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ENANTIOSELECTIVE EPOXIDATION OF UNFUNCTIONALIZED OLEFINS USING CHIRAL (SALEN)MANGANESE(III) COMPLEXES

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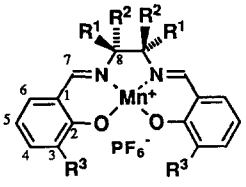
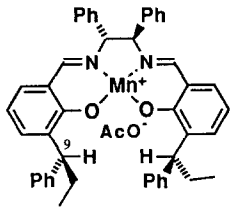
Summary: *Chiral (salen)manganese(III) complexes (3 and 4) were prepared and used for the enantioselective epoxidation of unfunctionalized olefins. The highest enantioselectivity of 48% ee for the catalytic epoxidation of (E)-stilbene was realized by using 3 as a catalyst though much lower enantioselectivity (7% ee) was obtained for that of (E)-1-phenyl-1-propene. In the epoxidation of (Z)-olefins, enantioselectivities were in the range of 68~72% ee by using 3 as a catalyst and 60% ee by using 4.*

The exploitation of various chiral transition metal complexes in the last decade enabled the realization of highly enantioselective reactions of olefins bearing a precoordinating functional group.[1] Still the achievement of the enantiofacial selection of unfunctionalized olefins is a challenging task.[2] As one of approaches for the problem, Jacobsen's[3] and our groups[4] independently reported that chiral (salen)manganese(III) complexes (**1**[3] and **2**[4]) were effective catalysts for the enantioselective epoxidation of unfunctionalized olefins, recently.

In the study of epoxidation using **2**, we found that the sense and degree of enantioface selection of olefins were affected by both the stereogenic centers on the aromatic ring part (C-3 and C-3' substituents) and those on the ethylenediamine part (C-8 and C-8' stereogenic centers).[4] Since aromatic ring part possesses conformational freedom though the ethylenediamine part is conformationally fixed by the formation of five-membered chelate ring, we considered that alteration in the conformation of C-9 and C-9' stereogenic centers in **2** would make the complex to show the varied catalytic activity and asymmetric induction. It was also expected that the results obtained here would provide the valuable insight into the mechanism of molecular recognition by chiral (salen)metal complexes. Along this line, we synthesized [(8*S*,8'*S*)-3,3'-bis[(1*R*)-1-phenylpropyl]-4,4'-dimethyl-8,8'-diphenylsalen]manganese(III) complex (**3**) and its (8*R*,8'*R*)-isomer (**4**), in which stereogenic centers in the C-3 and C-3' substituents were considered to take the hydrogen in plane conformation to the aromatic ring in order to minimize the allylic strain between the C-3 and C-4 aromatic substituents in **3** and **4**. Here we describe the synthesis of **3** and **4**, and epoxidation of olefins using these complexes as catalysts.



1a: R^1=Ph, R^2=R^3=H
1b: R^1=H, R^2=Ph, R^3=*t*-Bu



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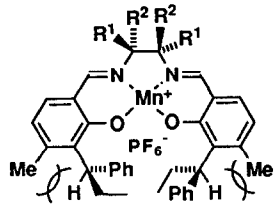
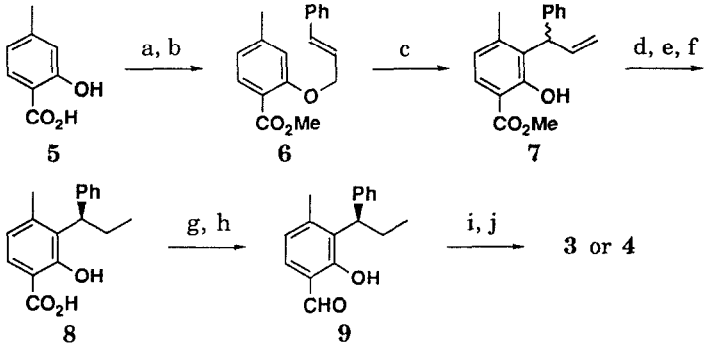


3: R^1=Ph, R^2=H
4: R^1=H, R^2=Ph

The manganese complexes (**3** and **4**) were prepared as follows (**Scheme 1**).[5] Esterification of 4-methylsalicylic acid (**5**) by heating with trimethyl orthoformate and subsequent cinnamylation in basic conditions gave methyl *O*-cinnamyl-4-methylsalicylate (**6**). Heating **6** at 170~180°C in the presence of calcium carbonate[6] caused Claisen rearrangement to produce **7**. Hydrogenation of **7** followed by hydrolysis afforded (*RS*)-4-methyl-3-(1-phenylpropyl)salicylic acid (*dl*-**8**) which could be resolved with the aid of (-)-brucine as a chiral base to give optically pure (*R*)-**8**.[7] Reduction of (*R*)-**8** with lithium aluminium hydride (LAH) and subsequent oxidation of the resulting benzyl alcohol with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ)[8] gave aldehyde (**9**). Treatment of **9** with (*S*,*S*)- or (*R*,*R*)-1,2-diphenylethylenediamine and $Mn(OAc)_2 \cdot 4H_2O$ under nitrogen atmosphere gave yellowish manganese(II) complexes which were further oxidized to manganese(III) complexes (**3** and **4**)[9] by bis(cyclopentadienyl)iron(III) hexafluorophosphate[10] with or without isolation of the divalent manganese complexes.[11]

