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Catalytic Asymmetric Sulfoxidation by Chiral Manganese Complexes: Acetylacetonate Anions as Chirality Switches

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Three manganese(II) complexes, namely [Mn(**1**)$(ClO_4)_2$] (**3**), [Mn(**1**)$(acac)_2$] (**4**), and [Mn_2(**1**)$(acac)_4$] (**5**), were isolated from solutions of $Mn(ClO_4)_2$ or $Mn(acac)_2$, and an easily accessible diimine ligand (1*S*,2*S*)-*N*,*N*′-bis-pyridin-2-ylmethylene-cyclohexane-1,2-diamine (**1**). Their structure was determined by X-ray crystallography, and these complexes proved to be catalysts for asymmetric sulfide oxidation by H_2O_2. Enantiomeric excesses ranging from 5% to 62% were obtained with a variety of aryl alkyl sulfides. We also observed an interesting "chirality switch" effect by the achiral acac anion reversing the enantioselectivity of the complex [Mn(**1**)$(ClO_4)_2$] from the *S* to the *R* sulfoxide enantiomer.

The asymmetric oxidation of sulfides has been widely studied in the last two decades due, in part, to the importance of chiral sulfoxides as auxiliaries in asymmetric synthesis.[1] Among the most relevant metal-dependent catalytic systems, one should note the chiral titanium/diethyl tartrate/hydroperoxide/H_2O system reported by Kagan and co-workers.[2] A high level of enantioselectivity was achieved, but with low turnover numbers. On the other hand, more robust catalysts such as chiral iron or manganese porphyrins[3] and Schiff base metal (titanium, vanadium or manganese) complexes offered better activity but a lower asymmetric induction.[4] Even the salen manganese complex developed by Jacobsen and co-workers and known as one of the best catalysts for asymmetric epoxidation of conjugated olefins[5] did not achieve as high a level of enantioselectivity for sulfoxidation as for epoxidation.[6] Yet, it is well-known that methodologies for asymmetric epoxidations are also useful ones for asymmetric oxidation of sulfides.

Currently, the best catalyst for asymmetric sulfoxidation was reported by the group of Katsuki.[7] Oxidation of a variety of sulfides was achieved with enantioselectivity up to 94% and moderate to good yields. The manganese catalyst contains a highly sophisticated salen ligand bearing, in addition to the chiral diimine moiety, two binaphthyl groups of axial chirality. However, the synthesis of the ligand is rather restricting.[7d] Moreover, iodosylbenzene, which is known to be relatively expensive, to be slightly unstable in the solid state, and to have a very low solubility, was used as the oxygen atom donor. One can also mention the system described by Mukaiyama and co-workers in 1995.[8] They disclosed that β-oxo aldiminatomanganese(III) complexes were able to catalyze the enantioselective oxidation of sulfides by molecular oxygen. The presence of an aldehyde was essential for the formation of a postulated acylperoxo-manganese intermediate. However, the enantiomeric excesses and the yields were both moderate.

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Table 1. Catalytic Asymmetric Oxidation of Methylphenyl Sulfide[a]

ligand	**1**	**1**	**2**	**2**	none	none
metal salt	$Mn(ClO_4)_2$	$Mn(acac)_2$	$Mn(ClO_4)_2$	$Mn(acac)_2$	$Mn(ClO_4)_2$	$Mn(acac)_2$
yield (%)	22 (72 h)[b]	15 (2 h)[b]	45 (24 h)[b]	6 (24 h)[b]	0 (24 h)	0 (24 h)
ee (%)	10 (*S*)[c]	25 (*R*)[c]	5 (*R*)[c]	0	0	0

[a] Ligand/manganese salt/substrate/H_2O_2 ratio = 1/1/600/10 mM in absolute ethanol. [b] In parentheses, the reaction time for completion. [c] In parentheses, the configuration of the major sulfoxide enantiomer.

Thus, there is still a crucial need for new catalysts with both good enantioselectivities and activities for the asymmetric oxidation of sulfides. Even though it is environnementally friendly (water is the only byproduct), few sulfoxidation catalytic reactions are using H_2O_2 as the oxygen atom donor so far. This is partly explained by its instability through metal-catalyzed dismutation and by its ability to generate free radicals. We have thus initiated a project aimed at finding enantioselective catalysts for asymmetric oxidation of sulfide by H_2O_2.[9] We describe here our investigations regarding the preparation of new and easily accessible manganese complexes for asymmetric sulfoxidation with H_2O_2 as a "green" oxidant. Most significantly, we found that a simple achiral anion could act as a chirality switch, allowing selective generation of one or the other sulfoxide enantiomer.

Experimental Section

Materials. Ethanol (Carlo Erba, analysis grade) was used after deoxygenation by argon bubbling. Starting materials were purchased from Fluka or Sigma Aldrich Co. Most of the reagents were of the best commercial grade available and were used without further purification. Column chromatography utilized Merck silica gel (230−400 mesh). Naphthyl methyl sulfide was prepared from the corresponding aryl thiol by alkylation with 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU) and iodomethane.[10] Commercial hydrogen peroxide 30% in water from Aldrich was used and titrated before utilization.

[**Caution:** Perchlorate salts are potentially explosive and should be used with care and appropriate safety precautions.]

