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Enantioselective Epoxidation of Unfunctionalized Olefins with Molecular Oxygen and Aldehyde Catalyzed by Optically Active Manganese(III) Complexes

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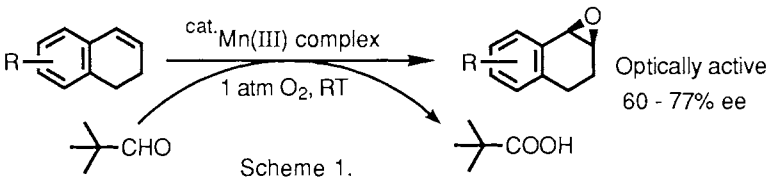
Enantioselective epoxidation of unfunctionalized olefins with combined use of molecular oxygen, an oxidant, and pivalaldehyde, a reductant, was demonstrated in the presence of a catalytic amount of optically active Mn(III)-salen complexes. Dihydronaphthalene derivatives were converted into the corresponding optically active epoxides in good yields with 60-77% enantiomeric excesses.

Optically active epoxides have attracted much attention as versatile intermediates[1] for the synthesis of a wide variety of chiral compounds, such as biologically active compounds[2] and ferroelectric liquid crystals,[3] etc. Sharpless and Katsuki developed the efficient titanium-catalyzed epoxidation of allylic alcohols by using *tert*-butyl hydroperoxide as an oxidant affording optically active 2,3-epoxy alcohols in good yields with very high enantiomeric excesses,[4] which has been successfully applied to the synthesis of a number of natural products.[2] Many efforts have been made to develop an efficient and widely applicable enantioselective epoxidation of simple olefins, and several enzymatic systems for terminal alkenes[5] have been reported. In the non-enzymatic systems, artificial metal-porphyrins have been designed as cytochrome P-450 modeling systems for enantioselective epoxidation of styrene analogues as the catalysts.[6] Recently, Jacobsen[7] and Katsuki[8] independently reported that Mn(III)-salen complexes are effective catalysts for enantioselective epoxidation of unfunctionalized olefins[9] by using terminal oxidants, such as iodosylbenzene[6-9] or sodium hypochlorite.[10] Except for artificial-bleomycin catalyzed epoxidation,[11] few have been reported on the utilization of molecular oxygen for enantioselective epoxidation of simple olefins. We have already reported an efficient method for the aerobic epoxidation of olefins catalyzed by metal complexes, such as nickel(II),[12] iron(III),[13] vanadium(IV),[14] and manganese(II)[15] coordinated by 1,3-diketone-type ligand, with combined use of aldehyde under mild reaction conditions. It is also observed that β-epoxides are stereoselectively obtained in manganese(II)-catalyzed epoxidation of cholesterol



Scheme 1.

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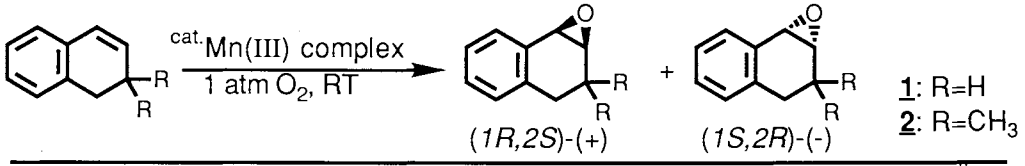
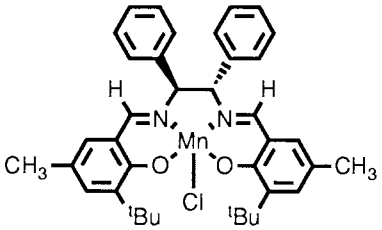
derivatives,[15, 16] while peracids afford α-epoxides of reversal configuration. These results suggest that the manganese(II) complex participates directly in the oxidation step of olefin. In this communication, we would like to report an aerobic enantioselective epoxidation of unfunctionalized olefins catalyzed by optically active manganese(III) complex in the coexistence of aldehyde (Scheme 1).

