# Optically active β-ketoiminato manganese(III) complexes as efficient catalysts in enantioselective aerobic epoxidation of unfunctionalized olefins

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**Abstract**

A novel manganese(III) complex having an optically active *N,N'*-ethylenebis-β-ketoimine ligand was prepared and characterized crystallographically. The manganese(III) complexes behave as effective catalysts in enantioselective epoxidation of unfunctionalized olefins by combined use of molecular oxygen, an oxidant, and pivalaldehyde, a reductant. Dihydronaphthalene derivatives were converted into the corresponding optically active epoxides with good to high enantioselectivities.

*Key words:* Catalysis; Enantioselectivity; Epoxidation; Manganese complexes; X-ray diffraction; Oxidation; Asymmetric synthesis; Molecular oxygen

## Introduction

Enantioselective non-enzymatic epoxidation of unfunctionalized olefins is one of the important and challenging targets in organic synthesis [1]. Several examples have been reported using artificial metal–porphyrins or manganese–salen complexes together with terminal oxidants, such as iodosylbenzene [2], sodium hypochlorite [3] and hydrogen peroxide [4], while few have been reported on the utilization of molecular oxygen in asymmetric epoxidation of unfunctionalized olefins [5]. Efficient methods for the aerobic epoxidation of olefins catalyzed by metal complexes, such as nickel(II) [6], iron(III) [7], vanadium(IV) [8] and manganese(II) [9], coordinated with β-diketonato ligand in the coexistence of an aldehyde, a reductant, were recently reported from our laboratory. It was also observed that β-epoxides are stereoselectively obtained in manganese(II) catalyzed epoxidation of cholesterol derivatives, while the conventional method of using peracids affords α-epoxide, a reversal configuration [9]. These results suggest that the manganese complex participates directly in the oxidation of olefin. Therefore, in the above method using an Mn catalyst, it was expected that manganese complexes having an optically active ligand derived from β-diketone would be effective in the aerobic enantioselective epoxidation of simple olefins. Recently we reported that the optically active *N,N'*-ethylenebis(α-alkoxycarbonyl-β-ketoiminato)manganese(III) complexes **A** (Fig. 1) were effective catalysts in aerobic enantioselective epoxidation of simple olefins, and the steric bulkiness of the ester moiety in the ligand enhanced the enantioselection [10]. In the present report, we describe the synthesis and crystallographical characterization of the new optically active ethylenebis-β-ketoiminato manganese(III) complexes first, and then illustrate the steric effect of the ester groups of the β-ketoiminato ligand linked to

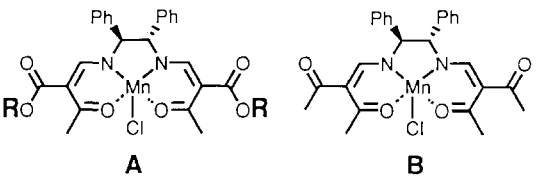


Fig. 1.

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manganese(III) complexes in the aerobic enantioselective epoxidation of unfunctionalized olefins.

## Experimental

IR spectra (KBr pellets) were taken on a JASCO model IR-700 spectrometer. $^1$H NMR spectra were recorded on a JEOL model FX-270 spectrometer using $CDCl_3$ as solvent and with TMS as an internal standard; $\delta$ values are given in ppm. GC analyses of the optical yield of the epoxide were performed on a Shimadzu GC-14A with a optically active glass capillary column (Chiraldex B-DA (20 m × 0.25 mm i.d. × 0.125 $\mu$m film), ASTEC Co.).

*Syntheses*

*Preparation of cyclopentyl acetoacetate (3)*

A mixture of cyclopentanol (**1**) (4.31 g, 50 mmol) and diketene (**2**) (5.04 g, 60 mmol) in benzene (100 ml) was stirred at 50 °C for 1 h in the coexistence of a catalytic amount of dimethylaminopyridine (10 mg). The resulting mixture was poured into a saturated solution of $NaHCO_3$ and extracted with ether. The organic extracts were dried over $Na_2SO_4$, concentrated and distillation afforded the acetoacetic acid cyclopentyl ester as a colorless oil (8.08 g, 95% yield); b.p. 97–98 °C/1.5 mmHg. $^1$H NMR ($CDCl_3$): $\delta$ 5.22 (m, 1H, CH–O), 3.41 (s, 2H, $COCH_2CO_2$), 2.26 (s, 3H, $CH_3$), 2.0–1.6 (m, 8H, $CH_2$). IR: 2964, 2874, 1740, 1718, 1649, 1412, 1361, 1324, 1151 cm$^{-1}$.

