Pergamon

Tetrahedron Letters 39 (1998) 4325–4328

TETRAHEDRON
LETTERS

What is the Origin of Highly Asymmetric Induction by a Chiral (Salen)manganese(III) Complex? Design of a Conformationally Fixed Complex and Its Application to Asymmetric Epoxidation of 2,2-Dimethylchromenes

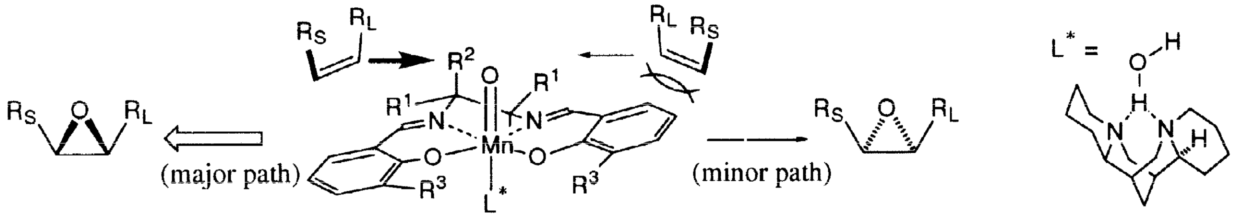
Yoshio N. Ito and Tsutomu Katsuki*

Department of Chemistry, Faculty of Science, Kyushu University, Hakozaki, Higashi-ku, Fukuoka 812-8581, Japan

Received 9 March 1998; revised 6 April 1998; accepted 8 April 1998

Abstract: The optically active (salen)manganese(III) complex **1** having a carboxylate group on the ethylenediamine moiety was found to be an efficient catalyst for the asymmetric epoxidation of several 2,2-dimethylchromene derivatives (up to 99% ee). A high level of turn-over number (up to 9,200) was also achieved in this epoxidation. The pseudo-axially oriented carboxylate in **1** was postulated to coordinate to the manganese ion and to fix the conformation of the salen ligand in the form enantiomeric to that of normal chiral (salen)manganese(III) complexes. This was supported by the absolute configurations of the produced epoxides.

Optically active (salen)manganese(III) complexes (hereafter referred to as Mn-salen complexes) are now well recognized as excellent catalysts for oxygen atom transfer reactions such as epoxidation,[1] oxidation of sulfides,[2] and hydroxylation of the C-H bond.[3] Their high asymmetry-inducing ability had been attributed to the location of the substituent of salen ligands: since they locate proximal to the metal center, they can interact intensely with the incoming substrate and effect high enantioface or enantiotopic selection.[4] However, we recently proposed that the ligand of the putative oxo salen species is not planar but folded as described in Figure 1 ($R^1 \neq H$, R^2= H, L*= achiral axial ligand) and that this folded chiral structure amplifies asymmetric induction by the Mn-salen complex.[5] The sense of chirality induced by folding the salen skeleton is controlled by the asymmetric center(s) at the ethylenediamine moiety, because the conformer bearing the substituents at the asymmetric center in pseudo-equatorial position (R^1) is more stable than that bearing the substituent in pseudo-axial position (R^2). The importance of the asymmetric induction by non-planarity of the salen ligand was demonstrated by our recent study on the asymmetric epoxidation with a new catalyst system using an achiral Mn-salen complex and a chiral axial ligand such as (-)-sparteine.[6] The coordination of the optically active axial ligand favors one of two enantiomeric non-planar conformers of the achiral complex and renders the complex chiral (Figure 1: R^1=R^2=Me, R^3=*t*-Bu, L*=chiral ligand). However, it is still unclear how much the non-planar structure of the ligand contributes to asymmetric induction by the Mn-salen complex. The answer to this question should shed light on the mechanism of asymmetric induction. Therefore, we further examined the effect of the conformation of the salen ligand on asymmetric induction with the expectation that, if the induction of asymmetry by the chirality of the salen ligand prevails over the induction by the asymmetric center(s) on the salen ligand, the sense of asymmetric induction would be reversed by inverting the conformation of the salen ligand. This analysis prompted us to synthesize the conformationally reversed Mn-salen complex.