At first, chiral catalysts, several Mn(III)-salen type complexes, and reductants, several aldehydes, were screened by taking the epoxidation of 1,2-dihydronaphthalene (**1**) as a model reaction. Optically active manganese(III) complexes **A** and **B** were prepared by Jacobsen's method,[10] and purified with column chromatography on silica-gel or washing the benzene solution with aqueous lithium chloride solution. It was found that *tert*-butyl group on C_3 position of salicylaldehyde in the chiral ligand was essential to realize enantioselection, and that pivalaldehyde was the most effective reductant for increasing both enantioselectivity and chemical yield. When optically active Mn(III)-salen complex **A** was employed as a catalyst with combined use of molecular oxygen and pivalaldehyde, 1,2-dihydronaphthalene (**1**) was converted into the corresponding epoxide in 42% yield, whose enantiomeric excess was determined by GC analysis (Chiraldex B-DA) to be 12% ee. The absolute configuration was (*1R, 2S*) by comparing the sign of optical rotation with the reported value[17](Entry 1). It should be noted here that the present enantioselection forming (*1R, 2S*)-epoxide by using (*S, S*)-catalyst is reversal to the results reported by Jacobsen[7, 10] or Katsuki.[8, 18] Furthermore, it is interesting to point out that in the coexistence of catalytic amount of *N*-methylimidazole, the absolute configuration of epoxide obtained in the epoxidation

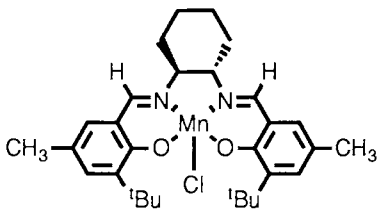
Table 1. Asymmetric epoxidation of 1,2-dihydronaphthalenes



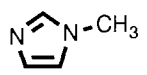
Entry	Catalyst	Olefin	Additive	Yield / %[c]	Optical yield / %ee[d] (1R,2S)-(+)	(1S,2R)-(-)
1[a]	**A**	**1**	—	42	**12**	
2[a]	**A**	**2**	—	51	**6**[e]	
3[a]	**B**	**1**	—	37	**6**	
4[b]	**A**	**1**	*N*-Me-Imd	62		**52**
5[b]	**A**	**2**	*N*-Me-Imd	67		**56**[e]
6[b]	**B**	**1**	*N*-Me-Imd	78		**63**
7[b]	**B**	**2**	*N*-Me-Imd	67		**72**[e]



A (*S,S*)-Ph-Salen-Cl



B (*S,S*)-Cyclo-Salen-Cl



N-Me-Imd

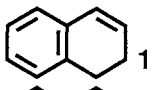
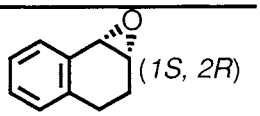
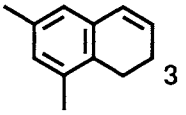
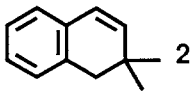
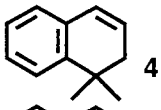
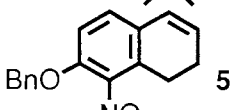
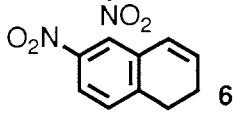
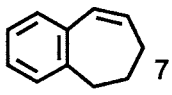
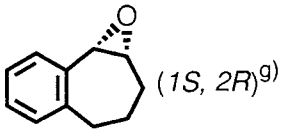
a) Reaction conditions; olefin 1.15 mmol, pivalaldehyde 3.5 mmol, Mn(III) catalyst 0.138 mmol (12 mol%) in benzene 4 ml, RT, 1 atm O_2, overnight. b) Reaction conditions; olefin 1.15 mmol, pivalaldehyde 3.5 mmol, Mn(III) catalyst 0.138 mmol (12 mol%), *N*-methylimidazole 0.55 mmol in fluorobenzene 4 ml, RT,1 atm O_2, overnight. c) Isolated yield. d) Determined by GC analysis (Chiraldex B-DA, ASTEC Co.). e) Absolute configuration were presumed from retention times of GC analysis and optical rotations.

catalyzed by (*S,S*)-complex **A** is completely reversed to give the epoxide of (*1S, 2R*) configuration and the enantiomeric excess is also improved up to 52% ee (Entry 4). Recently, it was reported that a donor ligand, such as 2-methylimidazole or pyridine *N*-oxide, was effective for the improvement of enantioselection in Mn(III)-catalyzed epoxidation by using iodosylbenzene as an oxidant, however, the absolute configuration was maintained even by addition of a donor ligand.[18] It was found that an aromatic hydrocarbon, such as toluene or benzene, was suitable solvent for the present epoxidation, and especially fluorobenzene was the most effective to improve the enantiomeric excess. Cyclo-Salen-Cl (**B**) was also a reliable complex to realize enantioselective epoxidation of simple olefins. In the presence of catalytic amounts of *N*-methylimidazole and Mn(III)-salen complex **B**, 1,2-dihydronaphthalene (**1**) and 3,3-dimethyl-3,4-dihydronaphthalene (**2**) were converted with molecular oxygen into the corresponding optically active epoxides with good enantioselectivities, 63% ee and 72% ee, respectively (Entries 6 and 7).

