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New ligands for manganese catalysed selective oxidation of sulfides to sulfoxides with hydrogen peroxide

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Abstract—In situ prepared manganese complexes with ligands **1**–**5** have been used in the catalytic oxidation of sulfides to sulfoxides using hydrogen peroxide at 0°C in acetone. Using ligand **4**, methyl phenyl sulfoxide is obtained in 55% yield and turnover numbers up to 250, while the formation of sulfone is almost suppressed. © 2001 Elsevier Science Ltd. All rights reserved.

The selective catalytic oxidation of sulfides to sulfoxides has been a challenge for many years, owing to the importance of sulfoxides as intermediates in organic synthesis.[1] The use of H_2O_2 as an oxidant has been extensively studied. Compared to catalytic methods that require oxidants such as NaOCl and ammonium periodates, the use of aqueous H_2O_2 offers the advantage that it is a cheap, environmentally benign and a readily available reagent.[2] Since water is the only expected side product, catalytic oxidation methods using this reagent are undoubtedly appealing, providing efficient catalysis is accomplished. The undesired sulfone is a common by-product in sulfide oxidation with H_2O_2 and its formation has to be suppressed. Much effort has also been devoted to the development of catalytic methods for the preparation of optically active sulfoxides owing to their importance as chiral ligands,[3] and bioactive products.[4] Since the first reports of Kagan[5] and Modena,[6] who used diethyltartrate, Ti(O*i*-Pr)$_4$ and hydroperoxides as oxidants yielding e.e.s higher than 90%, a number of publications related to this research followed.[7] Hydrogen peroxide has been

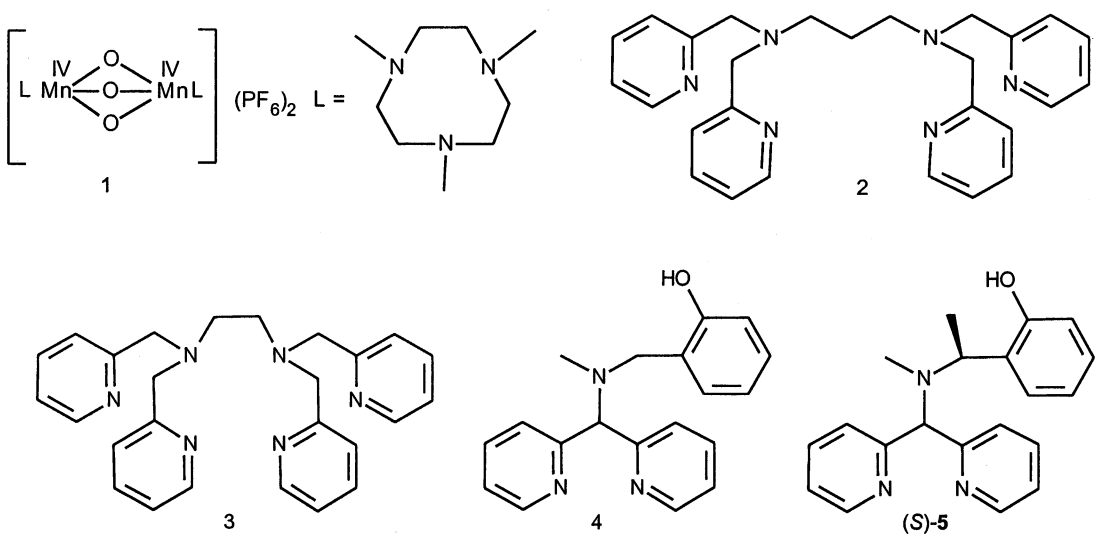

Figure 1.

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investigated as a terminal oxidant in the oxidation reactions with titanium derivatives supported on silica,[8] but only low enantioselectivities (13%) were obtained.[9] The use of the Jacobsen (salen) Mn(III) complexes provided good chemical yields and enantiomeric excesses in the range of 34–68% with a reaction system consisting of hydrogen peroxide, acetonitrile as solvent and 2–3 mol% of the salen complex.[10]

Considering that one could expect that a good epoxidation catalyst can also work as a promoter of the oxidation of thioethers, we report here the use of complex **1** and some in situ formed complexes with ligands **2**–**4** (Fig. 1) that were highly active in the oxidation of benzylic alcohols to aldehydes[11] and of olefins to epoxides[12] with H_2O_2. In addition, we report some preliminary results on the possibility of inducing enantioselectivity using the optically active Mn complex with ligand (*S*)-**5** (Fig. 1).