*Preparation of 2-formyl-3-oxo butylic acid cyclopentyl ester (4) (R = cyclopentyl)*

*N,N'*-Dimethylformamide dimethylacetal (7.14 g, 60 mmol) was added dropwise to cyclopentylacetoacetate (5.11 g, 30 mmol) at room temperature. The solution was kept stirring for an additional 2 h, then 1 N NaOH solution (MeOH–$H_2O$, 25 ml respectively) was added at 0 °C. After the stirring had continued for 2 h, the mixture was acidified with 1 N HCl (pH 3–4) at 0 °C, and then extracted with ether. Evaporation and purification by column chromatography on silica gel (ethyl acetate/hexane = 1/5) afforded the aldehyde **4** as a yellow oil (3.69 g, 62%). $^1$H NMR ($CDCl_3$): $\delta$ 9.16 (d, $J$ = 6 Hz; 1H, CHO), 5.32 (m, 1H, CH–O), 2.54 (s, 3H, $CH_3$), 2.0–1.6 (m, 8H, $CH_2$). IR: 2964, 2874, 1715, 1639, 1574, 1412, 1323, 1265, 1074 cm$^{-1}$.

*Preparation of N,N'-bis(2-cyclopentyloxycarbonyl-3-oxobutylidene)-(1S,2S)-diphenylethylenediaminato manganese(III) chloride (A-2)*

A mixture of 2-formyl-3-oxo-butylic acid cyclopentyl ester (**4**) (1.31 g, 6.60 mmol) and (*S,S*)-1,2-diphenylethylenediamine (0.64 g, 3.0 mmol) in 1,2-dichloroethane (10 ml) was added to a suspension of manganese(III) acetate ($Mn(OAc)_3 \cdot 2H_2O$) (0.68 g, 2.5 mmol) in ethanol–dichloroethane (5 ml/15 ml). The resulting mixture was refluxed for 3 h, followed by addition of lithium chloride (0.32 g, 7.6 mmol). After 1 h, the solvent was removed under reduced pressure. The residue was then extracted with dichloromethane, dried over sodium carbonate. Concentration *in vacuo* gave a crude Mn(III) complex. The pure manganese(III) complex **A-2** was isolated as a dark brown powder after purification by column chromatography on silica gel (acetone/dichloromethane = 1/9) and reprecipitation (dichloromethane/ether = 1/10). Yield 0.66 g (40%). Slow evaporation of the solvent (dichloromethane/hexane = 1/2) at room temperature for 3 days gave dark brown needles appropriate for X-ray crystallography.

*X-ray crystallography of A-2*

Accurate unit cell parameters were obtained on a Rigaku AFC-7R diffractometer with Mo K$\alpha$ radiation (graphite monochromator). The structure was solved by Patterson methods and refined by full-matrix least-squares calculations.

*Crystal data of A-2 ($C_{34}H_{38}ClMnN_2O_6$)*

$FW$ = 661.08, monoclinic, space group $C2$, $a$ = 32.616(10), $b$ = 9.663(7), $c$ = 11.277(10) Å, $\beta$ = 104.87(5)°, $V$ = 3434(4) Å$^3$, $Z$ = 4, $D_{calc}$ = 1.278 g/cm$^3$, $F(000)$ = 1384, $\mu$(Mo K$\alpha$) = 4.89 cm$^{-1}$, scan type $\omega$–2$\theta$, scan width 1.78 + 0.30 tan $\theta$, no. of reflections measured 4265 (total) and 4191 (unique), $R$ = 0.069 and $R_w$ = 0.067.