Physical Measurements. ^{1}H NMR spectra were recorded on a DPX 300 MHz Brüker spectrometer. UV−vis absorption spectra were recorded on a Varian Cary1Bio diode array spectrophotometer. GC-MS analyses were done with a Perkin-Elmer autosystem X coupled to a turbomass spectrometer. Electrospray mass spectrometry was performed on a Finnigan LC-Q instrument.

X-ray Crystallography. Data collection was performed at 298 K using a Bruker SMART diffractometer with a charged couple device (CCD) area detector, with graphite monochromated Mo Kα radiation ($\lambda = 0.71073$ Å). The molecular structure was solved by direct methods and refined on F^2 by full-matrix least-squares techniques using the SHELXTL package with anisotropic thermal parameters excepted for hydrogen atoms. Hydrogen atoms were placed in ideal positions and refined as riding atoms with individual isotropic displacement parameters. Pertinent crystallographic data are summarized in Table 2. Complex **3**: monoclinic, $P2_1$, a = 9.0550(6) Å, b = 19.8290(14) Å, c = 12.2059(8) Å, V = 2188.7(3) Å^3, Z = 4, R = 0.0357, R_w = 0.0678. Complex **4**: triclinic, $P\bar{1}$, a = 9.351(2) Å, b = 11.2540(19) Å, c = 13.0351(8) Å, V = 1405.5(6) Å^3, Z = 2, R = 0.0538, R_w = 01206. Complex **5**: monoclinic, $P2_1/c$, a = 13.0351(8) Å, b = 19.9146(9) Å, c = 20.3881(12) Å, V = 4097.4(4) Å^3, Z = 4, R = 0.0340, R_w = 0.0556.

Table 2. Selected Bond Lengths (Å) and Angles (deg) for Complexes **3**−**5**[a]

bond (Å)		angle (deg)	
	3		
Mn−N(1)	2.235(3)	N(1)−Mn−N(2)	70.98(10)
Mn−N(2)	2.267(3)	N(1)−Mn−N(3)	71.64(10)
Mn−N(3)	2.366(3)	N(3)−Mn−N(4)	147.77(12)
Mn−N(4)	2.338(3)	O(1)−Mn−O(11)	142.01(10)
Mn−O(1)	2.264(3)	O(1)−Mn−N(3)	87.00(10)
Mn−O(11)	2.203(3)	O(1)−Mn−N(1)	106.10(10)
	4		
Mn−N(1)	2.364(2)	N(1)−Mn−N(3)	72.10(8)
Mn−N(3)	2.278(2)	N(3)−Mn−O(21)	84.12(8)
Mn−O(21)	2.1562(19)	N(1)−Mn−O(22)	159.65(8)
Mn−O(22)	2.1130(19)	N(1)−Mn−O(21)	98.38(8)
Mn−O(31)	2.131(2)	N(1)−Mn−O(22)	94.79(8)
Mn−O(32)	2.148(2)	O(22)−Mn−O(31)	105.48(8)
	5		
Mn(2)−N(1)	2.3349(15)	N(3)−Mn(2)−N(1)	71.75(5)
Mn(2)−N(3)	2.2975(15)	N(1)−Mn(2)−O(41)	96.03(5)
Mn(2)−O(41)	2.1560(14)	N(1)−Mn(2)−O(42)	98.87(5)
Mn(2)−O(42)	2.1346(14)	N(1)−Mn(2)−O(51)	163.46(5)
Mn(2)−O(51)	2.1176(13)	N(1)−Mn(2)−O(52)	84.24(5)
Mn(2)−O(52)	2.1346(13)	O(51)−Mn(2)−O(41)	95.35(5)
Mn(1)−N(2)	2.3333(14)	O(51)−Mn(2)−O(42)	94.24(5)
Mn(1)−N(4)	2.3039(15)	N(3)−Mn(2)−O(41)	87.65(5)
Mn(1)−O(21)	2.1539(13)	N(3)−Mn(2)−O(42)	166.66(5)
Mn(1)−O(22)	2.1266(14)	N(3)−Mn(2)−O(51)	96.80(5)
Mn(1)−O(31)	2.1294(13)	N(3)−Mn(2)−O(52)	89.32(5)
Mn(1)−O(32)	2.1194(13)	O(21)−Mn(1)−O(31)	177.88(5)

[a] The estimated standard deviations in the least significant digits are given in parentheses.

Synthesis of Compounds. (1*S*,2*S*)-*N*,*N*′-Bis-pyridin-2-ylmethylene-cyclohexane-1,2-diamine (1). Under a nitrogen atmosphere, at 0 °C, a solution of freshly distilled 2-pyridincarboxaldehyde (209 mg; 1.95 mmol) in 5 mL of methanol was added over 1 h to a solution of (1*S*-2*S*)-(+)-1,2-diaminocyclohexane (100 mg; 876 μmoles) in 5 mL of methanol. The resulting clear solution was stirred for another hour at room temperature. Concentration in vacuo afforded the diimine as a white solid. Recrystallization in ether yielded the pure ligand **1** as colorless crystals (235 mg; 805 μmol, 92%): $[\alpha]^{25}_D = +24.6°$ (c 2, acetone); mp 181 °C; IR 3050, 3011, 2927, 2858, 1644, 1586, 1566, 1467, 1448, 992, 771 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (ddd, J = 4.8, 1.5, 0.9 Hz, 2H), 8,28 (s, 2H), 7.85 (d, J = 7.8 Hz, 2H), 7.60 (ddd, J = 7.8, 7.6, 1.5 Hz, 2H), 7.18 (ddd, J = 7.6, 4.8, 1.2 Hz, 2H), 3.50 (m, 2H), 1.83 (m, 6H), 1.48 (m, 2H); ^{13}C NMR (76 MHz, $CDCl_3$) δ 162.1 (CH), 155.3 (C), 149.9 (CH), 137.0 (CH), 125.1 (CH), 121.0 (CH), 74.2 (CH), 33.4 (CH_2), 25.0 (CH_2); mass spectrum (ESI), *m*/*z* (relative intensity) 315.3 ([**1** + Na]$^+$, 100); 347 ([**1** + Na + MeOH]$^+$, 52); 293.3 ([**1** + H]$^+$, 37). Anal. Calcd for $C_{18}H_{20}N_4$: C, 73.84; H, 6.95; N, 19.14. Found: C, 73.91; H, 6.90; N, 19.16.