Since we found that several manganese salts catalyse oxidation reactions with H_2O_2, we first examined the oxidation of methyl phenyl sulfide with H_2O_2 in the presence of only $Mn(OAc)_3{\cdot}2H_2O$. Different solvents, the effect of temperature and the amount of oxidant were investigated, and the results are collected in Table 1. The oxidation of methyl phenyl sulfide is almost completely suppressed in acetone and acetonitrile at 0°C using 2 equiv. of H_2O_2. Only 6% of methyl phenyl sulfide was converted to sulfoxide after 6 h in both solvents. When, under the same conditions, an excess (8 equiv.) of oxidant was used, 30% (in acetone) and 68% (in acetonitrile) of sulfide was converted.

Next the dinuclear manganese(IV) complex **1** based on the *N*,*N*′,*N*″-1,4,7-trimethyl-1,4,7-triazacyclononane (MeTACN) ligand[13] (used as catalyst in the selective oxidation of sulfides to sulfones with periodic acid in pyridine[14]) was used as catalyst for the oxidation of methyl phenyl sulfide with H_2O_2. Furthermore, the in situ-formed complexes with dinucleating ligands *N*,*N*,*N*′,*N*′-tetrakis(2-pyridylmethyl)-1,3-propanediamine (**2**, TPTN) and *N*,*N*,*N*′,*N*′-tetrakis(2-pyridylmethyl)-1,2-ethanediamine (**3**, TPEN) both featuring the three N-donor set for each Mn site, were used (Fig. 1). The ligands **2** and **3** contain a three- and two-carbon spacer, respectively, between the three N-donor sets.[12]

Typical catalytic reactions were performed[15] at 0°C under a nitrogen atmosphere using 1 equiv. of catalyst, 1000 equiv. of substrate and 8 equiv. of H_2O_2 with respect to substrate. The complexes and in situ-formed catalysts turned out to be very active in sulfide oxidation. For instance, the dinuclear manganese complex based on **1** performs very efficiently in the oxidation of methyl phenyl sulfide and generally resulted in full conversion in 1 h (Table 2). Unfortunately, besides the desired sulfoxide, overoxidation to sulfone was observed. Manganese complexes based on TPTN-**2** and TPEN-**3** were also found to be very active. However, overoxidation was also found. Based on the oxidation results with complex **1** and Mn complexes derived from ligands **2** and **3** (all featuring three N-donor sets) and because of the successful Jacobsen salen oxidation catalysts containing two N-donor and two O-donor sets,[10] we decided to use the new ligand 2-{[[di(2-pyridinyl)methyl](methyl)amino]methyl}phenol[16] (**4**,

Table 1. Oxidation of methyl phenyl sulfide with hydrogen peroxide (30% in water) in the presence of 0.2 mol% $Mn(OAc)_3{\cdot}2H_2O$ at 0°C

Entry	Solvent	Oxidant equiv.[a]	T.O.N.[b] 2 h sulfoxide[c] (sulfone[c])	T.O.N.[b] 4 h sulfoxide[c] (sulfone[c])	T.O.N.[b] 6 h sulfoxide[c] (sulfone[c])	Sulfide not reacted (%)
1	Acetone	2	14 (0)	15 (0)	16 (0)	94
2	Acetone	8	56 (53)	61 (62)	73 (78)	70
3	Acetonitrile	2	20 (5)	20 (5)	20 (5)	94
4	Acetonitrile	8	98 (51)	115 (149)	126 (181)	32
5[d]	Dichloromethane	8	21 (19)	27 (36)	35 (70)	75

[a] H_2O_2 with respect to substrate.
[b] T.O.N. = turnover number = mol product/mol catalyst.
[c] All products were identical to independent samples and identified by GC (HP 6890, column HP1 15×0.3 mm×2.65 μm, polydimethylsiloxane).
[d] Room temperature.