*Preparation of 3-methoxymethylene pentane-2,4-dione (6)*

A mixture of acetylacetone (**5**) (2.0 g, 20 mmol) and trimethylorthoformate (3.7 g, 35 mmol) in acetic anhydride (6.1 g, 60 mmol) was heated at 120 °C for 5 h. After the acetic anhydride was distilled off under reduced pressure, distillation afforded 3-methoxymethylene pentane-2,4-dione (**6**) as a yellow oil (1.5 g, 53%). $^1$H NMR ($CDCl_3$): $\delta$ 7.63 (s, 1H, =CHOMe), 4.05 (s, 3H, $CH_3OCH$=), 2.38 (s, 3H, $CH_3CO$), 2.33 (s, 3H, $CH_3CO$). IR 2998, 2946, 2852, 1678, 1623, 1587, 1388, 1360, 1292, 1134.

*Preparation of N,N'-ethylenebis(α-acetyl-β-ketoiminato)-manganese(III) chloride (B)*

The manganese(III) complex **B** was derived from the vinyl ether **6** by the template method described above. Yield 30%.

*Asymmetric aerobic epoxidation of dihydronaphthalene derivatives*

To a solution of (*S,S*)-**A-7** (83 mg, 0.104 mmol) in benzene (1.0 ml) was added a solution of 1,2-di-

hydronaphthalene (**7**) (104 mg, 0.8 mmol) and pivalaldehyde (241 mg, 2.8 mmol) in benzene (1.0 ml), and the resulting mixture was stirred at 30 °C for 1 h under an atmospheric pressure of oxygen. The crude product was poured into aqueous $NaHCO_3$ and extracted with ether. The organic layer was dried over sodium sulfate and concentrated *in vacuo*. Purification by column chromatography on silica gel (ethyl acetate/hexane) gave the corresponding optically active epoxide, (1*R*,2*S*)-(+)-1,2-epoxy-3,4-dihydronaphthalene (**8**), in 70% yield. The optical yield was determined to be 64% ee by GC analysis (Chiraldex B-DA, ASTEC Co.).

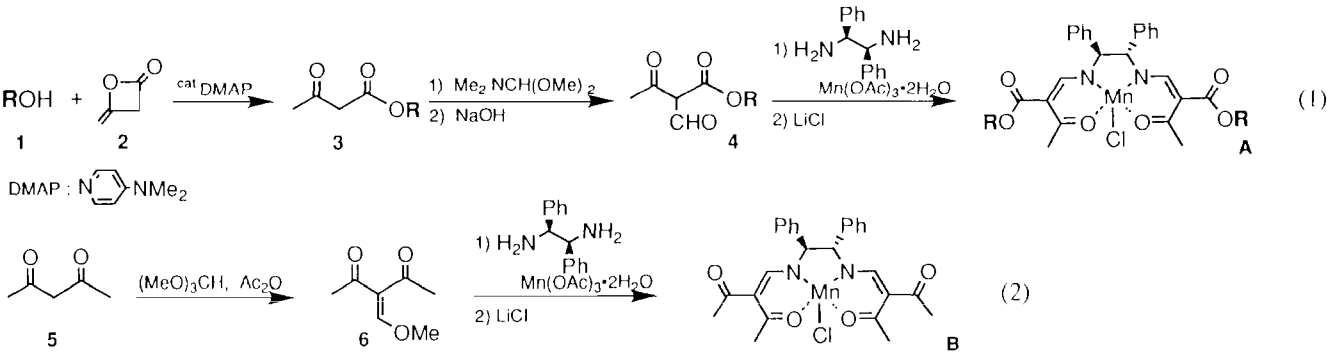
## Results and discussion

Syntheses of the optically active *N*,*N*′-ethylenebis-(α-alkoxycarbonyl-β-ketoiminato)manganese(III) complexes **A** are shown in Scheme 1. Preparation of the alkyl acetoacetate **3** was based on a previously reported method [11], and treatment of **3** with dimethylformamide dimethylacetal [12] and subsequent hydrolysis afforded the 2-formyl-3-oxo-butylate **4**. Formation of the keto-imine-type ligand and complexation with Mn(III) is based on a reported procedure for the preparations of Mn(III)–salen complexes [2d], that is, a mixture of **4**, (*S*,*S*)-1,2-diphenylethylenediamine and Mn(III) acetate was heated and followed by addition of lithium chloride [13]. Manganese(III) complex **A** was isolated as a dark brown powder after purification. In the present procedure, the use of an Mn(III) salt instead of an Mn(II) salt is crucial. A preparative procedure which involves the air oxidation of a mixture of a Mn(II) salt and the optically active ethylenebis-β-ketoiminato ligand afforded the corresponding Mn(III) complex in very low yield (<3%). On the other hand, manganese(III) complex **B** was prepared from the vinyl ether **6** by the same template method employed in the synthesis of complex **A**.