R_S=Alkyl, R_L=Aryl, R^1, R^2=H, alkyl, or aryl, R^3=bulky group

Figure 1

PII: S0040-4039(98)00763-1

Reversal of the conformation of a chiral Mn-salen complex forces the substituents at the ethylenediamine moiety to take the unfavored axial position. This unfavored conformation is, however, expected to be stabilized by the coordination of the substituent to the manganese ion (Fig. 2, B), if the substituent is a coordinating group such as a carboxylate. This type of intramolecular coordination has already been reported: a salen-type manganese complex bearing an imidazole substituent at the C7 carbon was synthesized by Berkessel and its C7-substituent was demonstrated to serve as the axial ligand.[7] However, most of the Mn-salen complexes so far reported possess C2-symmetry, that is, 1,2-disubstituted ethylenediamine derivatives are used as their chiral source. In this type of Mn-salen complexes, the uncoordinated other substituent (Z) is also forced to take axial orientation with reversal of the conformation, which might cause steric repulsion with the incoming olefin and deteriorate catalytic reactivity and asymmetric induction. Thus, a complex bearing a mono-substituted diamine moiety is considered to be the choice for the present study.

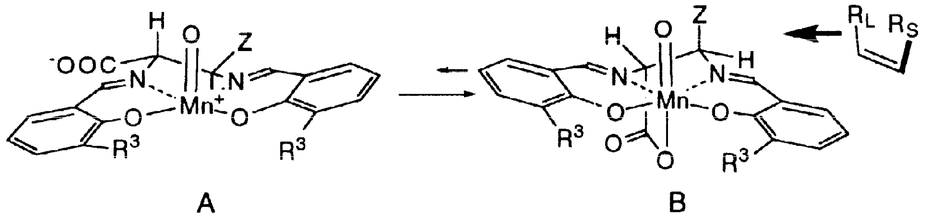
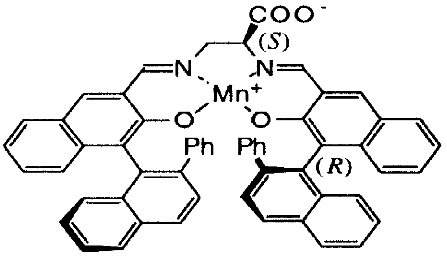
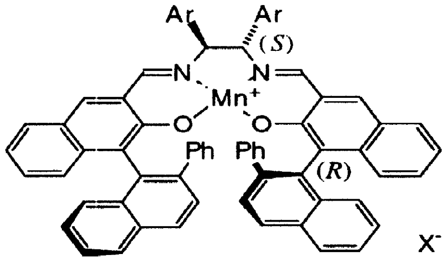


Figure 2



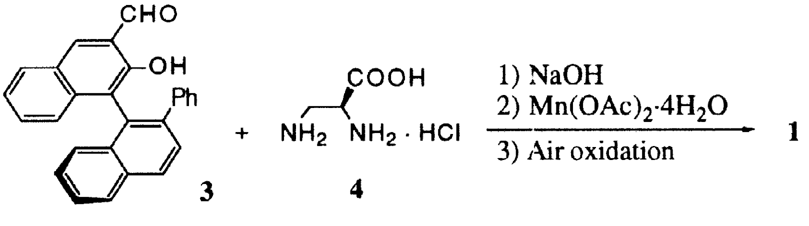
1



2

Based on these working hypotheses, asymmetric epoxidation of 2,2-dimethylchromenes catalyzed by complex **1** having a mono-carboxylate group on the ethylenediamine moiety was examined. Complex **1** has a 2'-phenylnaphthyl group as a bulky C3-substituent, which has been shown to be highly effective for controlling the orientation of incoming olefins.[8] In the case that the substituents at the ethylenediamine moiety are not a coordinating group, Mn-salen complexes **2** having (*R*,*S*)-configuration are better catalysts for epoxidation than those having (*R*,*R*)- or (*S*,*S*)-configuration. However, since the coordination of the carboxylate reverses the conformation of the salen ligand (*vide supra*), **1** possessing (*R*,*S*)-configuration was considered to be the complex of choice.[9] Note that the relative configurations of complexes **1** and **2** are not identical, though both complexes have the same (*R*,*S*)-configuration due to the CIP-nomenclature system.