Scheme 1



(a) $(MeO)_3CH$, 120°C, 2d; (b) NaH, $PhCHCHCH_2Br$, in DMF, 77% (2 steps); (c) $CaCO_3$, 170~180°C, 1d, 73%; (d) H_2-Pd/C in AcOEt, 100%; (e) NaOH (5M) in EtOH, then HCl, 100%; (f) (–)-Brucine·$2H_2O$, three repeated recrystallizations from acetone, then HCl, 22% from *dl*-**8**; (g) LAH in THF, 99%; (h) DDQ in AcOEt, 86%; (i) (*S*,*S*)- or (*R*,*R*)-1,2-diphenylethylenediamine, $Mn(OAc)_2 \cdot 4H_2O$, in EtOH or MeCN; (j) Cp_2FePF_6 in MeCN, 34% (2 steps) for **3** (two pot procedure), 72% (2 steps) for **4** (one pot procedure)

With the chiral catalysts (**3** and **4**) in hand, the asymmetric epoxidation of unfunctionalized olefins using **3** and **4** as catalysts was next examined with iodosobenzene as a terminal oxidant.

The results were summarized in **Table 1**. The epoxidation of (*E*)-stilbene underwent smoothly and 48% ee was realized by using **3** as a catalyst (entry 1).[12] This is the highest one to date observed for the metal-catalyzed epoxidation of (*E*)-stilbene. Although the another chiral catalyst **4** was not effective for the epoxidation in terms of chemical yield and enantioselectivity (entry 2), it was note worthy that the sense of asymmetric induction was the same to that catalyzed by **3** (entries 1 and 2). This was also observed for the epoxidation of (*E*)-1-phenyl-1-propene (entries 3 and 4). These results suggest that the chirality of C-3 and C-3' substituents has stronger influence upon the sense of asymmetric induction than that of ethylenediamine moiety. It is also interesting note that **3** showed higher ee for the epoxidation of (*E*)-stilbene than for that of (*E*)-1-phenyl-1-

propene while **2** showed higher ee for the epoxidation of (*E*)-1-phenyl-1-propene,[4] suggesting that the best conformation of C-3 and C-3' substituents changed with substrates for the epoxidation of (*E*)-olefins.

On the other hand, in the epoxidation of (Z)-olefins such as (Z)-1-phenyl-1-propene and dihydronaphthalene, the enantiofacial selection was found to be mainly controlled by the chirality of the diamine moiety (entries 5~7). In another words, the chirality of C-3 and C-3' substituents had only small influence, differing from the epoxidation of (*E*)-olefins (*vide supra*). Although the enantioselectivities were slightly decreased as compared with those of Jacobsen's complex (**1b**) having bulky *t*-butyl group at C-3 and C-3', **3** and **4** showed superior asymmetric induction to **2** having the same C-3 and C-3' substituents. These results implied that C-3 and C-3' substituents in **1b**, **3**, and **4** have similar conformations each other in which C-9 alkyl group (methyl group for **1b** or ethyl group for **3** and **4**) is synclinal to (C-2)-(C-3) bond of aromatic ring but those in **2** have a different conformation.[13] Therefore, the bulkiness and conformation of C-3 and C-3' substituents are important in affecting the degree of enantiofacial selection of this type of olefins.

Based on the above analysis, syntheses of new chiral (salen)metal complexes which might bring about better asymmetric induction are under investigation in our laboratory.

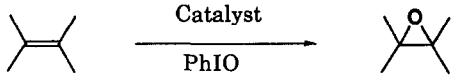


Table 1. Asymmetric Epoxidation of Unfunctionalized Olefins[a]

Entry	Substrate	Catalyst	Yield(%)	% Ee[b]	Abs. Config[c]
1	(*E*)-stilbene	**3**	95	48 (33[d])	1*R*,2*R*
2	(*E*)-stilbene	**4**	19	6	1*R*,2*R*
3	(*E*)-1-phenyl-1-propene	**3**	32[e]	7 (50[f])	1*R*,2*R*
4	(*E*)-1-phenyl-1-propene	**4**	25[e]	17	1*R*,2*R*
5	(*Z*)-1-phenyl-1-propene	**3**	12[g]	68 (84[h])	1*S*,2*R*
6	dihydronaphthalene	**3**	65	72 (50[f]), 76[h])	1*S*,2*R*
7	dihydronaphthalene	**4**	24	60	1*R*,2*S*

a) Reactions were conducted in acetonitrile at room temperature with molar ratio of substrate:catalyst:iodosobenzene=1:0.02:2.

