Enantioselective Epoxidation of Conjugated *Z*-Olefins with Newly Modified Mn(salen) Complex

Hiromichi Egami, Ryo Irie, Ken Sakai, and Tsutomu Katsuki*
Department of Chemistry, Faculty of Science, Graduate School, Kyushu University 33, Hakozaki, Higashi-ku, Fukuoka 812-8581

(Received September 19, 2006; CL-061083; E-mail: katsuscc@mbox.nc.kyushu-u.ac.jp)

Chiral Mn(salen) complex **3** bearing a 1-ethyl-1-methylpropyl group at C3, C3′, C5, and C5′ was found to induce higher asymmetry in the epoxidation of conjugated *Z*-olefins, especially less nucleophilic ones, in the presence of 4-phenylpyridine *N*-oxide than complex **1** bearing a *t*-butyl group at the same carbons. The higher enantioselectivity was considered to be attributable to Me-in-plane conformation of the 1-ethyl-1-methylpropyl group at C3 and C3′.

In 1986, Kochi et al. reported that Mn(salen) complexes served as catalysts for epoxidation of olefins[1] and subsequently Jacobsen's and our groups independently reported chiral Mn(salen)-catalyzed asymmetric epoxidation in 1990.[2] Although many chiral Mn(salen) complexes have been synthesized from then on, they are roughly classified into two groups, complexes developed by Jacobsen (J-type) and by us (K-type). They differ in the presence or absence of a chiral substituent at C3 and C3′: K-type catalysts are constructed based on the diastereomeric strategy and show higher asymmetric induction and wider scope of applicability, while J-type catalysts are more easily available.[3] Thus, it is still of value to improve asymmetric induction by J-type catalysts. Although asymmetric induction by Mn(salen) complexes is governed by many factors, steric repulsion between the olefinic substituent and the substituent at C3 or C3′ plays a crucial role.[3,4] Second generation K-type catalysts bear a 2-phenylnaphthyl group at C3 or C3′ and direct the 2-phenyl group close to an incoming olefin,[5] while J-type catalysts generally bear *t*-butyl (*t*-Bu) groups that locate rather away from the olefin, at C3 and C3′. Recently, Bu et al. reported that replacement of the *t*-Bu group with a 1,1-dimethylpropyl (*t*-Pen) group improved asymmetric induction by J-type complexes, because the *t*-Pen group exerts better steric effectiveness than the *t*-Bu group due to the presence of the free rotational ethyl group in *t*-Pen group.[6] However, the improvement of asymmetric induction by complex **2** does not seem as large as expected, probably because the *t*-Pen group at C3 and C3′ can take two conformers, the desired (R^1 = Et) and the undesired (R^2 = Et), almost equally (Figure 1).

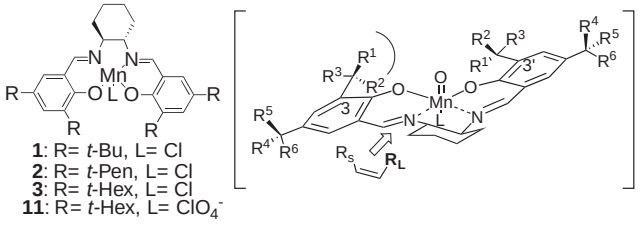
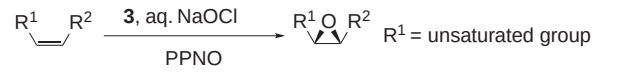


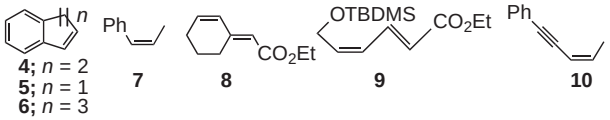
Figure 1. J-type catalysts and the possible conformation of 3- and 3′-substituents in the corresponding O=Mn(salen) species.

Table 1. Asymmetric epoxidation using J-type catalysts[a]



Entry	Sub.	Temp. /°C	Time /h	Yield[b] /%	% ee	(% ee)[c]	(% ee)[d]
1	**4**	4	0.5	12	88[e]	75[f]	
2	**4**	4	4	82	88[e]	86[f](86[g])	79(85[h])
3	**5**	0	4	61	88[e]	86[i](88[g,j])	
4	**6**	0	4	53	96[k]	89[f]	
5	**7**	4	8	89	96(96[j])[l]	92[m]	92(94[j])
					(*trans*/*cis* = 1/5)[n]	(*trans*/*cis* = 1/11.5)[m]	
6	**8**	0	24	34	92[e]	77[o]	
7	**9**	0	48	50	94[p,q]	83[o,q]	
					(*trans*/*cis* = 10/1)[n]	(*trans*/*cis* = 7.3/1)[o]	
8	**10**	rt	4	93	97[q](71[r])[l]	93[q](58[r])[j,s]	
					(*trans*/*cis* = 1.8/1, 88[t])[n]	(*trans*/*cis* = 2/1, 81[t])[s]	