Preparation of **1** was achieved in a one-pot procedure (Scheme 1). Two equivalents of sodium hydroxide in ethanol were added slowly to a suspension of two equivalents of (*R*)-aldehyde **3**[10] and one equivalent of commercially available (*S*)-2,3-diaminopropionic acid hydrogen chloride (**4**) in ethanol. After



Scheme 1

stirring for 2 h, one equivalent of manganese(II) acetate tetrahydrate was added to the mixture in one portion. Stirring the resulting yellow suspension in air for one day changed the color to dark brown. Purification with column chromatography on silica gel afforded **1** in 85% as brown crystals.[11]

With the complex **1** in hand, we examined the epoxidation of 2,2-dimethylchromene derivative **5a** using **1** as the catalyst and iodosylbenzene as the terminal oxidant.[12] The reaction proceeded smoothly to afford the corresponding epoxide **6a** in high yields and enantiomeric excesses; some representative results are shown in Table 1 (entries 1-12). The absolute configuration of **6a** was found to be 3*S*,4*S* from the sign of its optical

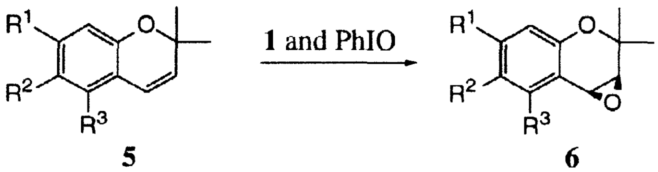
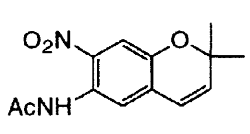


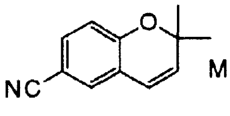
Table 1. Asymmetric epoxidation of **5a-e** catalyzed by **1**.[a)]

Entry	Substrate	Catalyst (mol%)	Solvent	Temp. (℃)	Time	Yield[b)] (%)	Ee[c)] (%)
1	**5a**	5	CH_2Cl_2	rt	2 h	92	96
2	**5a**	2	CH_2Cl_2	0	1 d	80	91
3	**5a**	2	CH_3CN	rt	2 h	100	95
4	**5a**	2	CH_3CN	0	6 h	100	98
5	**5a**	0.2	CH_3CN	0	6 h	95	98
6	**5a**	0.1	CH_3CN	-20	2 d	94	99
7	**5a**	0.1	CH_3CN	-30	6 d	80	98
8	**5a**	0.01	CH_3CN	-30	6 d	22	99
9	**5a**	0.01	CH_3CN	0	10 d	92	99
10	**5a**	2	AcOEt	0	6 h	94	94
11	**5a**	2	Me_2CO	0	6 h	99	95
12	**5a**	2	aqMe_2CO[d)]	0	6 h	94	92
13	**5b**	2	CH_3CN	0	1 d	88	93
14	**5b**	0.01	CH_3CN	0	10 d	40	95
15	**5b**	2	CH_3CN	-20	20 h	96	96
16	**5c**	2	CH_3CN	0	1 d	84	83
17	**5c**	2	CH_3CN	-20	20 h	80	90
18	**5d**	2	CH_3CN	-20	20 h	86	97
19	**5e**	2	CH_3CN	-20	20 h	91	98
20	**5e**	0.01	CH_3CN	0	10 d	67	98

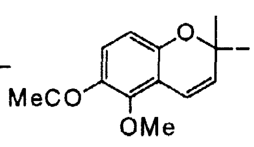
a) All the reactions were carried out using 1-1.5 equiv. of iodosylbenzene as a terminal oxidant. b) Isolated yield. c) The enantiomeric excesses of the epoxides were determined by HPLC analyses (column: Daicel Chiralcel OJ). Every epoxide has 3*S*,4*S* configuration as described in the above scheme. d) The ratio of acetone and water is 7:1.



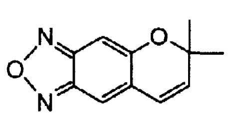
5a



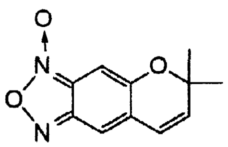
5b



5c



5d



5e

rotation and retention time in the HPLC analysis using a chiral column. Several solvents were employed and, among them, acetonitrile was found to be the most effective for the present reaction. With 2 mol% of **1**, the reaction proceeded at 0 ℃ quantitatively and 98% ee was observed (entry 4). Contrary to the previously reported (salen)manganese(III) catalysts having uncoordinating substituents on their ethylenediamine moiety, high asymmetric induction was observed without addition of an axial ligand such as pyridine *N*-oxide or an imidazole derivative. Accordingly, the present procedure is very simple. Furthermore, it was found that **1** was highly stable in the epoxidation conditions. The catalyst could be recovered by column chromatography after the reaction and recycled for another run. Moreover, reduction of the catalyst amount of **1** from 2 mol% to 0.01 mol% maintained the high yield and high ee (>98% ee) though prolonged reaction time was required at 0 ℃ (entry 9). The turn-over number of the catalyst could be estimated 9,200 times. For the other substrates **5b-e**, similar high asymmetric inductions of more than 90% ee were observed (entries 13-20).