The structure of the *N*,*N*′-ethylenebis(α-cyclopentyloxycarbonyl-β-ketoiminato)manganese(III) complex **A-2** was determined by X-ray diffraction methods and a view of the molecule is shown in Fig. 2(a). The complex has a near square planar geometry. The four coordinated oxygen and nitrogen atoms of the ligand are coplanar to within 0.135 Å, and the manganese atom is comprised in that square base. The two carbon atoms (C4, C5) of the five-membered chelate ring with the phenyl groups of the ethylenediamine unit in pseudoequatorial positions are displaced out of the plane of the square base (by 0.3–0.4 Å). It should be noted that the alkyl group (cyclopentyl group) in the ester unit and one of the phenyl groups of the diphenylethylenediamine unit are located near each other (*c.* 4 Å).

The reactions were carried out at room temperature under the atmospheric pressure of oxygen in the coexistence of the optically active manganese(III) complex catalyst and pivalaldehyde, a reductant.

In our previous communication [10], the steric effect of an alkyl group in the ester moiety of the manganese(III) complex upon the optical yield of the produced 1,2-dihydronaphthaleneoxide was described; namely, as shown in Table 1, it has been found that the (*S*,*S*)-**A** catalyst derived from a bulkier alcohol improved the enantioselectivities. Compared with the cases using (*S*,*S*)-**A-1** (33% ee) derived from methyl acetoacetate, optically active epoxide **8** was obtained with better enantioselections when using the Mn(III) complexes (*S*,*S*)-**A-2**, **A-3**, **A-4** and **A-5**, having bulkier substituents, such as cyclopentyl, cyclohexyl, cyclooctyl and 2-adamantyl groups (37% ee, 42% ee, 43% ee and 44% ee, respectively). When (*S*,*S*)-**A-6** and (*R*,*R*)-**A-6** derived from chiral (−)-borneol were used as catalysts, the absolute configurations and optical yields of epoxide **8** were (1*R*,2*S*)-(+) (50% ee) and (1*S*,2*R*)-(−) (45% ee), respectively (entries 6 and 7). These results indicate that enantioselection in the present asymmetric reaction is dependent upon the optically active 1,2-diphenylethylenediamine unit and that the contribution of chirality in the ester moiety is not influential. Moreover, when the Mn(III) complex **A-7**, with a bulky alcohol, DL-isoborneol, in the ester moiety, was used, the optical




Scheme 1.