(1*S*,2*S*)-*N*,*N*′-Bis-pyridin-2-ylmethyl-cyclohexane-1,2-diamine (2). $NaBH_4$ (72 mg; 1.92 mmol) was added to a previously cooled to 0 °C solution of **1** (140 mg; 480 μmol) in 5 mL of methanol. After stirring for 1 h at room temperature, the solution

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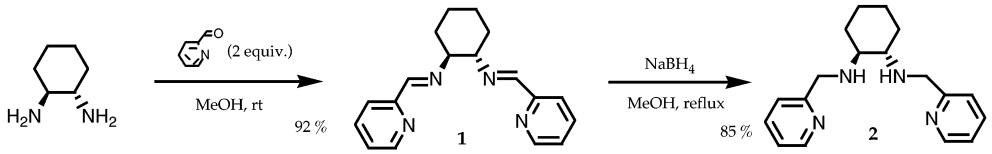
Scheme 1. Synthesis of Ligands **1** and **2**



was heated to reflux for 1 h. The solution was cooled to room temperature and hydrolyzed by addition of water (1 mL). After concentration in vacuo, the crude residue was dissolved in CH_2Cl_2 (20 mL), washed sequentially with saturated aqueous $NaHCO_3$ solution (2 × 4 mL), water (2 × 4 mL), and brine (2 × 4 mL), and dried over Na_2SO_4. The product was isolated as a yellow solid after removal of the solvent. Recrystallization from ether afforded colorless crystals (235 mg; 805 μmol, 85%): $[\alpha]^{25}_D = +0.5°$ (*c* 2, acetone); mp 143 °C; IR 3057, 3015, 2932, 2858, 1596, 1479, 1438, 1134, 761 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.43 (dd, $J = 4.8$, 1.2 Hz, 2H), 7.68 (ddd, $J = 7.8$, 7.8, 1.2 Hz, 2H), 7.42 (d, $J = 7.8$ Hz, 2H), 7.18 (ddd, $J = 7.8$, 4.8, 1.2 Hz, 2H), 4.26 (d, $J = 14.7$ Hz, 2H), 4.02 (d, $J = 14.7$ Hz, 2H), 2.73 (m, 2H), 2.14 (m, 2H), 1.75 (m, 2H), 1.49 (m, 2H), 1.20 (m, 4H); ^{13}C NMR (76 MHz, $CDCl_3$) δ 161.3 (C), 149.7 (CH), 137.1 (CH), 123.0 (CH), 122.4 (CH), 62.0 (CH_2), 53.2 (CH), 32.2 (CH_2), 25.7 (CH_2); mass spectrum (ESI), *m*/*z* (relative intensity) 319.2 ([**2** + Na]$^+$, 21); 297.3 ([**2** + H]$^+$, 100). Anal. Calcd for $C_{18}H_{24}N_4$: C, 72.94; H, 8.16; N, 18.90. Found: C, 73.15; H, 8.02; N, 18.83.

[Mn(dii-picchxn)(ClO$_4$)$_2$] (3). To a solution of **1** (30 mg; 103 μmol) in 1.5 mL of MeCN was added dropwise a solution of $Mn(ClO_4)_2 \cdot 6H_2O$ (37 mg; 103 μmoles) in 1.5 mL of MeCN. The resulting yellow solution was reduced a third of its volume, and a large excess of ether was added to precipitate the complex. The yellow precipitate was filtered off (51 mg, 94 μmol, 91%). X-ray quality crystals were obtained by vapor diffusion of diethyl ether into an acetonitrile solution of the complex (49 mg, 90 μmol, 87%): IR 3070, 2938, 2860, 2364, 2349, 1656, 1597, 1143, 1110, 1091, 1032, 1010, 6228 cm^{-1}; mass spectrum (CH_3CN, ESI$^+$), *m*/*z* (relative intensity) 446.1 ([**3** − $(ClO_4)^-$]$^+$, 100); 173.7 ([**3** − 2$(ClO_4)^-$]$^{2+}$, 67]; 193.9 ([**3** − 2$(ClO_4)^-$ + (CH_3CN)]$^{2+}$, 30). Anal. Calcd for $MnC_{18}H_{20}N_4Cl_2O_8$: C, 39.58; H, 3.69; N, 10.26; Cl, 12.98; Mn, 10.06. Found: C, 39.29; H, 3.71; N, 10.28; Cl, 13.09; Mn, 9.98.

