atoms in **2** (O2···O4 5.32 Å) and **3** (O2···O2A 6.24 Å). The short bridge in **2** leads to more important geometrical constraints for the aromatic systems when compared to the longer one. This is reflected by the angles between the aromatic rings (123° for **2** and 52° for **3**) and by the distances between the oxygen atoms of the phenolic functions (6.37 Å for **2** and 4.36 Å for **3**).

All the complexes, obtained as dark brown microcrystalline powders, were characterized by usual methods. Elemental analyses C, H, N, Cl, Mn are consistent with the proposed formula Mn^{III}(Salen)Cl · S (S = solvent molecule(s)). The principal feature of the IR spectra is the intense band ranging from 1616 to 1621 cm^{-1} which is assigned to the $\nu_{C=N}$ stretch. From the ES mass spectrometry data, complexes **6**–**11** exist exclusively as monomers, except for complex **7** where a dimeric compound $[Mn_2^{III}(Salen)_2Cl]^+$ (m/z = 1213.6) is detected as a minor species.

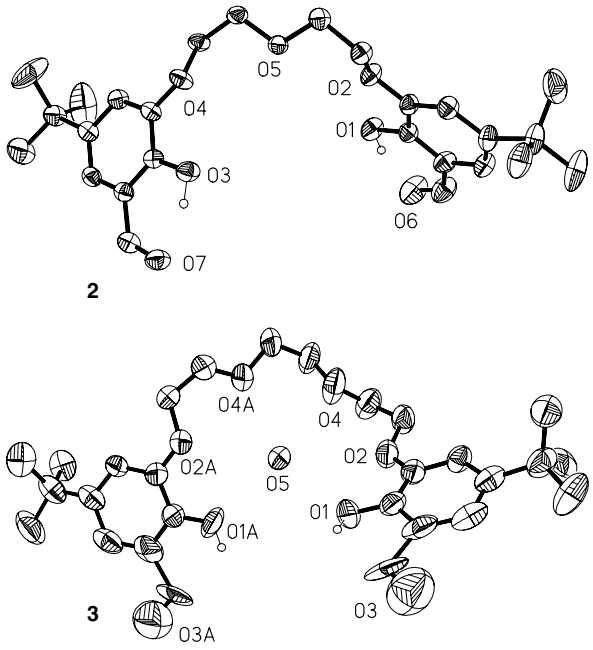
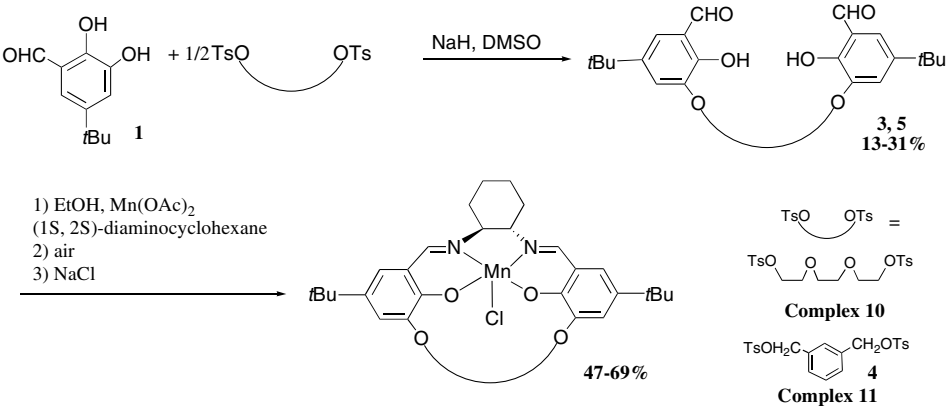


Fig. 2. Crystal structures of **2** and **3**. H atoms are omitted for clarity.

Recrystallization of complex **8** in acetone/pentane afforded red crystals, suitable for X-ray analysis (Fig. 3). The structure of catalyst **8** was found to be monomeric. Complex **8** adopts a square-pyramidal geometry, with the manganese center located only slightly above the basal plane (0.24 Å).

All attempts to crystallize the other complexes in a wide range of solvent mixtures and even by exchanging the chloride anion by non-coordinatinative counterions, i.e., NO_3^-, BF_4^- and PF_6^-, were disappointing and we have only obtained amorphous rectangular crystals in the case of nitrate-containing complexes.