Table 2. Oxidation of methyl phenyl sulfide with 8 equiv. of hydrogen peroxide (30% in water) in the presence of 0.2 mol% $Mn(OAc)_3{\cdot}2H_2O$ and 0.2 mol% of ligand at 0°C

Complex ligand[a]	T.O.N.[b] 2 h sulfoxide (sulfone)	T.O.N.[b] 4 h sulfoxide (sulfone)	T.O.N.[c] 6 h sulfoxide (sulfone)
1	574 (395)[c]	N.d.	N.d.
2	349 (222)	563 (342)	N.d.
3[d]	330 (220)	342 (343)	357 (464)
4	247 (58)	248 (69)	255 (74)

[a] See Fig. 1.
[b] T.O.N. = turnover number = mol product/ mol catalyst.
[c] T.O.N. result after 1 h.
[d] Room temperature.

Table 3. Oxidation of sulfides using Mn-catalysts based and (*S*)-**5**[a]

Entry	Ar	R	Sulfoxide (%)[b]	ee[c]	Absolute configuration[d]
1	Ph	Me	55	18	*R*
2	*p*-MeC_6H_4	Me	50	8	*R*
3	*p*-$MeOC_6H_4$	Me	48	5	*R*
4	Ph	CH_2Ph	50	5	*R*
5	2-Naphthyl	Me	52	6	*R*
6	1-Naphthyl	Me	52	7	*R*

[a] Acetone, $T=0°C$ under a N_2 atmosphere, reaction time 2 h, 8 equiv. of 30% H_2O_2 in water as oxidant.
[b] Isolated yield after column chromatography (SiO_2, EtOAc).
[c] Determined by HPLC on a Daicel Chiralcel OB-H column.
[d] Determined by Daicel Chiralcel OJ column; determined by comparison with literature values.[7b]

Fig. 1), featuring a three N-donor and one O-donor ligand. Using the complex formed in situ from ligand **4** with $Mn(OAc)_3·2H_2O$ and methyl phenyl sulfide as a test compound, high selectivity was observed, while only slight overoxidation was found. After 4 h, 248 turnover numbers to sulfoxide and only 69 turnover numbers to sulfone were detected (Table 2). After column chromatography a 55% isolated yield of pure sulfoxide was obtained.

Even in the case of slow oxidant addition (over a 1 h period), only a negligible effect in increasing the conversion was found. Using $Mn(ClO_4)_2·6H_2O$ instead of $Mn(OAc)_3·2H_2O$ caused an increase in overoxidation to sulfone, whereas switching from acetone to acetonitrile or dichloromethane as solvent resulted in a dramatic decrease in conversion. It turned out that the best conditions for ligand **4** are acetone as the solvent, and performing the oxidation at 0°C and 8 equiv. of hydrogen peroxide. In summary, the Mn complex with ligand **4** is a promising catalyst in the selective oxidation of methyl phenyl sulfide using hydrogen peroxide: with a very low amount of catalyst (0.2 mol%) we obtained the corresponding sulfoxide with 55% chemical yield, without formation of sulfone. We decided to test ligand (*S*)-**5**,[16] a chiral version of ligand **4**, reasoning that we should obtain sulfoxides with conversion comparable with those obtained using ligand **4**, but in optically active form. The results of oxidation of several substrates using this new ligand are presented in Table 3.

Employing the catalyst formed in situ by reacting the enantiopure ligand (*S*)-**5** (Fig. 1) with manganese acetate, sulfoxides are obtained in good yields ranging from 48 to 55%. It seems that the structure of the substrate does not affect the chemical yield of the reaction. An important feature is that only minor amounts of by-products resulting form overoxidation were found. Using (*S*)-**5** we always obtained sulfoxides with (*R*)-configuration and e.e.s up to 18% (methyl phenyl sulfoxide). Increasing the amount of catalyst from 0.2 to 2 mol% did not improve the enantioselectivity.

In conclusion, the Mn complex based on ligands **4** and **5** is a highly selective and active system for catalytic oxidation of sulfides to sulfoxides using aqueous hydrogen peroxide as a terminal oxidant. Studies to enhance the enantioselectivity in this new catalytic system are in progress.

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