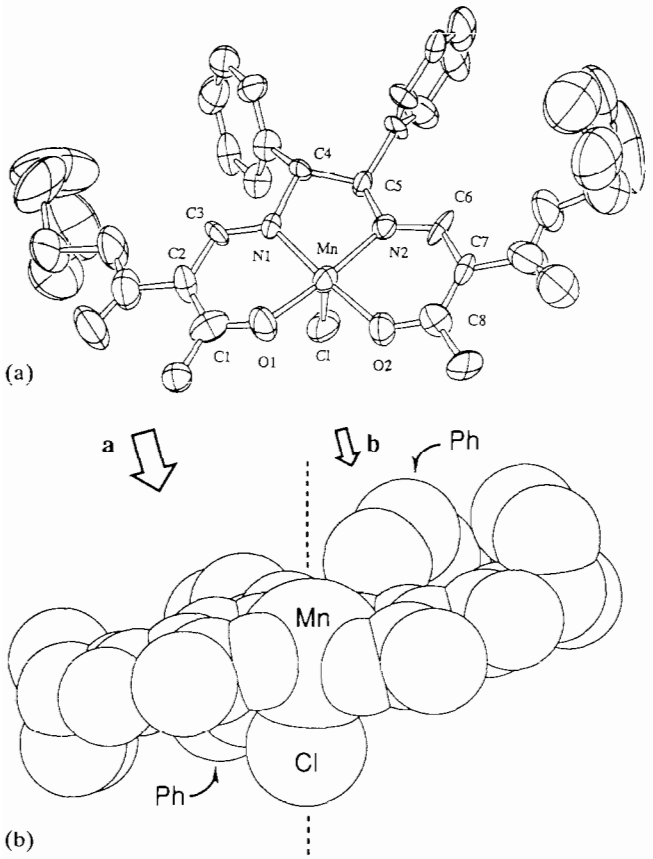


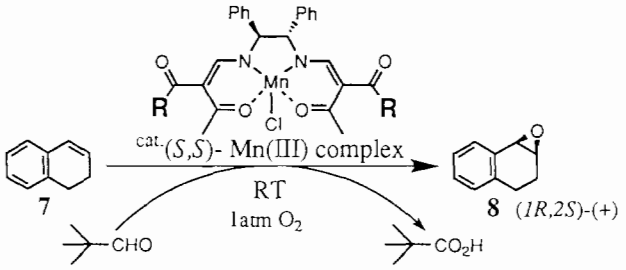

Fig. 2. Crystal structure of (*R,R*)-α-cyclopentyloxycarbonyl-β-ketoiminato manganese(III) chloride **A-2**: (a) ORTEP view. Selected bond lengths (Å) and bond angles (°) are as follows: Mn–Cl, 2.574(9); Mn–O(1), 1.92(1); Mn–O(2), 1.91(1); Mn–N(1), 1.94(1); Mn–N(2), 1.95(1); Cl–Mn–O(1), 95.0(5); Cl–Mn–O(2), 95.5(5); Cl–Mn–N(1), 84.2(5); Cl–Mn–N(2), 88.2(5); O(1)–Mn–N(2), 173.8(7); O(2)–Mn–N(1), 176.9(6); O(1)–Mn–O(2), 93.5(5); O(1)–Mn–N(1), 89.7(6); O(2)–Mn–N(2), 91.5(6); N(1)–Mn–N(2), 85.4(6); (b) side view (space filling model based on the X-ray crystal structure).

yield was also improved up to 52% e.e. (entry 8). This steric effect was revealed by X-ray analysis as illustrated in Fig. 2(b); the location of the alkyl group in the ester moiety, which is residing near the phenyl group of the diamine unit, resulted in an improvement in enantioselection (approach **a** > approach **b**). Consequently, it should be noted that the bulky alkyl substituents may serve only to control the approach of the olefins to the chiral diphenyldiamine unit.

In addition, it was found that the optical yield of the epoxide was also affected by the electronic property of the side chain of the bis-β-diketonato ligands, namely, the trifluoroethyl ester (in **A-8**) and the acetyl group (in **B**) gave good results (entries 9 and 10).

Asymmetric aerobic epoxidation catalyzed by the optically active manganese(III) complex **A-7** was successfully applied to several simple olefins, 1,2-dihydronaphthalene derivatives (Table 2). Dihydronaphthalenes without any functional groups, **7**, **9** and **10**, were converted into the corresponding epoxides by combined use of molecular oxygen and pivalaldehyde at 30 °C * in good yields with good enantioselections, 64% e.e., 53% e.e., and 70% e.e., respectively (entries 1–3). In the case of enantioselective epoxidation of 6,7-dihydro-5*H*-benzocycloheptene (**13**), the optically active (3*R*,4*S*)-(+)-epoxide was obtained with highly enantiomeric excess (84% e.e., entry 6). (Absolute configuration was determined by optical rotation [14].)