[a]All the reactions were carried out in dichloromethane in the presence of PPNO by using NaOCl as the terminal oxidant, unless otherwise mentioned. [b]Isolated yield. [c]The highest % ee reported for asymmetric epoxidation using **1** as a catalyst. [d]The reactions with complex **2** as catalyst. The % ees were taken from Ref. 6. [e]Determined by HPLC analysis (DAICEL CHIRALCEL OB-H). [f]The reaction was carried out by us using **1** purchased from Aldrich, as the catalyst according to the reported procedure. [g]Taken from Ref. 3a. [h]The reaction was carried out in the presence of pyridine *N*-oxide. [i]Taken from Ref. 11. [j]The reaction was carried out in the absence of 4-PPNO. [k]Determined by HPLC analysis (DAICEL CHIRALCEL AS-H). [l]Determined by HPLC analysis of the *cis*-epoxide (DAICEL CHIRALCEL OJ-H). [m]Taken from Ref. 12. [n]The present study. [o]Taken from Ref. 13. [p]Determined by HPLC analysis (DAICEL CHIRALCEL OD-H). [q]The number stands for ee of the *trans*-epoxide. [r]The number stands for ee of the *cis*-epoxide. [s]Taken from Ref. 14. [t]The number stands for the face selectivity. Face selectivity = $ee_{trans} \times \%trans + ee_{cis} \times \%cis$.



On the other hand, we recently found that an (ON)Ru(salen) complex possessing a 1-ethyl-1-methylpropyl (*t*-Hex) group at C3, C3′, C5, and C5′ served as an efficient catalyst for chemoselective aerobic oxidation of primary alcohols even in the presence of activated secondary alcohols.[7] The *t*-Hex groups at C3 and C3′ have been proved or by NOE experiment to adopt Me-in-plane (Mip) conformation. We anticipated that Mn(salen) complex **3** bearing the same salen ligand would induce much larger asymmetry than complexes **1** and **2**, because the *t*-Hex groups at C3 and C3′ would also adopt Mip conformation (R^1, R^2 = Et, R^3 = Me, Figure 1) and show much larger steric effectiveness than *t*-Pen.

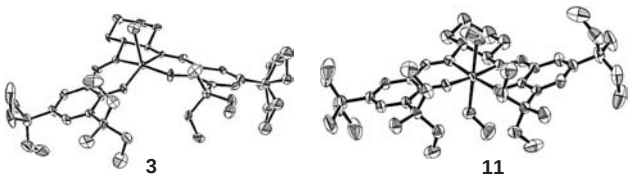


Figure 2. ORTEP diagrams for the X-ray structures of **3** and **11**. The *t*-Hex group at C5 in **3** and the perchlorate ion in **11** show orientational disorder. The perchlorate ion and hydrogen atoms are omitted for clarity.

Thus, we synthesized complex **3** in a conventional manner[2,7] and examined epoxidation of dihydronaphthalene **4** in the presence of 4-phenylpyridine *N*-oxide (PPNO) (Table 1).[8] The enantioselectivity of the epoxidation of **4** using **1** as catalyst under the same conditions was 75% ee.[9] Bu et al. have reported that epoxidation with **2** shows 79% ee at 4 h (Entry 2).[6,10] The epoxidation with **3** showed the highest ee of 88%. It is noteworthy that the enantioselectivity did not vary during the reaction (Entries 1 and 2). On the other hand, enantioselectivity of epoxidation of indene **5** with **3** was almost identical to that with **1** (Entry 3). However, the epoxidation of **6** with **3** showed much better enantioselectivity than that with **1** (Entry 4). Epoxidation of **7** also showed a similar trend (Entry 5). We inferred from these results that **3** could exert better catalytic performance, as coplanarity of the double bond and aromatic substituent becomes smaller, that is, olefins become less nucleophilic. In order to ascertain this assumption, we further examined the epoxidation of (2*E*,4*Z*)-2,4-dienoates **8** and **9**. Indeed, **3** showed much better enantioselectivity in the epoxidation of these olefins than **1** (Entries 6 and 7). Epoxidation of enyne **10** was also better effected by **3** than by **1** (Entry 8). Steric effectiveness of *t*-Bu, *t*-Pen, and *t*-Hex groups is mainly caused by van der Waals repulsion and is limited in a short range. Thus, their steric effectiveness can be fully exerted only when a substrate comes close to the substituents. As substrate becomes less nucleophilic, the transition state (TS) of the oxidation shifts to a later stage and the substrate is more accessible to the substituents at TS. This general discussion agrees with the above results.

