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CATALYTIC ASYMMETRIC EPOXIDATION OF UNFUNCTIONALIZED OLEFINS

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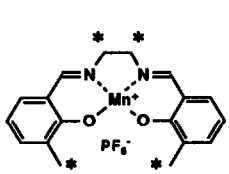
Summary: Manganese complex of the optically active salen ligand [*N,N'*-bis[(*S*)-3-(1-phenylpropyl)salicylidene]-(1*R*,2*R*)-1,2-diphenylethylenediaminato] was found to be an effective catalyst for the enantioselective epoxidation of unfunctionalized olefins. The highest enantioselectivity of 50% ee was realized for (*E*)-1-phenyl-1-propene.

Optically active epoxides are known as versatile chiral building blocks in organic synthesis.[1] Many efforts have been directed toward developing asymmetric epoxidation reaction of olefins and it was found that epoxidation of allylic alcohols using $Ti(O^iPr)_4$/diethyl tartrate/*t*-butyl hydroperoxide derived system proceeded with high enantioselectivity.[2] However, enantioselective epoxidation of olefins which do not bear a specific adjacent functionality like hydroxyl group still remains unsettled.[3]

In connection with studies of developing the model compound for the cytochrome P-450 family,[4] iron complexes of chiral porphyrins were found to be effective for the asymmetric epoxidation of unfunctionalized olefins showing up to 72% ee in the epoxidation of (*Z*)-1-phenyl-1-propene.[3c] On the other hand, manganese salen complex **1** was also reported to be a useful catalyst for the epoxidation of olefins by Kochi *et al.*[5] We assumed that replacement of carbons with asterisk in **1** by stereogenic carbons would provide the reaction site of the high asymmetric inducing ability, because there the asymmetric centers located closer to the metal center than those in porphyrin complexes. According to these assumptions, we studied the epoxidation of olefins using newly designed chiral manganese-salen complexes (**2** and **3**) as catalysts. Quite recently, Jacobsen *et al.* reported the enantioselective epoxidation using chiral manganese-salen complex (**4**) wherein the diamine part carries the same stereogenic carbons to our proposed complex but bulky *t*-butyl group was placed *ortho* to phenoxide oxygen atom.[6] This prompts us to disclose our own results.



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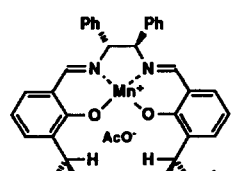

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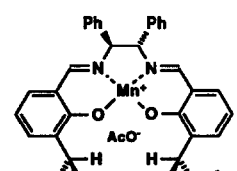

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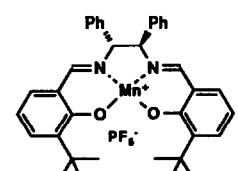

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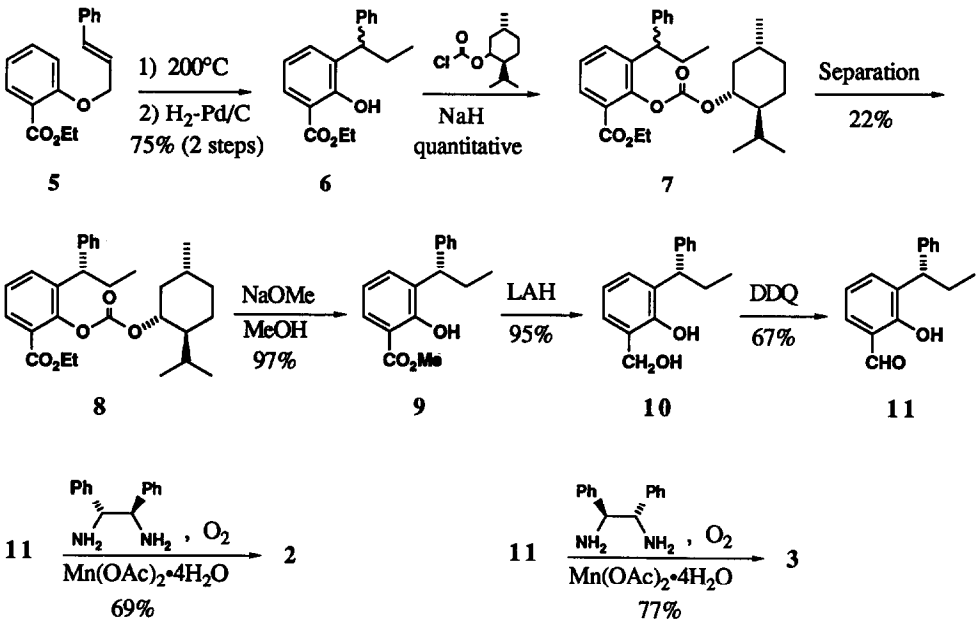