TABLE 1. Asymmetric epoxidation of 1,2-dihydronaphthalene

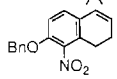
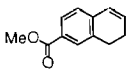
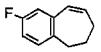



| Entry[a] | R | | Yield (%)[c] | Optical yield (% e.e.)[f] |
|---|---|---|---|---|
| 1 | $CH_3O$–⟨ | **A-1** | 64 | 33 |
| 2 | O–⟨ | **A-2** | 45 | 37 |
| 3 | O–⟨ | **A-3** | 42 | 42 |
| 4 | O–⟨ | **A-4** | 39 | 43 |
| 5 | O–⟨ | **A-5** | 46 | 44 |
| 6[b] | O–⟨ | ***(R,R)*-A-6** | 50 | 45[b] |
| 7[c] | O–⟨ | ***(S,S)*-A-6** | 47 | 50 |
| 8[d] | O–⟨ | **A-7** | 51 | 52 |
| 9 | $CF_3CH_2O$–⟨ | **A-8** | 50 | 45 |
| 10 | $CH_3$–⟨ | **B** | 51 | 45 |

[a]Reaction conditions: 1,2-dihydronaphthalene 0.8 mmol, pivalaldehyde 2.8 mmol, Mn(III) catalyst 0.104 mmol (13 mol%) in benzene 2 ml, r.t., 1 atm $O_2$, 1 h. [b](*R,R*)-Diamine/(−)-borneol-catalyst was used, then the absolute configuration of the epoxide was (1*S*,2*R*)-(−). [c](*S,S*)-Diamine/(−)-borneol-catalyst was used. [d](*S,S*)-Diamine/DL-isoborneol-catalyst. [e]Isolated yield. [f]Determined by GC analysis (Chiraldex B-DA (20 m × 0.25 mm i.d. × 0.125 μm film), ASTEC Co.). Absolute configurations were (1*R*,2*S*)-(+) except entry 6.

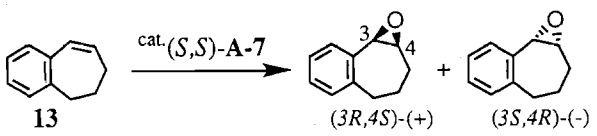
*The enantioselectivity in the present reaction was affected by temperature. In the present asymmetric epoxidation, reaction temperature between 25 (r.t.) and 30 °C is suitable for higher enantioselection.

TABLE 2. Asymmetric epoxidation of dihydronaphthalene derivatives with catalyst **A-7**

| Entry[a] | Olefin[b] | | Yield (%)[c] | Optical yield (% e.e.)[d] |
|---|---|---|---|---|
| 1 |  | **7** | 70 | 64 |
| 2 |  | **9** | 40 | 53 |
| 3 |  | **10** | 43 | 70 |
| 4 |  | **11** | 73 | 43 |
| 5 |  | **12** | 67 | 59 |
| 6 |  | **13** | 52 | 84 |
| 7 |  | **14** | 32 | 79 |

[a]Reaction conditions; olefin 0.8 mmol, pivalaldehyde 2.8 mmol, Mn(III) catalyst (**A-7**) 0.104 mmol (13 mol%) in benzene 2 ml, 30 °C, 1 atm $O_2$, 1 h. [b]Olefins were prepared from the corresponding tetralone derivatives. [c]Isolated yield. [d]Determined by GC analysis (Chiraldex B-DA).

TABLE 3. Absolute configuration of epoxide obtained from asymmetric oxidation with catalyst (*S,S*)-**A-7**




**13** (*3R,4S*)-(+) (*3S,4R*)-(-)

| Oxidant | Optical yield (% e.e.) | |
|---|---|---|
| | (*3R,4S*)-(+) | (*3S,4R*)-(−) |
| $O_2$ | 84 | |
| NaOCl | | 41 |

Moreover, it is noteworthy that the face selectivity in aerobic asymmetric epoxidation of olefins is the reverse of that of conventionally employed terminal oxidants, such as sodium hypochlorite and iodosylbenzene; for example, in the oxidation reaction of olefin **13** catalyzed by (*S,S*)-**A-7**, the gaseous oxygen–pivalaldehyde system afforded the (*3R,4S*)-(+)-epoxide in 84% ee, while the reverse (NaOCl) gave the (*3S,4R*)-(−)-epoxide in 41% ee (Table 3). Although the detailed mechanism is not yet clear, the results suggest the possible generation of a new class of intermediates [15] composed of a chiral complex catalyst and oxygen, which is very important in achieving the effective enantioselective epoxidation of unfunctionalized olefins.

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