[Mn(dii-picchxn)(acac)$_2$] (4). To a solution of **1** (60.6 mg; 207.5 μmol) in 0.5 mL of MeCN was added dropwise a solution of $Mn(acac)_2$ (50.5 mg; 200 μmol) in 0.5 mL of MeCN under a nitrogen atmosphere. Cooling at 4 °C of the resulting solution afforded **4** as pale orange crystals suitable for X-ray analysis (68 mg, 90 μmol, 61%): IR 3062, 2930, 2853, 2364, 2333, 1593, 1511, 1458, 1402, 1306, 1254, 1013, 918, 779 cm^{-1}; mass spectrum (CH_3CN, ESI$^+$), *m*/*z* (relative intensity) 446.2 ([**4** − $(acac)^-$]$^+$, 100); 699.2 ([**5** − $(acac)^-$]$^+$, <1). Anal. Calcd for $MnC_{18}H_{20}N_4Cl_2O_8$: C, 61,65; H, 6,28; N, 10,27; Mn, 10.07. Found: C, 61.26; H, 6.33; N, 10.27; Mn, 10.00.

Standard Conditions for Sulfoxidation. Under a nitrogen atmosphere, the manganese salt (10 μmol) and the ligand (10 or 100 μmol) were dissolved in absolute ethanol (10 mL). The sulfide (6 mmol) was added (final volume, 10 mL), and the mixture was stirred for 15 min. The reaction was initiated by addition of H_2O_2 (100 μmol; ratio of complex/sulfide/H_2O_2 = 1/600/10). An internal standard (20 μL of a 1 M solution of benzophenone or fluorenone in MeCN) was added to the reaction mixture. The characterization of the sulfoxides was done by GC-MS. Unambiguous identification of the products was made by comparison with pure compounds, which were either prepared independently or commercially available. All the sulfoxides were isolated by column chromatography on silica gel (ethyl acetate−hexane 20:80. then 80:20). The enantiomeric excesses were determined by ^1H NMR in $CDCl_3$ for the purified products. Chiral (*R*)-(+)-2,2′-binaphthol (1-2 equiv) was added by small portions until a good splitting of the CH_3 singlet (between 2.7 and 3.0 ppm) was obtained.[11] The ee was calculated from the deconvolution of these two peaks.

Results

Synthesis of the Ligands 1 and 2. We investigated the potential of manganese complexes bearing new C_2-symmetric chiral nitrogen containing ligands as catalysts, for asymmetric oxidation of sulfides. The two selected ligands were both constituted by a chiral cyclohexyl diamine backbone and two pyridines (Scheme 1). Our choice was first driven by their easy accessibility. Second, we expected that the Schiff base ligand (1*S*,2*S*)-dii-picchxn (dii-picchxn= *N*,*N*′-bis-pyridin-2-ylmethylene-1,2-cyclohexanediamine) (**1**) would adopt a nonplanar stepped conformation similar to that of the salen ligand,[12] whereas **2** ((1*S*,2*S*)-picchxn = picchxn = *N*,*N*′-bis-pyridin-2-ylmethyl-1,2-cyclohexanediamine),[13] thanks to a higher flexibility, would adopt a cis-β or a cis-α topology around the metal. During the course of this study, Que and co-workers[14] and very recently the group of Stack[15] used related chiral BPMCN (*N*,*N*′-bis-(2-pyridylmethyl)-*N*,*N*′-dimethyl-1,2-cyclohexanediamine) iron and manganese complexes for asymmetric *cis*-dihydroxylation of olefins and for epoxidation of electron-deficient olefins, respectively, illustrating the potential of such ligands for asymmetric catalysis.

The Schiff base ligand (1*S*,2*S*)-dii-picchxn, **1**, was easily and efficiently prepared (92% yield) in one step from the commercially available (1*S*,2*S*)-1,2-diaminocyclohexane and a small excess of 2-pyridinecarboxyaldehyde in methanolic solution. Compound **1** can be further reduced by sodium borohydride in refluxing methanol to afford **2** in a good yield.

Manganese-Dependent Sulfoxidation Reactions. Oxidation of methylphenyl sulfide by hydrogen peroxide in the presence of manganese(II) salts was then investigated as a probe reaction. Preliminary studies were carried out with *rac*-**1** and *rac*-**2** (1 mM) in the presence of $Mn(ClO_4)_2$ or $Mn(acac)_2$, the substrate, and H_2O_2 (1:1:600:10, ligand/manganese salt/substrate/H_2O_2) in absolute ethanol and under