The observed enantioface selectivity is consistent with that expected from our working hypothesis (*vide supra*). The equilibration in Figure 2 should shift exclusively to conformer B where the carboxylate group coordinates with the manganese ion. Differing from a Mn-salen complex, external axial ligand, and iodosylbenzene system in which excess external ligand might doubly coordinate with the manganese ion and retard the formation of the oxo-manganese species, the present system which does not use any additional axial ligand allows the new complex **1** to leave one axial coordination site unoccupied. This may partly explain the high catalytic activity of **1**.

As described here, we have succeeded in developing a novel type of catalyst. The present study provides a conceptually new catalyst for asymmetric reaction. Further application of **1** to other asymmetric reactions, further elucidation of the mechanism, and the optimization of the catalyst are under investigation in our laboratory.[13]

Acknowledgment: Financial support from a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports and Culture, Japan and from Asahi Glass Foundation is gratefully acknowledged. The authors also thank Nissan Chemical Industries Co. Ltd. for generous supply of some chemicals.

References and Notes

1) Katsuki, T. *J. Mol. Catalyst A*, **1996**, *113*, 87-107.
2) Kokubo, C.; Katsuki, T. *Tetrahedron,* **1997**, *52*, 13895-13900, and references cited therein.
3) Miyafuji, A.; Katsuki, T. *Synlett,* **1997**, 836-838.
4) Katsuki, T. *Coord. Chem. Rev.*, **1995**, *140*, 189. Katsuki, T. *J. Synth. Org. Chem. Jpn.*, **1995**, *53*, 940. Jacobsen, E. N. In "*Catalytic Asymmetric Synthesis*" ed by I. Ojima, VCH publishers, Inc., New York (1993), pp. 159-202.
5) Hamada, T.; Fukuda, T.; Imanishi, H; Katsuki, T. *Tetrahedron,* **1996**, *52*, 515-530. Noguchi, Y.; Irie, R.; Fukuda, T.; Katsuki, T. *Tetrahedron Lett.*, **1996**, *37*, 4533-4536.
6) Hashihayata, T.; Ito, Y; Katsuki, T. *Synlett,* **1996**, 1079-1081. Hashihayata, T.; Ito, Y.; Katsuki, T. *Tetrahedron*, **1997**, *53*, 9541-9552.
7) Schwenkreis, T.; Berkessel, A. *Tetrahedron Lett.*, **1993**, *34*, 4785-4788.
8) Sasaki, H.; Irie, R.; Hamada, T.; Suzuki, K.; Katsuki, T. *Tetrahedron*, **1994**, *50*, 11827-11838.
9) The epoxidation of **5a** using a complex prepared from **3** and ethylenediamine where the carboxylate group was eliminated, produced (3*S*,4*S*)-epoxide in 92% with 37% ee.
10) Sasaki, H.; Irie, R.; Katsuki, T. *Synlett,* **1994**, 356-358. Hosoya, N.; Hatayama, A.; Irie, R.; Sasaki, H.; Katsuki, T. *Tetrahedron*, **1994**, *50*, 4311-4322. Sasaki, H.; Irie, R.; Hamada, T.; Suzuki, K.; Katsuki, T. *Tetrahedron*, **1994**, *50*, 11827-11838.
11) Recrystallization from AcOEt and hexane gave analytical sample of **1**. Calcd for $C_{57}H_{37}N_2O_4Mn\cdot H_2O$: H, 4.43, C, 77.19, N, 3.16%. Found: H, 4.29, C, 77.18, N, 3.11%.
12) Representative asymmetric epoxidation procedure is as follows (Table 1, entry 4). Iodosylbenzene (23 mg, 0.1 mmol) was added in one portion to a suspension of **5a** (26 mg, 0.1 mmol) and **1** (1.8 mg, 2 μmol) in acetonitrile (0.8 ml) at 0 ℃. After stirring for 6 h, the mixture was concentrated. The residue was chromatographed on silica gel (hexane/AcOEt 4:1-7:3) to afford **6a** (28 mg, 100 %) as yellow crystals. $[\alpha]_D^{24}$ +24.0° (*c* 0.90, $CHCl_3$).
13) The results described in this paper are not compatible with the hypothesis that the salen ligands of oxo-species are planar: Palucki, M.; Finney, N. S.; Pospisil, P. J.; Güler, M. L.; Ishida, T.; Jacobsen, E. N. *J. Am. Chem. Soc.*, **1998**, *120*, 948-954.