The proposal that Mn(salen)-catalyzed epoxidation in the presence of PPNO proceeds through a PPNO-bound oxo Mn(salen) species has been accepted.[3] In order to prove our assumption on the conformation of the 3,3′-Hex groups, we performed an X-ray analysis of **3** and cationic Mn complex **11** coordinated by methanols at the apical positions[15] (Figure 2). Complex **11** was prepared as the model compound of the O = Mn(salen)-PPNO adduct. Many Mn(salen)Cl complexes take a square pyramidal configuration, in which the salen ligands mostly adopt a planar or stepped conformation. However, the salen ligand of **1** has been reported to adopt an umbrella-shape (US) conformation.[11] The salen ligand of **3** also adopted a distorted US conformation, but it is noteworthy that one of the 3,3′-*t*-Hex groups in **3** took Et-in-plane conformation, reflecting their steric effectiveness.[16] In contrast, **11** possessed octahedral configuration and both the 3 and the 3′-*t*-Hex groups were found to adopt the desired Mip conformation (Figure 2).[17,18]

In conclusion, we were able to synthesize a new Mn(salen) complex **3** bearing a *t*-Hex group at C3, C3′, C5, and C5′ and to achieve highly enantioselective epoxidation with it in the presence of PPNO. Moreover, this study demonstrated that the enantioselectivity of the epoxidation using J-type catalyst could be further enhanced by introducing suitably designed 3,3′-substituents.

Financial support from CREST, Japan Science and Technology Agency (JST), Banyu Pharmaceutical Co., and Nissan Chemical Industries is gratefully acknowledged. H. E. acknowledges Research Fellowships of the Japan Society for the Promotion of Science for Young Scientists.

This paper is dedicated to Professor Teruaki Mukaiyama on the occasion of his eightieth birthday.

References and Notes

1 K. Srinivasan, P. Michaud, J. K. Kochi, *J. Am. Chem. Soc.* **1986**, *108*, 2309.
2 a) W. Zhang, J. L. Loebach, S. R. Wilson, E. N. Jacobsen, *J. Am. Chem. Soc.* **1990**, *112*, 2801. b) R. Irie, K. Noda, Y. Ito, N. Matsumoto, T. Katsuki, *Tetrahedron Lett.* **1990**, *31*, 7345.
3 a) E. N. Jacobsen, in *Catalytic Asymmetric synthesis*, ed. by I. Ojima, VCH Publishers, New York, **1993**, pp. 159–202. b) T. Katsuki, *Coord. Chem. Rev.* **1995**, *140*, 189. c) T. Katsuki, *J. Mol. Catal. A: Chem.* **1996**, *113*, 87. d) E. M. McGarrigle, D. G. Gilheany, *Chem. Rev.* **2005**, *105*, 1564.
4 T. Katsuki, *Adv. Synth. Catal.* **2002**, *344*, 131.
5 H. Sasaki, R. Irie, T. Hamada, K. Suzuki, T. Katsuki, *Tetrahedron* **1994**, *50*, 11827.
6 A. Gaquere, S. Liang, F.-L. Hus, X. R. Bu, *Tetrahedron: Asymmetry* **2002**, *13*, 2089.
7 H. Egami, H. Shimizu, T. Katsuki, *Tetrahedron Lett.* **2005**, *46*, 783.
8 A typical procedure: complex **3** (2 μmol) and PPNO (0.02 mmol) were weighed into a Schlenk tube, followed by addition of dry CH_2Cl_2 (1 mL) and olefin (0.1 mmol). The mixture was cooled to the specified temperature described in Table 1 and aqueous NaOCl (0.44 M, pH = 11.35, 1.2 mL) pre-cooled to the specified temperature was added. The whole mixture was stirred at the temperature for the time given in the Table, and worked up in a conventional manner. The enantiomer excesses of the products were determined as described in the footnotes to Table 1.
9 It has been reported that the ee of the resulting epoxide increases with the reaction time, because of enantiomer-differentiating C–H oxidation of the epoxide under the condition using a J-type catalyst: F. J. Larrow, E. N. Jacobsen, *J. Am. Chem. Soc.* **1994**, *116*, 12129.
10 The epoxidation proceeded with higher enantioselectivity of 85% ee in the presence of pyridine *N*-oxide. However, whether C–H oxidation occurred under this condition or not was not described in the paper.
11 P. J. Pospisil, D. H. Carsten, E. N. Jacobsen, *Chem. Eur. J.* **1996**, *2*, 974.
12 E. N. Jacobsen, W. Zhang, A. R. Muci, J. R. Ecker, L. Deng, *J. Am. Chem. Soc.* **1991**, *113*, 7063.
13 S. Chang, N. O. Lee, E. N. Jacobsen, *J. Org. Chem.* **1993**, *58*, 6939.
14 O. N. Lee, E. N. Jacobsen, *Tetrahedron Lett.* **1991**, *32*, 6533s.
15 Complex **11** was prepared by treating **3** with $AgClO_4$. Single crystals of **3** and **11** were obtained by recrystallization from MeOH–CH_3CN and MeOH–*i*-PrOH, respectively.
16 CCDC No. 618956.
17 CCDC No. 616680.
18 In general, the ligand of octahedral Mn(salen) complexses adopts a planar or stepped conformation.

Published on the web (Advance View) December 16, 2006; doi:10.1246/cl.2007.46