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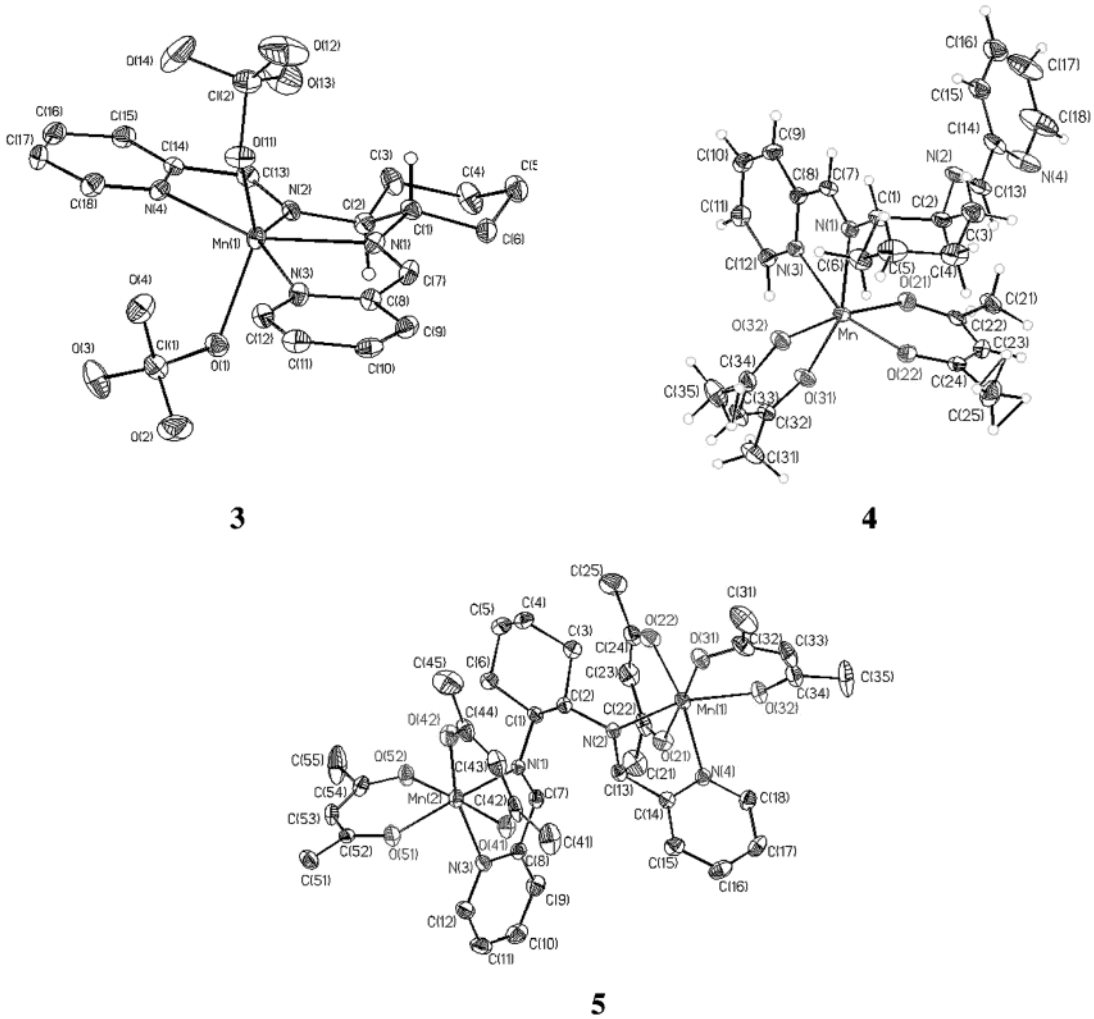

Figure 1. Structures of [Mn(**1**)(ClO_4)$_2$] (**3**); [Mn(**1**)(acac)$_2$] (**4**); [Mn$_2$(**1**)(acac)$_4$] (**5**).

air atmosphere. The reaction products were identified and quantified by GC-MS during the course of the reaction. It was observed that Mn(ClO_4)$_2$/*rac*-**1**, Mn(acac)$_2$/*rac*-**1**, and Mn(ClO_4)$_2$/*rac*-**2** systems were able to oxidize the sulfide selectively into the corresponding sulfoxide with 22%, 15%, and 45% yields, respectively. No sulfone could be detected. In the presence of *rac*-**1**, 72 h was needed to complete the oxidation with Mn(ClO_4)$_2$ as a catalyst as compared to 2 h with Mn(acac)$_2$. On the other hand, the reaction went to completion after 24 h when Mn(ClO_4)$_2$ and *rac*-**2** were used. No oxidation could be observed in the absence of the manganese salt.

Despite the low reaction yields, the asymmetric induction ability of the optically pure ligands was explored under the same experimental conditions as described. After completion, the sulfoxide was purified by column chromatography. The enantiomeric excesses (ee's) were measured by ^{1}H NMR spectroscopy in the presence of 2 equiv of (*R*)-(+)-2,2′-binaphthol as a chiral shift reagent with regard to the isolated sulfoxide.[16] The results are reported in Table 1 and show that (i) no oxidation product was formed when the reaction was carried out in the absence of the ligand, (ii) whatever manganese salt used, the Schiff base ligand **1** induced a better enantioselectivity during the oxidation than the ligand **2**, and (iii) a higher yield was achieved with Mn(ClO_4)$_2$ and **2**. Once again, we wish to emphasize the important effects of the two anions regarding the reactivity. While the Mn(ClO_4)$_2$/**1** system yielded the *S* sulfoxide enantiomer with a 10% ee preferentially, its acac homologues had a reverse and higher enantioselectivity (25% ee in favor of the *R* enantiomer). Consequently, due to the lower asymmetric induction of **2**, the study was pursued with ligand **1** only.