Scheme 1

Our chiral manganese-salen complexes (**2** and **3**) were prepared as follows (Scheme 1): Claisen rearrangement of ethyl *O*-cinnnamylsalicylate (**5**) followed by hydrogenation gave ethyl 3-[(*RS*)-1-phenylpropyl)salicylate (**6**).[7] Treatment of **6** with (-)-menthyl chloroformate gave a mixture of diastereomeric carbonates **7** as crystals. A short column chromatography on silica gel and three recrystallizations from hexane gave a pure single isomer **8**, the stereochemistry of which was determined by X-ray analysis. **8** was exposed to sodium methoxide and the resulting methyl ester **9** was reduced to the diol **10**. DDQ oxidation of **10** gave (*S*)-aldehyde **11**. Successive treatments of **11** with (*R*,*R*)- or (*S*,*S*)-1,2-diphenylehthylenediamine and $Mn(OAc)_2 \cdot 4H_2O$ in air gave **2** and **3**, respectively, which were used for the following experiments after the recrystallization from hexane-dichloromethane.[8]

Epoxidation catalyzed by **2** or **3** was examined with (*E*)- and (*Z*)-1-phenyl-1-propene (**12** and **13**) and dihydronaphthalene (**14**) as substrates and iodosobenzene as a terminal oxidant.

Both **2** and **3** showed catalytic activity. As described in Table 1, **2** exhibited a higher level of asymmetric induction (44~50% ee, entries 1, 2, and 6) than **3** (21~43% ee, entries 3 and 7). The sense of asymmetric induction by **2** and **3** were found to be opposite (entries 1 to 3 and 6 to 7). These results suggested that (*S*)-salicylaldehyde and (*R*,*R*)-diamine moieties constituted a matched pair in terms of double diastereoselection.[9] Actually, **15** which did not have a stereogenic carbon on the C-3 substituent showed a level of asymmetric induction between those obtained by **2** and **3**. Addition of 2-methylimidazole in the epoxidation of **12** improved the

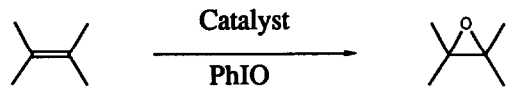


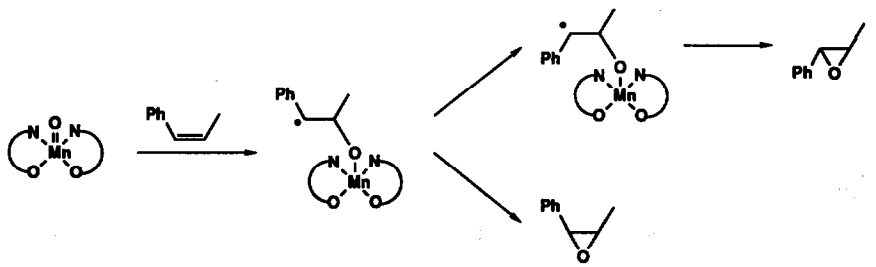
Table 1. Catalytic asymmetric epoxidation using **2** or **3** as a catalyst.[a)]