The present system was applied to the enantioselective epoxidations of various simple olefines. 1,2-Dihydronaphthalenes **1-4**, which contained no function groups, were converted into the corresponding optically active epoxides in good yields with good enantioselectivities (52-72% ee, Entries 1-4). The enantioselective aerobic epoxidation of 1,2-benzo-1,3-cycloheptadiene (**7**) afforded the corresponding epoxide with high enantiomeric excess in the coexistence of Mn(III) complex (Cyclo-Salen-Cl **B**) (Entry 7).

A typical procedure is described for the asymmetric epoxidation of 3,3-dimethyl-3,4-dihydronaphthalene (**2**, see Entry 3 in Table 2): To a mixture of (*S,S*)-Cyclo-Salen-Cl (**B**) (76 mg, 0.138 mmol, 12 mol%) and *N*-

Table 2. Examples of asymmetric epoxidation

Entry[a]	Olefin[b]	Yield / %[c]	Optical yield / %ee[d]	Note
1	 **1**	78	63	 (*1S, 2R*)
2	 **3**	73	52	
3	 **2**	80	72	
4	 **4**	35	63	
5	 **5**	38	66[e]	
6	 **6**	43	43[f]	
7	 **7**	52	77	 (*1S, 2R*)[g]

a) Reaction conditions; olefin 1.15 mmol, pivalaldehyde 3.5 mmol, *N*-methylimidazole 0.55 mmol, (*S,S*)-Cyclo-Salen-Mn(III)-Cl (**B**) 0.138 mmol (12 mol%) in fluorobenzene 4 ml, RT, 1 atm O_2, overnight. b) Olefins were prepared from the corresponding tetralone derivatives, see Ref. 19. c) Isolated yield. d) Determined by GC analysis unless otherwise stated. ASTEC Co. Chiraldex B-DA (20 m x 0.25 mm ID x 0.125 μ film). e) Determined by HPLC analysis. Daicel OD(+) (Hexane : 2-propanol). f) Determined by NMR analysis. $Eu(hfc)_3$ was used as a shift reagent in $CDCl_3$. g) Absolute configuration was determined by optical rotation, see Ref. 20.

methylimidazole (45.3 mg, 0.552 mmol) in fluorobenzene (2.0 ml) was added a solution of **2** (182 mg, 1.15 mmol) and pivalaldehyde (300 mg, 3.5 mmol) in fluorobenzene (2.0 ml) and stirred overnight at room temperature under an oxygen atmosphere. The crude product was purified by column chromatography on silica-gel (hexane / ethyl acetate 20 : 1) to afford the corresponding optically active epoxide in 67% yield (133 mg). The enantiomeric excess was determined by GC analysis (Chiraldex B-DA, ASTEC Co.) to be 72% ee.

It is noted that with combined use of molecular oxygen and pivalaldehyde, unfunctionalized olefins, 1,2-dihydronaphthalene derivatives, were converted into the corresponding epoxides with good enantioselections in the coexistence of catalytic amount of optically active Mn(III) complexes and *N*-methylimidazole. Further investigation of the present reaction and development of more effective ligands are under way.

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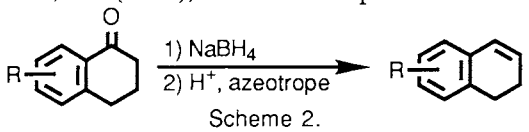
19) 1,2-Dihydronaphthalene (**1**) was purchased from Aldrich Co., and other olefins were prepared by reduction and dehydration as shown in Scheme 2 from the corresponding tetralone derivatives, which were purchased from Aldrich Co. (**3**), Lancaster Co. (**6**), or Tokyo Kasei Kogyo Co. (**7**), respectively, or prepared by reported methods (**2**: I. Crossland, *Acta Chem. Scand.*, **B30**, 787 (1976), **4**: R. D. Campbell and N. H. Cromwell, *J. Am. Chem. Soc.*, **77**, 5169 (1955), **5**: H. Sugihara, K. Ukawa, A. Miyake, K. Itoh, and Y. Sanno, *Chem. Pharm. Bull.*, **26**, 394 (1978)).



Scheme 2.

20) D. R. Boyd, M. R. J. Dorrity, J. F. Malone, R. A. S. McMordie, N. D. Sharma, H. Dalton, and P. Williams, *J. Chem. Soc., Perkin Trans. 1*, **1990**, 489.

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