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Asymmetric Epoxidation of Unfunctionalized Olefins Catalyzed by Novel Manganese-Picolinamide-Salicylidene Complexes

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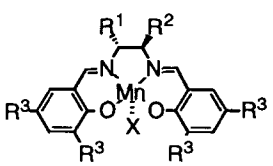
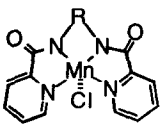
Abstract: A new class of tetradentate chiral picolinamide-salicylidene ligands and their corresponding manganese complexes as catalysts for epoxidation of olefins have been designed and synthesized. The manganese complexes catalyzed asymmetric epoxidation of olefins by sodium hypochlorite with up to 74% ee for cis olefins and 53% ee for *trans*-β-methyl styrene. These novel catalysts exhibited higher turnover numbers than chiral Mn-salen catalysts. Copyright © 1996 Elsevier Science Ltd

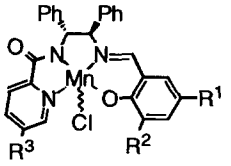
Commonly studied metal catalysts for the asymmetric epoxidation of unfunctionalized olefins are chiral metalloporphyrins and manganese-salen complexes.[1] Metalloporphyrins usually exhibit high turnover numbers and moderate enantioselectivities.[2] Chiral manganese-salen systems[3] are highly enantioselective for epoxidation of *cis* olefins, but their turnover numbers are relatively low. Recently, several other types of metal catalysts for the asymmetric epoxidation of olefins have been reported. These include: nickel complexes bearing cyclic or acyclic tetraaza multidentate ligands;[4] a biomimetic Mn-dihydrosalen complex;[5] a chiral ruthenium-bis(oxazolinyl)bipyridine complex;[6] and β-ketoiminato manganese complexes.[7] The development of novel epoxidation catalysts, in addition to salen and porphyrin systems, is important as it would open new avenues for the discovery of improved catalysts. We report here our results on the design, preparation and evaluation of novel oxidation resistant catalysts (**5**, **6a-b**) for asymmetric epoxidation of unfunctionalized olefins.



1: $R^1=R^2=R^3=H$
2: R^3=t-Bu; $R^1+R^2=(CH_2)_4$



3: R = *o*-C_6H_4
4: R = CH(Ph)CH(Ph)



5: $R^1=R^2=R^3=H$
6a: R^1=t-Bu; R^2=trityl; $R^3=H$
6b: R^1=t-Bu; R^2=1,1-diethylpropyl; R^3=n-Bu

The discovery[3,9] of Jacobsen's chiral manganese salen catalyst **2** was based on Kochi's work on the achiral manganese-salen catalyst **1**.[8] The easily oxidizable imine and phenoxide moieties in **2** were proposed to be responsible for the oxidative degradation of the catalyst during the epoxidation reaction.[9]

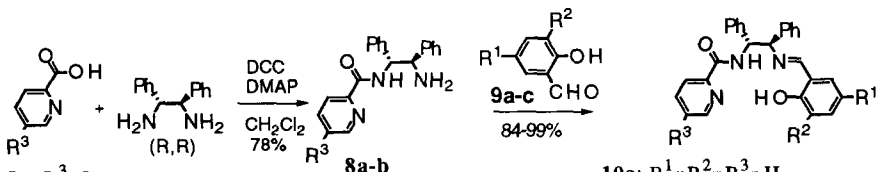
The manganese complex **3** of a bisamide has been reported to be an active catalyst for epoxidation of simple olefins by iodosylbenzene.[10] Using Jacobsen's strategy for his invention of the chiral Mn-salen complex based on Kochi's achiral complex, we reasoned that by replacing phenylenediamine with a chiral diamine, the resulting complex **4** might be an enantioselective catalyst for olefin epoxidation. The amide and pyridine moieties are much more stable than phenol or imine moieties under oxidative conditions. Therefore,

the catalyst life time may be longer than the Mn-salen complex, resulting in higher catalyst turnover numbers.

The free ligand in **4** was synthesized from picolinic acid and (1R,2R)-(+)-1,2-diphenylethylenediamine.[11] Reaction of the chiral ligand with $Mn(OAc)_3 \cdot 2H_2O$ and LiCl in the presence of KO*t*-Bu gave **4** only in very low yield (<10%).[12] Furthermore, no catalytic activity was observed when **4** was used in epoxidation of styrene using Clorox® bleach as the oxidant. This dramatic change in catalytic activity of **4** compared with **3** may be attributed to the change of the conjugation system when using a chiral diamine instead of phenylenediamine. We also made the corresponding nickel complex using a literature procedure.[11] The epoxidation of *trans*-β–methylstyrene under Mukaiyama's conditions[7] gave the corresponding epoxide in 88% yield with 1 mol% of the nickel catalyst. However, the ee of the product epoxide was not significant (<8%).

Next, we were interested in investigating the catalytic activity and selectivity of complex **5**, which contains a salicylidene moiety and a picolinamide moiety. Complex **5** may be viewed as a hybrid of the structures of Mn-salen **2** and Mn-bispicolinamide **3**, hence the "hybrid" complex. The hybrid ligand **10a** was synthesized by reaction of picolinic acid with one equivalent of the chiral diamine in the presence of DCC and catalytic amount of DMAP in CH_2Cl_2 at room temperature to form a monoamide **8a**, followed by condensation with 1 equiv. of salicylaldehyde (**9a**). Treatment of **10a** with $Mn(OAc)_3$ dihydrate and LiCl in ethanol afforded **5**, which was isolated by column chromatography on silica gel in 67% yield.[12]

Scheme 1



7a: R^3=H
7b: R^3=n-Bu

8a-b

10a: R^1=R^2=R^3=H
10b: R^1=t-Bu; R^2=trityl; R^3=H
10c: R^1=t-Bu; R^2=1,1-diethylpropyl; R^3=n-Bu

With 3.4 mol% of **5**, the epoxidation of *cis*-β–methylstyrene by sodium hypochlorite under Jacobsen's conditions[3c] gave 40% ee and 66% yield (Table 1, entry 1). Epoxidation of dihydronaphthalene with 0.8 mol% of **5** gave the epoxide in 80% yield and 39% ee, implying a turnover number of about 100. The turnover number of Jacobsen's catalyst was reported to be < 25 in the epoxidation of dihydronaphthalene.[1a] These results were rather encouraging despite the low ee's. The observed high turnover numbers of the hybrid catalyst **5** supported our rationale for the design of robust epoxidation catalysts.

