Synthesis of Mn-Salen Catalyst Bearing (1*R*,2*R*,3*R*,6*R*)-3,6-Dimethylcyclohexane-1,2-diamine as an Ethylenediamine Part and Its Application to Asymmetric Epoxidation

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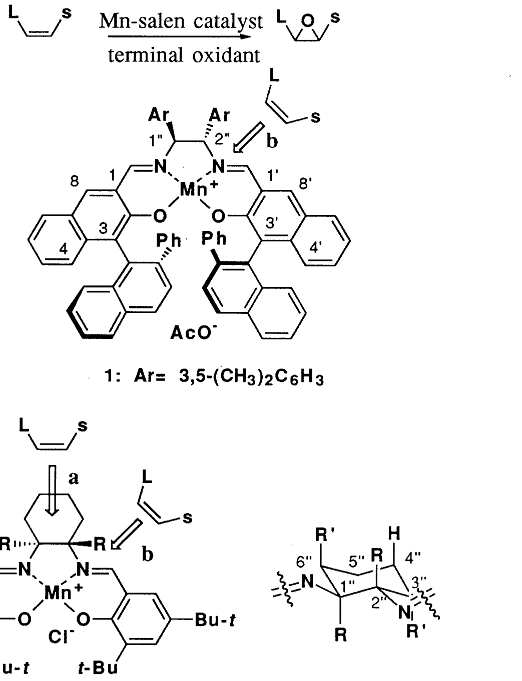
The new Mn-salen catalysts bearing (1*R*,2*R*,3*R*,6*R*)-3,6-dimethylcyclohexane-1,2-diamine as an ethylenediamine part was found to show higher asymmetric induction in the epoxidation of conjugated *cis*-olefins than the Mn-salen catalyst bearing optically active cyclohexanediamine as an ethylenediamine part. This result supports our proposal that olefins approach metal-oxo bond along nitrogen-manganese bond axis in salen-catalyzed epoxidation.

Mn-salen complexes have been found to be effective catalysts for the asymmetric epoxidation of simple olefins and for the asymmetric oxidation of sulfides.[1] These Mn-salen complexes are composed of an optically active ethylenediamine and the salicylaldehyde bearing optically active or sterically bulky aromatic substituent. Recently we found that (a*R*)-3-formyl-2-hydroxy-2'-phenyl-1,1'-binaphthyl was a highly efficient chiral salicylaldehyde part and that the combination of this salicylaldehyde and (*S*,*S*)-1,2-diamino-1,2-bis(3,5-dimethylphenyl)ethane offered so far the best Mn-salen catalyst (**1**) for the epoxidation of conjugated *cis*-disubstituted and trisubstituted olefins.[2] However, there seems to be still a room for the improvement of chiral ethylenediamine part. Thus far, 1,2-diphenylethylenediamine and its derivative, cyclohexane-1,2-diamine, and 4-azacyclopentane-1,2-diamine have been used as a chiral ethylenediamine part.[1] Among them, optically active cyclohexanediamine was originally used by Fujita et al.[3] for the construction of V-salen catalyst that served as a catalyst for asymmetric oxidation of sulfides and later used by Jacobsen[4] and our group[5] for the construction of Mn-salen catalyst. However, there is some controversy on the chirality transfer process by Mn-salen catalysts bearing chiral cyclohexanediamine. Jacobsen et al. has reported that Mn-salen catalyst (**2**) exhibits high enantioselectivity in the epoxidation of *cis*-olefins, wherein the sense of asymmetric induction was explained by assuming that olefins approach metal-oxo bond along the pathway **a**: the larger substituent on olefins is directed away from the C2"-axial hydrogen atom.[4] Catalyst (**3**) prepared from *trans*-1,2-diamino-1,2-dimethylcyclohexane, however, showed considerably diminished enantioselectivity, despite that it has an axial methyl group at C2" that is more bulky than the axial hydrogen atom.[4]

We have proposed the different pathway **b** along nitrogen-manganese bond axis for the olefin's approach based on our own results.[6] Although the pathway **ent-b** seems equally favorable, it is disfavored for the following reasons. Both pathways **b** and **ent-b** are sterically hindered due to the presence of C2"- and C6"-axial hydrogen atoms, respectively, but olefins on the pathway **b** can undergo HOMO-LUMO interaction with metal-oxo bond before they collide with C2"-axial hydrogen atom.[6] The HOMO-LUMO interaction overrides the steric hindrance by C2"-axial hydrogen atom. Despite this description, there seems to be some possibilitiy that olefins approach metal-oxo bond along the pathway **ent-b** producing the undesired enantiomer of the epoxide, since the steric requirement of hydrogen atom is not considered to be large enough to intercept the pathway **ent-b** completely.