b) Enantiomeric excess was determined by ^{1}H NMR analysis (400MHz) in the presence of Eu(hfc)$_3$ or by HPLC (Daicel Chiralcel OD).

c) Absolute configuration was determined by comparing the specific rotation with the reported value.

d) Reported value using **1a** as a catalyst (reference 3).

e) A trace amount of 1-phenyl-2-propanone was also produced.

f) Reported value using **2** as a catalyst (reference 4).

g) (1*R*,2*R*)-Epoxide (1.8%, 38% ee), 1-phenyl-2-propanone (12%), and 2-phenylpropanal (<5%) were also obtained.

h) Reported value using **1b** as a catalyst (reference 3).

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References and Notes

1) R. Noyori and M. Kitamura, in "*Modern Synthetic Methods*" ed. by R. Scheffold, Springer-verlark, New York, Vol. 5, p. 115 (1989).

2) For the recent reviews for the catalytic enantioselective reactions of unfunctionalized olefins, see: a) E. N. Jacobsen, I. Markó, W. S. Mungall, G. Shroder, and K. B. Sharpless, *J. Am. Chem. Soc.*, **110**, 1968 (1988). b) R. L. Halterman, K. P. C. Vollhardt, M. E. Welker, D. Bläser, R. Boese, *J. Am. Chem. Soc.*, **109**, 8105 (1987). c) J. T. Groves and P. Viski, *J. Org. Chem.*, **55**, 3628 (1990).

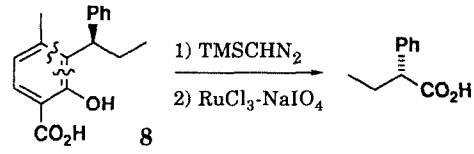
3) W. Zhang, J. L. Loebach, S. R. Wilson, and E. N. Jacobsen, *J. Am. Chem. Soc.*, **112**, 2801 (1990).

4) R. Irie, K. Noda, N. Matsumoto, Y. Ito, and T. Katsuki, *Tetrahedron Lett.*, in press.

5) All the compounds obtained gave the satisfactory spectroscopic analyses, except for **3** and **4** which gave broad ^{1}H NMR spectra.

6) Addition of one equivalent of calcium carbonate to the reaction was found to be effective for minimizing the side reaction of rearrangement of the cinnamyl moiety to C-5 position instead of C-3 position of the aromatic ring.

7) The absolute configuration of **8** was determined to be *R* by its chemical correlation. Namely, treatments of the resolved **8** with trimethylsilyldiazomethane followed by catalytic ruthenium tetroxide oxidation [P. H. J. Carlsen, T. Katsuki, V. S. Martin, and K. B. Sharpless, *J. Org. Chem.*, **46**, 3936 (1981)] gave (*R*)-2-phenylpropionic acid in 52% yield (2 steps) as a colorless oil, $[\alpha]_D^{26}$ –76.1° (c 0.74, EtOH). (*S*)-2-Phenylpropionic acid was reported to show $[\alpha]_D^{25}$ +78.5° (EtOH) [C. Aaron, D. Dull, J. L. Schmiegel, D. Jaeger, Y. Ohashi, and H. S. Mosher, *J. Org. Chem.*, **32**, 2797 (1967)].



8) The DDQ oxidation of the benzylic alcohol to aldehyde (**9**) was proceeded smoothly without serious oxidative dimerization which was observed for the oxidation to 4-unsubstituted aldehyde (see reference 4). R. Irie, Y. Ito, and T. Katsuki, unpublished result.

9) **3** gave satisfactory elementary analysis. Found: C, 63.51; H, 5.31; N, 3.02%. Calcd for $C_{48}H_{46}N_2O_2MnPF_6 \cdot 1.5H_2O$: C, 63.37; H, 5.43; N, 3.08%.

10) K. Srinivasan, S. Perrier, and J. K. Kochi, *J. Am. Chem. Soc.*, **108**, 2309 (1986).

11) Since the divalent manganese complex prepared from (*R,R*)-diamine was relactant to crystallize, the reaction mixture was treated directly with an oxidant.

12) Employment of 2-methylimidazole as an additive did not give any favorable results in the epoxidation of (*E*)-stilbene or (*E*)-1-phenyl-1-propene though improvement of enantioselectivities by the same additive was observed for the epoxidation of (*E*)-1-phenyl-1-propene catalyzed by **2** (see reference 4).

13) While the effect of counter ion should be considered to account for the stereoselectivity, almost the same results to **2** were observed by exchange the counter ion of **2** from acetate to hexafluorophosphate. R. Irie, Y. Ito, and T. Katsuki, unpublished result.

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