Enantioselectivity of the manganese salen or porphyrin epoxidation catalysts has been tremendously enhanced by the alteration of substituents on the ligand.[2,3,9] Therefore, we synthesized complexes (**6a-b**) with different substituents. The requisite substituted salicylaldehydes (**9b**: R^1=t-Bu; R^2 = trityl; **9c**: R^1=t-Bu; R^2=1,1-diethylpropyl) were synthesized by alkylation of 4-*tert*-butylphenol with trityl alcohol or triethyl carbinol in the presence of concentrated sulfuric acid, followed by formylation with hexamethylenetetramine under Duff reaction conditions.[13] The hybrid complexes (**6a-b**) were obtained in 30-60% overall yield from the corresponding 2-pyridinecarboxylic acids according to the reaction sequence outlined in Scheme 1.

Table 1. Asymmetric Epoxidation Catalyzed by Mn-Picolinamide-Salicylidene Complexes[a]

Entry	Olefin:	Catalyst: (mol%)	Mol% Mn-salen required in lit.[b]	Epoxides: cis/trans	yield%[c]	ee[d] of major epoxide
1	Z–β–methylstyrene	**5** (3.4)	4[1a]	76/24	66	40 (1R,2S)[14]
2	"	**6a** (0.8)		85/15	78	67 (1R,2S)
3	*E*–β–methylstyrene	**5** (4)	~7[16]	0/100	92	31 (1R,2R)
4	"	**6b** (5.2)		0/100	100	53 (1R,2R)
5	"	**6b** (0.8)		0/100	55	51 (1R,2R)
6	1,2-dihydronaphthalene	**5** (0.8)	4[1a]	n/a	80	39 (1R,2S)
7	"	**6a** (0.54)		n/a	82	74 (1R,2S)

[a] Buffered 5% NaOCl (pH=11.3);[3c] CH_2Cl_2 as solvent; 0°C; 15-40h. [b] Literature amount (mol%) of a manganese salen catalyst required for complete conversion. [c] Yields were determined by GC using decane as internal standard. For epoxidation of *cis*-β–methylstyrene, the total yield of both cis and trans epoxides is shown. [d] Ee's were determined by chiral GC using cyclodex-B or Chiraldex G-PN column.

Similar to Jacobsen's system, increased enantioselectivities were observed with bulky substituents (Table 1). With complex **6a**, bearing a trityl group, the ee for epoxidation of *cis*-β–methylstyrene was increased to 67% (entry 2). The ee of cis epoxides in the epoxidation of *cis*-β–methylstyrene catalyzed by **6a** was constant during the course of the reaction. Epoxidation of 1,2-dihydronaphthalene catalyzed by 0.54 mol% of **6a** gave 74% ee and the catalyst turnover number was about 150 (entry 7). The ee for epoxidation of *trans*-β-methyl styrene catalyzed by **6b**, made from Fusaric acid (**7b**), was 53% (entry 4, 5). To our knowledge, this is the highest ee ever obtained in metal catalyzed epoxidation of *trans*-β-methylstyrene using bleach as oxidant.[15]

In contrast to the Jacobsen's system, the use of (R, R)-1,2-diaminocyclohexane instead of (R, R)-1,2-diphenylethylenediamine did not increase the ee for epoxidation of *cis*-β–methylstyrene. Another characteristic of the epoxidation reactions catalyzed by the hybrid catalysts was that the reaction rates for *cis*-β–methylstyrene and *trans*-β–methylstyrene were similar.[16] One should note that, unlike the salen ligands, the hybrid ligands **10a-c** are devoid of C_2 symmetry.[17] In complexes **5** and **6a-b**, the picolinamide moiety forms a 5-membered metallacycle with manganese, whereas the salicylidene moiety forms a 6-membered metallacycle. This results in significant geometrical differences between the left half and the right half of the hybrid complexes. The active form of the hybrid catalysts in the epoxidation reaction is probably a manganese oxo complex by analogy to the Mn-salen or Mn-porphyrin catalysts.[1] The lack of C_2 symmetry in the hybrid system can therefore result in either of two diastereomeric species. At present time, it is not clear to us which diastereomer is preferentially formed or more reactive.

In conclusion, a number of picolinamide based ligands and their manganese complexes have been synthesized and evaluated in the asymmetric epoxidation of simple olefins. As expected, the hybrid manganese-picolinamide-salicylidene complexes exhibited higher catalyst turnover numbers in the cases studied than manganese-salen systems reported in literature. They are a new class of epoxidation catalysts in addition to manganese salen and porphyrin complexes. These complexes, although currently affording moderate ee's (< 74%), have potential to be improved, particularly for the epoxidation of trans olefins which still remains as an unsettled important problem in asymmetric catalysis.

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14. The absolute configuration of the major enantiomer was determined by comparing the retention time on the chiral columns with that of the authentic chiral epoxide samples.
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