Determination of the Metal Complexes Involved in the Oxidation Catalysis. In the following, we describe the experiments aimed at identifying the metal complexes formed during the reaction of each of the two manganese salts with **1**. The crystallization by slow diffusion of ether in a 1:1 mixture of Mn(ClO_4)$_2$ and ligand **1** in acetonitrile afforded crystals suitable for X-ray analysis (Figure 1). The structure of the [Mn(ClO_4)$_2$(dii-picchxn)] (**3**) complex formed from Mn(ClO_4)$_2$ revealed the unexpected presence of two perchlorate anions as monodentate ligands, yet known to be poor ligands, in a trans position. Moreover, the structure showed an important distortion of the octahedral coordination with a O−Mn−O angle of 142° (Table 2). This could be due to

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Table 3. Catalytic Asymmetric Oxidation of Aryl Methyl Sulfides[a]

sulfide R^1-S-R^2		**1** + $Mn(ClO_4)_2$ = **3**		**1** + $Mn(acac)_2$ = **4**, **5**			
R^1	R^2	yield[a] (%)	ee[a] (%)	yield[a]	ee[a]	yield[b]	ee[b]
4-$CH_3O-C_6H_4-$	$-CH_3$	32	12 (*S*)	32	20 (*R*)	70	31 (*R*)
C_6H_5-	$-CH_3$	22	10 (*S*)	15	25 (*R*)	42	34 (*R*)
4-Br$-C_6H_4-$	$-CH_3$	13	5 (*S*)	11	38 (*R*)	58	50 (*R*)
4-$NO_2-C_6H_4-$	$-CH_3$	11	0	8	62 (*R*)	25	61 (*R*)
C_6H_5-	$-CH_2CH_3$	8	0	12	35 (*n.d*)	32	44 (n.d.)
naphthyl$-$	$-CH_3$	12	5 (*S*)	15	49 (*R*)	41	52 (*R*)

[a] Ligand/manganese salt/substrat/H_2O_2 ratio = 1/1/600/10. [b] Ligand/manganese salt/substrat/H_2O_2 ratio = 10/1/600/10.

the formation of the three strained contiguous 5-membered chelate rings in the equatorial plane of the complex as compared to the 6-5-6-membered chelate rings observed with salen ligands. The $N_{Py}-Mn-N_{Py}$ angle is thus opened to 147° which differs significantly from 90°, pushing away the two perchlorate anions from their apical positions. It was also observed that the two pyridine planes adopted a slightly unparalleled conformation of about 6°. The average $Mn-N_{amine}$ and $Mn-N_{pyridine}$ distances of 2.25 and 2.35 Å, respectively, are in agreement with a high-spin manganese-(II) center.[17]

Complex **4** ([$Mn(acac)_2$(dii-picchxn)]), whose crystals were obtained from the cooling at 5 °C of a saturated equimolar solution of $Mn(acac)_2$ and **1** in acetonitrile, showed an unexpected crystallographic structure (Figure 1). The ligand was coordinated to the metal center by a single arm constituted by one imine and one pyridine. The four remaining positions were occupied by two acac anions which, in contrast to the monodentate perchlorate anion, prevented an equatorial coordination of the whole ligand. The Mn−O distances ranged from 2.11 to 2.15 Å while the Mn−N bonds are slightly longer than in **3** with $Mn-N_{amine}$ distance of 2.28 Å and $Mn-N_{pyridine}$ distance 2.36 Å (Table 2). Interestingly, a faster crystallization yielded, in addition to **4**, another type of single crystal suitable for X-ray analysis. It was found that this new complex (**5**) was the C_2-symmetric di-manganese homologue of **4**, in which each arm of the ligand binds one manganese center coordinated by two acac anions (Figure 1). Both **4** and **5** presented a slightly distorted octahedral coordination with cis angles ranging from about 71° for $N_{py}-Mn-N_{imine}$ to about 84° for O−Mn−O angles and trans angles from 160° to 177° (Table 2).

Positive ESI-MS mass spectral analysis of solutions of **3** and **4** afforded mainly two intense *m*/*z* fragmentations of 446.2 and 446.1 corresponding to the parent ions [Mn(**1**)-(ClO_4)]$^+$ and [Mn(**1**)(acac)]$^+$, respectively. Furthermore, these cationic species were also observed from a 1:1 mixture of a manganese salt and **1** indicating the formation of these two complexes in solution. The dinuclear complex **5** was hard to detect by positive ESI-MS analysis in a 1:1 mixture of **1** and $Mn(acac)_2$, 699.2 *m*/*z* for [Mn_2(**1**)$(acac)_3$]$^+$ and 599.1 *m*/*z* for [Mn_2(**1**)$(acac)_2$ − H^+]$^+$. Complex **5** could also be detected in a solution formed by redissolution of **4** in acetonitrile.

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Catalytic Asymmetric Oxidation of Aryl Methyl Sulfides by 3 and 4. The catalytic activities of complexes **3** and **4** (1 mM) were then assayed during the oxidation of a variety of sulfides (600 mM) by 10 equiv of H_2O_2 with regard to the catalyst, in absolute ethanol. In each case, the yields and enantiomeric excesses were the same whether the isolated complex or a 1:1 mixture of the ligand and the corresponding manganese salt was used. This demonstrated that the active catalyst was indeed **3** or **4**, respectively. Table 3 reports the yields and the enantiomeric excesses for the sulfoxide products. In both cases, the yields were moderate and did not exceed 32%. An active dismutation of the H_2O_2 by traces of uncoordinated manganese salt might be at the origin of this problem (see following description). The enantioselectivity of the **1**/$Mn(ClO_4)_2$ system was low and afforded selectively the *S* enantiomer. On the contrary, a better stereoselectivity was achieved with the **1**/$Mn(acac)_2$ system with ee's ranging from 20% to 62% in favor of the *R* enantiomer. It is important to note the drastic effect of the anion on the reactivity and the selectivity of the catalyst. First of all, for similar yields, the **1**/$Mn(acac)_2$ system proved to be much faster than the **1**/$Mn(ClO_4)_2$ one (2 h compared to 72 h, respectively, for completion). Second, whereas the latter afforded preferentially the *S* sulfoxide in all cases, the *R* isomer was the major product when the oxidation was carried out with the **1**/$Mn(acac)_2$ system. Third, while the selectivity increased with electron-withdrawing groups on the phenyl moiety of the arylmethyl sulfide in the case of $Mn(acac)_2$, it tended to decrease with $Mn(ClO_4)_2$.