Scheme 2. Reaction pathways used for the preparation of complexes **10** and **11.**

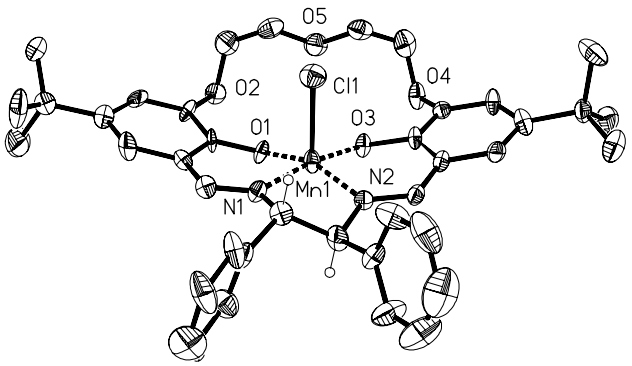


Fig. 3. Crystal structure of **8**. H atoms and non-coordinated solvent molecules are omitted for clarity. Two identical molecules of the complex are present in the asymmetric unit, only one molecule is shown. Selected bond distances (Å) and angles (°) of **8**: Mn1–Cl1 2.431(4), Mn1–O1 1.913(9), Mn1–O3 1.846(9), Mn1–N1 1.987(12), Mn1–N2 2.011(11), Cl1–Mn1–O1104.9(3), Cl1–Mn1–O3 97.5(3), Cl1–Mn1–N1 90.1(3), Cl1–Mn1–N2 95.2(3), O1–Mn1–O3 90.7(4), O1–Mn1–N1 91.6(5), O1–Mn1–N2159.0(4), O3–Mn1–N1171.2(5), O3–Mn1–N2 92.6(4), N1–Mn1–N2 82.2(5), O1···O3 2.675, O2···O4 5.483.

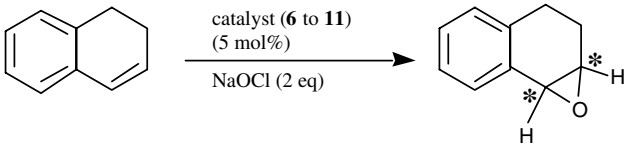
3.2. Asymmetric epoxidation catalyzed by Mn(III) complexes 6–11

The asymmetric epoxidation of 1,2-dihydronaphthalene using the six complexes **6**–**11** described above has been evaluated. Reactions were carried out using NaOCl as oxidant at room temperature. The epoxidations were typically performed with a substrate, oxidant and catalyst ratio of 1:2:0.05. The results obtained are summarized in Table 1.

With NaOCl as oxidant in a biphasic system, enantiomeric excesses were modest (16–23%) and similar for complexes **6**–**7** and **8**–**9** which differ in the chiral auxiliary. This suggested that the bulky diphenylethylene diimine has not a strong influence in the stereoinduction step for these catalysts. The best, but still modest, ee value (23%) was achieved with complex **10**, involving the long and flexible triethylene glycol bridge. For complex **11**, a complete bleaching was observed at the end of the reaction (disappearence of the brown color). This could be explained by the fact that the two fragile benzylic positions of the bridge are sensitive towards oxidative degradation. From these first results, catalyst **10** was selected to be tested with two *cis*-disustituted olefins, namely 1,2-dihydronaphthalene and 2,2′-dimethylchromene, and several oxygen atom donors, namely NaOCl, PhIO and *n*-Bu_4NHSO_5 (Table 2).

The reactions were conducted at 0 °C in the presence of the donor ligand 4-phenylpyridine *N*-oxide (4-PPNO). The addition of a nitrogenous base (4-PPNO) is supposed to avoid the formation of unreactive μ-oxo dimers [28] and to enhance the activity of the high valent Mn(V) species [29]. Indeed, with 1,2-dihydronaphthalene as substrate, the epoxide yield was enhanced: 56% with NaOCl (entry 1, Table 2) compared to 31% (entry 5, Table 1). The ee value slightly increased (28% to be compared with 23%). Tetrabutylammonium monopersulfate is easily prepared from oxone [18] and is soluble in various organic solvents. With the catalytic system **10**/*n*-Bu_4NHSO_5, a complete conversion of the substrate was reached within 30 min with a good selectivity in epoxide (78%) but the reaction was not enantioselective. In addition, it should be noted that this oxidant gives the lowest ratio of naphthalene, a dehydrogenation product in this catalytic oxidation. For the two *cis*-disubstituted olefins, the best enantiomeric excesses were reached with PhIO as oxidant (42% and 74% with 1,2-dihydronaphthalene and 2,2′-dimethylchromene, respectively) and this is a general trend for all the synthesized complexes (data not shown).