Entry	Substrate	Catalyst	Time (h)	Yield (%)	% Ee[b)]	Confign
1[c)]	**12**	**2**	8.0	37	44 (20[d)], 65[e)])	(1*R*,2*R*)
2[c,f)]	**12**	**2**	14	12	50	(1*R*,2*R*)
3[c)]	**12**	**3**	8.5	28	21	(1*S*,2*S*)
4[c)]	**12**	**15**[g)]	6.0	15	20	(1*S*,2*S*)
5	**13**[h)]	**2**	12	26[i)]	44 (84[d)])	(1*R*,2*S*)
6	**14**	**2**	1.5	93	49 (78[d)])	(1*R*,2*S*)
7	**14**	**3**	2.0	25	43	(1*S*,2*R*)

a) Reaction was conducted in acetonitrile at room temperature with molar ratio of substrate:catalyst:iodosobenzene=1:0.09:2.
b) Enantiomeric excess was determined by ^{1}H NMR analysis (400 MHz) in the presence of Eu(hfc)$_3$.
c) The reaction was carried out in the presence of 0.5 eq. of 2-methylimidazole.
d) The highest % ee previously reported for nonenzymatic catalytic epoxidation (reference 6).
e) The highest % ee previously reported for nonenzymatic stoichiometric epoxidation (reference 3c).
f) The reaction was conducted in dichloromethane.
g) Manganese-salene complex (**15**) was prepared from 3-methylsalicylaldehyde, (*S*,*S*)-1,2-diphenylethylenediamine and Mn(OAc)$_2$•4H$_2$O in a similar manner to that described for **2** and **3**.
h) **13** contained 3% of **12**.
i) (1*S*,2*S*)-Epoxide of 47% ee (17%) together with 1-phenylpropan-2-one (8%) was also obtained.

enantioselectivity up to 50% ee.[10)] This is the highest one to date observed for a series of the metal-catalyzed epoxidation of unfunctionalized (*E*)-olefins, while any favorable result was not observed for **13** and **14**. Epoxidation proceeds in acetonitrile or dichloromethane[11)] but the better stereoselectivity to a small extent was observed for the reaction of **12** in dichloromethane (entries 1 and 2).[12)]

Interestingly, epoxidation of **13** gave a mixture of (1*R*,2*S*)- (44% ee) and (1*S*,2*S*)-epoxides (47% ee) together with a small amount of 1-phenylpropan-2-one (entry 5). Although the precise reaction mechanism is unclear at present, this result suggests the intervention of a radical intermediate in the course of the reaction as shown in the Scheme 2.[13)]



Scheme 2

The studies on the reaction mechanism and the modification of the catalyst for the improvement of enantioselectivity are now under investigation in our laboratory.

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1) See, e.g. ; B. E. Rossiter, In "*Asymmetric Synthesis*" ed. by J. D. Morrison, Academic Press, New York, 1986, vol. 5, p. 193.
2) T. Katsuki and K. B. Sharpless, *J. Am. Chem. Soc.*, **102**, 5974 (1980).
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4) For the review of transition metal catalyzed epoxidation, see: K. A. Jφrgensen, *Chem. Rev.*, **89**, 431 (1989).
5) K. Srinivasan, S. Perrier, and J. K. Kochi, *J. Am. Chem. Soc.*, **108**, 2309 (1986).
6) W. Zhang, J. L. Loebach, S. R. Wilson, and E. N. Jacobsen, *ibid.*, **112**, 2801 (1990).
7) All the compounds obtained gave the satisfactory spectroscopic analyses, except for **2** and **3** which gave broad ^{1}H NMR spectra.
8) **2** gave satisfactory elementary analyses. Found: C, 74.30; H, 5.86; N, 3.53%. Calcd for $C_{48}H_{45}N_2O_4Mn \cdot 0.5H_2O$: C, 74.12; H, 5.96; N, 3.60%.
9) Groves *et al.* observed a similar phenomenon in the epoxidation using iron-chiral porphyrin complexes as catalysts (reference 3c).
10) 32 % and 3 % ee's were observed for the epoxidation of **12** catalyzed by **2** and **3** in acetonitrile, respectively, in the absence of 2-methylimidazole.
11) The reaction in benzene or propan-2-ol was very slow.
12) In the epoxidation of **14**, the same level of asymmetric induction was observed both in dichloromethane and acetonitrile.
13) Kochi *et al.* suggested the intervention of a radical intermediate in the epoxidation using **1** as a catalyst (reference 5).

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