Catalytic Enantioselective Oxidation of Alkanes and Alkenes Using (Salen)Manganese Complexes Bearing a Chiral Binaphthyl Strapping Unit

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Abstract: A (salen)manganese(III) complex bearing a chiral binaphthyl strapping unit catalyzes the enantioselective hydroxylation of indane (up to 34% ee) and the epoxidation of alkenes (up to 93% ee) with iodosylbenzene.

Keywords: asymmetric epoxidation; asymmetric hydroxylation; C–H activation; hydrocarbons; iodosylbenzene; salen-manganese complex

Catalytic asymmetric oxidation of hydrocarbons is an important and rapidly growing area in organic synthesis, and much effort has been devoted to create a new chiral metal complex directed towards asymmetric oxidations.[1]

For asymmetric hydroxylation of C–H bonds of alkanes, it is important to control the direction of substrate's approach to the active metal-oxo center. For this purpose, chiral metalloporphyrin complexes such as bridged iron-porphyrins bearing a chiral binaphthyl vaulted unit[2] and D_4-symmetric chiral ruthenium porphyrins[3] and a concave type (salen)manganese complex **4** bearing a chiral environment[4] were designed and used for asymmetric hydroxylation of hydrocarbons. The (salen)manganese complexes **3**[5] and **4**[6] are also known to be effective for the asymmetric epoxidation of alkenes (Figure 1).

During the course of our study on the biomimetic oxidation of alkanes,[7,8] we found that enantioselective oxidation of symmetrical alkanes using the catalyst **3** proceeds to give the corresponding optically active ketones in up to 70% ee.[9] In order to aim at asymmetric hydroxylation of alkanes, we synthesized new bridged Mn(salen) complexes bearing a strapping unit (**1** and **2**).[10] The strategy is the generation of oxo-manganese species in a cage. Herein, we wish to report that the novel manganese salen complex (**1**) bearing a chiral strapping unit is an effective catalyst for the enantioselective hydroxylation of alkanes and epoxidation of alkenes.

The strapped Mn(salen) complexes were synthesized as shown in Scheme 1. (*S*)-2,2′-Binaphthol was allowed to react with *p*-bromobenzaldehyde in the presence of copper. The dialdehyde was converted to the corresponding diol **5** by reduction with $LiAlH_4$. 3-*tert*-Butyl-5-formyl-4-methoxymethoxyphenylacetic acid[11] was prepared in four steps; that is, Friedel–Crafts alkylation

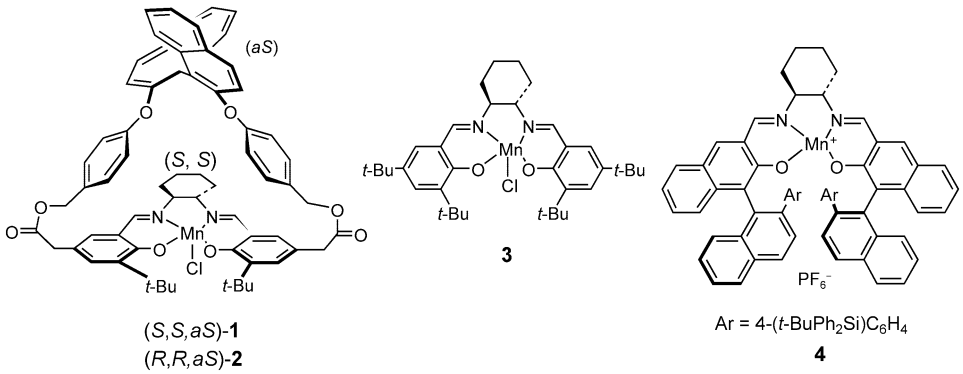

Figure 1. (Salen)manganese(III) complexes.

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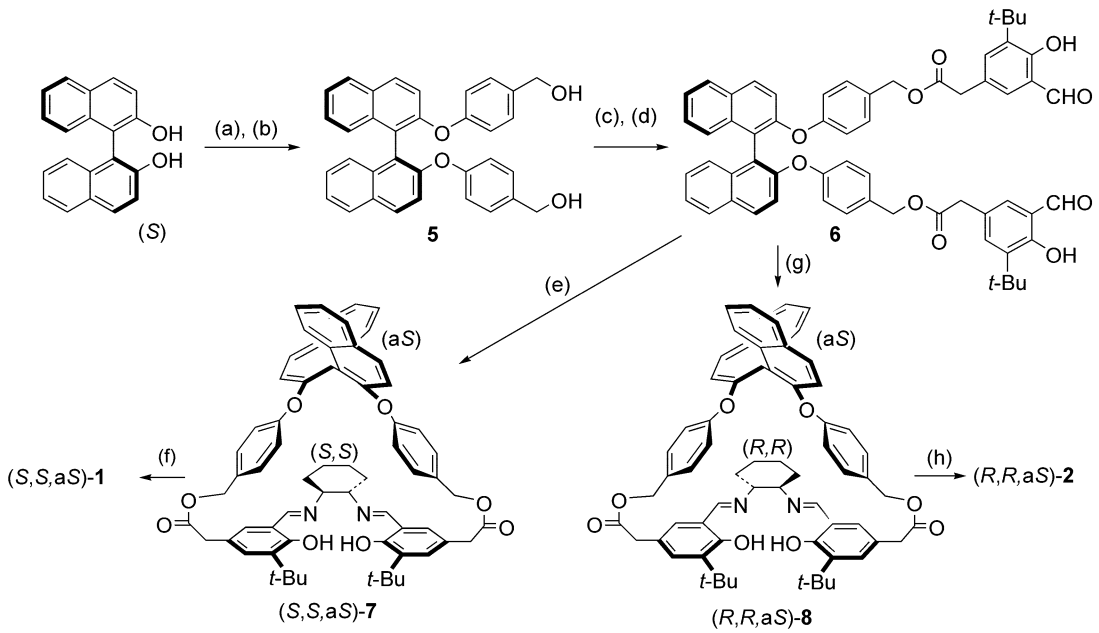
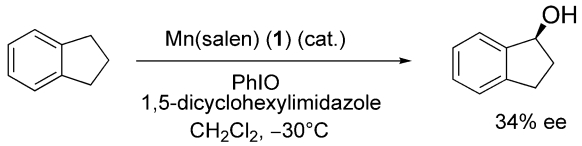