In order to improve the reaction yields, several modifications were attempted. It was found that only alcoholic solvents such as absolute ethanol were suitable for the oxidation of methylphenyl sulfide. Under the described conditions, when acetonitrile or dichloromethane was used, no oxidation products could be observed even after 24 h of reaction. Furthermore, various oxidants such as iodosylbenzene (PhIO), *t*-butylhydroperoxide (TBHP), and sodium periodate were compared to H_2O_2. The latter gave the best results in terms of the enantioselectivity of the reaction whereas PhIO and TBHP afforded higher yields but low enantiomeric excesses (0% and 5% (*R*), respectively, for the oxidation of methylphenylsulfide). Furthermore, slow addition of 10 equiv of H_2O_2 over 24 h did not change the yields when **1**/$Mn(ClO_4)_2$ was used as the catalytic system. On the other hand, with $Mn(acac)_2$, the slow addition of the oxidant over a 2 h period resulted in a significant increase of the yield of the oxidation of methylphenyl sulfide (from 15%

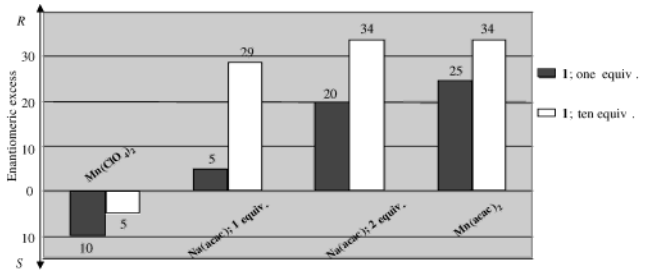

Figure 2. Effect of Na(acac) on the enantioselectivity of the sulfoxidation of methylphenylsulfide catalyzed by the **1**/$Mn(ClO_4)_2$ system. Ligand/metal/H_2O_2/sulfide ratio/1/1/10:/600 (dark) and 1/10/10/600 (white).

to 32% yield). Interestingly, an unexpected improvement of the enantiomeric excess from 25% to 38% was also observed.

Finally, the best results were obtained with a large excess of the ligand with regard to the catalyst (ligand/$Mn(acac)_2$/substrate/H_2O_2 ratio = 10/1/600/10; Table 3). A significant increase of both yields (now ranging from 25% to 70%) and enantioselectivity (ee's now ranging from 31% to 61%) was observed (Table 3).

In contrast, addition of an excess of **1** to a solution of $Mn(ClO_4)_2$ resulted in a drastic drop of the efficiency of the catalyst further illustrating the difference between the two systems.

Stability of the Catalytic System. The stability of the catalytic system **1**/$Mn(acac)_2$ was explored. Successive portions of 10 equiv of hydrogen peroxide with regard to the catalyst were added every second hour for the oxidation of methylphenylsulfide under the described conditions. Both yields and enantioselectivity remained almost unchanged after addition of 60 equiv of H_2O_2 (36% overall yield, 31% ee). Thus, after 25 turnovers, the catalyst retained full activity and enantioselectivity.

Acac Anion as a Chirality Switch. The observed drastic effect of the nature of the anion (acac versus perchlorate) on the reactivity of the manganese catalyst led us to investigate the behavior of the $Mn(ClO_4)_2$/**1** system in the presence of sodium acetylacetonate during the oxidation of methylphenylsulfide. To a mixture of $Mn(ClO_4)_2$ (1 mM), ligand **1** (1 and 10 mM), and methylphenyl sulfide (600 mM) in ethanol, sodium acetylacetonate was added just before the addition of 10 equiv of hydrogen peroxide. The results for one and two equiv of Na(acac) are reported in Figure 2 and compared to those obtained with the **1**/$Mn(acac)_2$ and the **1**/$Mn(ClO_4)_2$ systems.

As soon as 1 equiv of acac was added, the enantioselectivity of the sulfoxidation was shifted from the *S* to the *R* enantiomer but with an ee lower than that achieved with the $Mn(acac)_2$ salt. A comparable stereoselectivity was reached with 2 equiv of sodium acetylacetonate indicating a conversion of the catalyst **3** into complexes **4** and **5** upon addition of acac. This hypothesis was confirmed by ESI-MS analysis. It clearly showed the disappearance of the parent ions $[Mn(\mathbf{1})(ClO_4)]^+$ in favor of the $[Mn(\mathbf{1})(acac)]^+$ when 2 equiv of Na(acac) was added to an ethanolic solution of $Mn(ClO_4)_2$ and **1**.