1: Ar= 3,5-$(CH_3)_2C_6H_3$

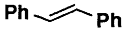
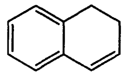
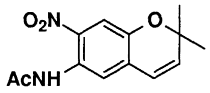
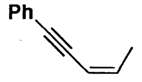
2: R= H
3: R= Me

Figure 1. The olefin's approaches in Mn-salen catalyzed epoxidation.

Accordingly, we assumed that the replacement of C3"- and C6"-axial hydrogen atoms with sterically more bulky methyl group (R = H, R' = Me, Figure 1) would improve asymmetric induction. It was also expected that, if olefins approach along the pathway **a**, the sense of asymmetric induction by the 3",6"-dimethylcyclohexanediamine moiety would be opposite to that by cyclohexanediamine moiety, since C6"-axial methyl group would direct the larger olefinic substituent closer to C2"-axial hydrogen atom. Accordingly, the Mn-salen catalyst bearing 3,6-dimethylcyclohexane-1,2-diamine was expected to be a good probe for the investigation on the mechanism of asymmetric induction by Mn-salen catalyst. Under these expectations, we synthesized the Mn-salen catalysts (**4** and **5**) bearing (1*R*,2*R*,3*R*,6*R*)-3,6-dimethylcyclohexane-1,2-diamine[7] and (1*S*,2*S*)-cyclohexanediamine as a chiral ethylenediamine part, respectively, and examined epoxidation.

The results are summarized in Table 1. Both the catalysts showed the same sense of asymmetric induction as expected from

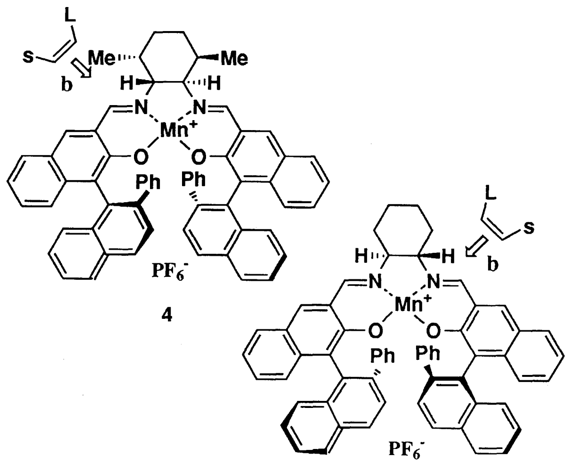
Table 1. Asymmetric epoxidation using **4** and **5** as catalysts

Entry	olefin	catalyst	oxidant	temp	additive	epoxide (yield/%	% ee	configuration)
1		**4**	PhIO	rt		56	43	(1*S*,2*S*)
2	"	**5**	"	"		58	27	(1*R*,2*R*)
3		**4**	NaClO	0 °C	PPNO[a]	43	97	(1*R*,2*S*)
4	"	**5**	"	"	"	45	91	(1*S*,2*R*)
5		**4**	"	"	"	63	>99	(3*R*,4*R*)
6	"	**5**	"	"	"	77	98	(3*S*,4*S*)
7		**4**	"	"	"	70[b]	97	(1*R*,2*S*)
8	"	**5**	"	"	"	75[c]	91	(1*S*,2*R*)

a PPNO = 4-phenylpyridine *N*-oxide.

b A mixture of *cis*- and *trans*-epoxides in a ratio of 3.5:1. The % ee of the *trans*-epoxide was 90%. The face selectivity of the starting enyne was calculated to be 95% ee.

c A mixture of *cis*- and *trans*-epoxides in a ratio of 1.2:1. The % ee of the *trans*-epoxide was 98%. The face selectivity of the starting enyne was calculated to be 94% ee.



4

5

our proposal. Note that the configurations of the ethylenediamine part of **4** and **5** are opposite to each other and, therefore, the epoxides obtained by using **4** as the catalyst are enantiomeric to the epoxides obtained by using **5** as the catalyst. Furthermore, the epoxidation with **4** showed higher asymmetric induction than **5** in all the epoxidation in accord with our assumption that the axially oriented C3"- and C6"-substituents effectively block the undesired pathway **ent-b** leading to the improved asymmetric induction.

In conclusion, our new results strongly support the hypothesis that olefins approach metal-oxo bond along the pathway **b**.

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References and Notes

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7 Synthesis of (1*R*,2*R*,3*R*,6*R*)-3,6-dimethylcyclohexane-1,2-diamine has been described in the preceding paper. Mn-salen catalysts (**4** and **5**) were synthesized from the corresponding salicylaldehyde and diamines according to the reported procedure: R. Irie, K. Noda, Y. Ito, N. Matsumoto, and T. Katsuki, *Tetrahedron: Asymmetry*, **2**, 481 (1991).