Table 1
Catalytic asymmetric epoxidation of 1,2-dihydronaphthalene with Mn^{III}–Salen complexes **6**–**11** in the presence of NaOCl as oxidant



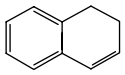
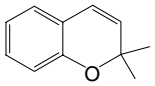
Entry	Catalyst	Yield (%)[a]	Ee (%)[b]
1	**6**	20 (21)	18
2	**7**	40 (26)	16
3	**8**	22 (9)	16
4	**9**	40 (26)	16
5	**10**	31 (15)	23
6	**11**	32 (12)	20

Reactions were carried out with substrate (0.1 mmol), catalyst (5 μmol) and oxidant (0.2 mmol) at room temperature. For details informations, see Section 2.

[a] Epoxide yield (naphthalene yield).

[b] Ee were determined by chiral GC (see Section 2); epoxide configurations are 1*S*,2*R* for catalysts **6**, **8**, **10** and **11** and 1R,2S for catalysts **7** and **9** [24].

Table 2
Catalytic asymmetric epoxidation of *cis*-disubstituted olefins with complex **10** in the presence of several oxidants

Entry	Substrate	Oxidant	Conversion (%)	Yield (%)[a]	Selectivity[b] (%)	Ee[c] (%)
1		NaOCl	90	56 (19)	62	28
2		PhIO	93	62 (19)	67	42
3		*n*-Bu_4NHSO_5	99	78 (7)	78	4
4		NaOCl	86	64	75	56
5		PhIO	68	51	75	74

Reactions were carried out with substrate (0.1 mmol), catalyst **10** (5 μmol) and oxidant (0.2 mmol) at 0 °C in the presence of 5 eq. of 4-PPNO with respect to the catalyst. For details informations, see Section 2.

[a] Epoxide yield (naphthalene yield).

[b] Selectivity of epoxide.

[c] Ee were determined by chiral GC (see Section 2); epoxide configurations are 1*S*,2*R* for 1,2-dihydronaphthalene and non-determined for 2,2′-dimethylchromene [24].

With the different oxygen atom donors used, catalyst **10** exhibits a large range of enantiomeric excesses, suggesting that the nature of the active high valent metal-oxo species should be different depending on the oxidant itself. One explanation could be a participation of the leaving group of the oxidant in the transition state corresponding to the oxygen atom transfer from the high-valent metal-oxo-like species, as previously described in metalloporphyrins-catalyzed oxygenation reactions [30]. In the case of PhIO, the PhI group could be involved in the transition state of the ''Mn(Salen)-oxo like'' species (PhIO–(Salen)Mn^{V}=O or (Salen)Mn^{IV}–OIPh), being more bent than a pure Mn^{V}=O entity and thus inducing a better stereoinduction than with NaOCl. This hypothesis is in agreement with the recent results obtained by Roschmann et al. and Collman et al. [31,32].

A cationic (Salen)Cr^{V}=O and its pyridine *N*-oxide adduct have been unambiguously determined to adopt non-planar structures by Kochi et al. on the basis of X-ray crystallography [33]. (Salen)Mn^{V}=O active species are too reactive to be isolated however they are also considered to adopt non-planar structures. Plattner et al. have established by theoretical studies the steplike or cup shaped conformations for (Salen)Mn^{V}=O intermediates bearing an axial *N*-oxide ligand [34]. Katsuki has also evidenced the non-planarity of Mn^{V}=O species by using an achiral Mn^{III}(Salen) with a chiral axial bipyridine-*N*,*N*′-dioxide [16]. In this context, the better results obtained with complex **10** exhibiting the long bridge could be related to the essential flexibility of the macrocycle during the oxygen atom transfer step, allowing stepped or bent conformations for the active high-valent metal-oxo species.

4. Conclusion

In summary, we have synthesized and characterized six chiral macrocyclic Schiff base complexes, involving aliphatic polyether or benzylic diether bridges linked in the 3 and 3′ positions of the salicylidene moieties. They have been tested as catalysts for the asymmetric epoxidation of a *cis*-disubstituted olefin. The strategy of preparing a macrocyclic ligand with a junction arm in positions 3 and 3′ has not been previously reported for chiral Mn(III)Salen catalysts to the best of our knowledge and remains attractive. 2,2′-Dimethylchromene oxide has been obtained with an ee value of 74% with PhIO as oxidant and complex **10** as catalyst. Indeed, introducing sterically hindered linkers with bulky substituents in the vicinity of the strategic 3 and 3′ positions should probably increase the asymmetric induction of the corresponding catalysts. Moreover, such bridges could be functionalized in their middle to immobilize the resulting catalysts on organic supports since the development of recyclable supported catalysts with efficient activities and enantioselectivities is still a challenge.

Acknowledgement

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version at doi:10.1016/j.jorganchem.2005.01.055.

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