Discussion

Manganese (Mn) chiral complexes have been extensively studied as catalysts for enantioselective oxidation reactions. The most developed systems are those based on Mn porphyrins[3,18] and Mn salen complexes.[5] However, the former requires costly synthesis of chiral porphyrins which furthermore display large sensitivity to oxidative degradation unless more extensive and difficult modifications are incorporated into the tetrapyrrolic macrocycle. The latter are easily accessible from readily available precursors and are much more stable. However, whereas Mn salen complexes proved to be very efficient for epoxidation of olefins using sodium hypochlorite or iodosylarenes as oxidants, they have been only rarely used for the oxidation of sulfides by hydrogen peroxide.[6]

In this paper, we report a novel class of simple ligands, exemplified by ligand **1**, which in combination with Mn−acetylacetonate (acac) provide enantioselective catalysts for the oxidation of sulfides to sulfoxides by H_2O_2. These systems have the following advantages: (i) the ligands are easy to synthesize and to modify; (ii) the resulting catalyst is rather stable; (iii) the enantiomeric excesses (ee's) are in the range of those obtained with the Mn−salen complexes for the same reaction;[6] (iv) the yields are reasonable under conditions (excess of ligand; slow addition of H_2O_2) optimized for limiting H_2O_2 dismutation.[19] Thus, although synthetically useful enantioselectivities have not yet been attained with the system presented here, it is likely that significant improvements will result from further modification of the ligands, both in terms of yields and ee's. Reduction of ligand **1** results in ligand **2**, which proved to provide much less enantioselectivity to the catalytic system. This is rather surprising considering that BPMCN, a homologue of **2**, was shown, during the course of our work, to form an iron complex with large enantioselectivity during *cis*-dihydroxylation of olefins.[14] This suggests that slight modifications of this type of ligand might result in a great variety of chiral Mn catalysts, with modulable substrate selectivities and enantioselectivities, further illustrating the potential of these ligands.

The active catalyst in the system **1**/$Mn(acac)_2$ is likely to be complex **4**. This complex is present in reaction mixtures containing **1** and $Mn(acac)_2$ and can be crystallized from these mixtures. The three-dimensional structure of complex **4** was unexpected since the ligand is occupying only two coordination sites whereas the four other positions are occupied by two acac ligands. As a consequence, no labile coordination site is present in the catalyst raising the question of how the peroxide or the substrate or both are activated at the metal site and how the chirality of the ligand is transferred to the oxidation product during oxo transfer. Clearly, further experiments are required to understand the mechanism of

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the reaction and the origin of the enantioselectivity of complex **4**. A second complex, the dinuclear complex **5**, is also present in reaction mixtures. However, considering that it represents only a minor proportion of total Mn content in the presence of an excess of ligand, we assume that the effect of **5** during catalysis is of limited importance. However, again, more experiments are needed to identify subtle differences between the two complexes.

Finally, we observed that the catalytic properties of the Mn−**1** combination could be finely tuned by varying the anion of the Mn salt, which thus provides an additional tool for increasing the diversity of the catalysts derived from this class of ligands. With the same ligand **1**, addition of Mn-$(ClO_4)_2$ or Mn$(acac)_2$ resulted in two structurally very different complexes, **3** and **4**, respectively. Furthermore, these complexes had opposite enantioselectivities, which is so far difficult to explain on the basis of the three-dimensional structures reported here. Surprisingly, complex **4** in which the two stereogenic centers are relatively far away from the metal site afforded better stereoselectivity than complex **3**. Among several explanations, one should consider the possibility that the optically pure ligand **1** induces a specific chirality (Δ or Λ)[20] at the manganese center of complex **4**, given the recent demonstration that a stereogenic metal center has the potential to transfer its chiral information to the substrate during catalysis.[21] Finally, the electronic properties of the para substituents on aryl methyl sulfides had opposite effects on the ee's of the reactions catalyzed by **3** and **4** (Table 3). With **4**, better ee's were obtained with electron-withdrawing substituents whereas with **3**, better enantioselectivity was obtained with electron-donating substituents. All these results (stereoselectivity, electronic effects) strongly suggest that the reactions catalyzed by **3** proceed by a mechanism different from that catalyzed by **4**.[22] In the case of Mn(salen) complexes which are structurally related to complex **3**, ee's increased with increased electron-withdrawing properties of the para substituents on aryl alkyl sulfides.[23]

The effect of the anion was illustrated in an experiment shown in Figure 2. Complex **3**, responsible for the stereoselective formation of *S*-sulfoxides, can be converted to complex **4**, responsible for the stereoselective formation of *R*-sulfoxides, upon addition of sodium acetylacetonate. As far as we know, this is the only reported example in which an achiral anion plays the role of a chirality switch allowing the selective formation of either one or the other enantiomeric product.[24]

Conclusion

In this paper, we described the development and the application of manganese(II) systems with C_2-symmetric bis-diimine chiral ligand for catalytic asymmetric sulfoxidation. Three original and unexpected complexes were isolated and structurally characterized by X-ray analysis. One of these catalytic systems afforded chiral sulfoxides with moderate to good enantioselectivities. Thanks to the simplicity of the ligand and its straightforward synthesis, optimization of this system is currently under investigation, and results will be reported in due course. We also reported the effect of an achiral anion as a chirality switch on the stereoselectivity of the oxidation of sulfides allowing the formation of either one or the other sulfoxide enantiomer via the transformation of one active complex into another one.

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Supporting Information Available: Crystallographic data for [Mn(**1**)$(ClO_4)_2$], [Mn(**1**)$(acac)_2$], and [Mn_2(**1**)$(acac)_4$] (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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