Scheme 1. For (*S*,*S*,a*S*)-**1**: (a) *p*-bromobenzaldehyde, Cu, CuO, K_2CO_3, pyridine, reflux, 100%; (b) $LiAlH_4$, THF, reflux, 97%; (c) 3-formyl-4-methoxymethoxy-5-*tert*-butylphenylacetic acid, DCC, DMAP, CH_2Cl_2, 50%; (d) TMSBr, CH_2Cl_2, 85%; (e) (*S*,*S*)-cyclohexanediamine, EtOH, 71%; (f) $Mn(OAc)_2 \cdot H_2O$, LiCl, EtOH, reflux, 93%. For (*R*,*R*,a*S*)-**2**: (g) (*R*,*R*)-cyclohexanediamine, EtOH, 53%; (h) $Mn(OAc)_2 \cdot H_2O$, LiCl, EtOH, reflux, 66%.

of methyl *p*-hydroxyphenylacetate with *t*-butanol, formylation, protection of the hydroxy group with methoxymethyl group (MOM), and hydrolysis of the methyl ester under basic conditions, and then was allowed to condense with the diol **5**. Subsequent deprotection of the methoxymethyl group with trimethylsilyl bromide gave the corresponding disalicylaldehyde **6**. Diastereomeric pairs of the strapped salen ligands **7** and **8** were prepared by the condensation of **6** with optically active (*S*,*S*)- and (*R*,*R*)-cyclohexanediamine, respectively. Metalation of the salen ligands **7** and **8** with $Mn(OAc)_4 \cdot 4\,H_2O$ gave the corresponding diastereomeric isomers of the strapped Mn(salen) complexes **1** and **2**, respectively.

Asymmetric hydroxylation of an alkane with iodosylbenzene in the presence of the chiral strapped Mn(salen) complex catalyst **1** can be carried out. Typically, treatment of indane with PhIO in the presence of 0.2 mol % of Mn(salen) catalyst **1** in CH_2Cl_2 at $-30\,^{\circ}C$ under argon gave (*S*)-1-indanol (20% yield) with 34% ee along with a small amount of 1-indanone (Scheme 2).

In the present reaction, coordination of a fifth ligand to the Mn(salen) complex as an axial ligand[12] is important to control the reaction site; that is, either inside or outside the cavity (Figure 2). A sterically hindered ligand favors coordination to the opposite side of the strapped unit, resulting in formation of the active oxo-manganese species in the chiral cavity. In contrast, a small ligand coordinates to the Mn from both non-strapped and strapped sides. An interesting effect of the



Scheme 2. Enantioselective oxidation of indane with Mn (salen) catalyst **1**.

fifth ligand was observed (Table 1). The Mn(salen) **1**-catalyzed oxidation of indane without an axial ligand gave 1-indanol with only 5% ee (entry 1). When the non-substituted imidazole was used, the enantioselectivity was not influenced (8% ee) (entry 2). In contrast, when bulky 4-phenylpyridine *N*-oxide and 1,5-dicyclohexylimidazole were used as the fifth ligand, the enantioselectivity was improved to 14% ee and 25% ee, respectively (entries 3 and 4). Furthermore, the enantioselectivity was improved, when the reaction temperature was low (at $-30\,^{\circ}C$, 34% ee) (entry 5). A substrate seems to approach to the cage with recognition of the slope of the bridging naphthyl group [(A) in **9** in Figure 2]. Actually, the Mn(salen) **2** which is a diastereomer of **1** and an unmatched pair gave the (*R*)-alcohol with only 15% ee (entry 6). The non-bridging complex **3** gave the (*S*)-alcohol with 15% ee (entry 7).

Enantioselective epoxidation of alkenes can be also carried out using the chiral strapped Mn(salen) complex **1** (Scheme 3). Typically, treatment of 2,2-dimethylchromene with PhIO in the presence of the catalyst **1** and 4-phenylpyridine *N*-oxide in CH_2Cl_2 under argon gave the

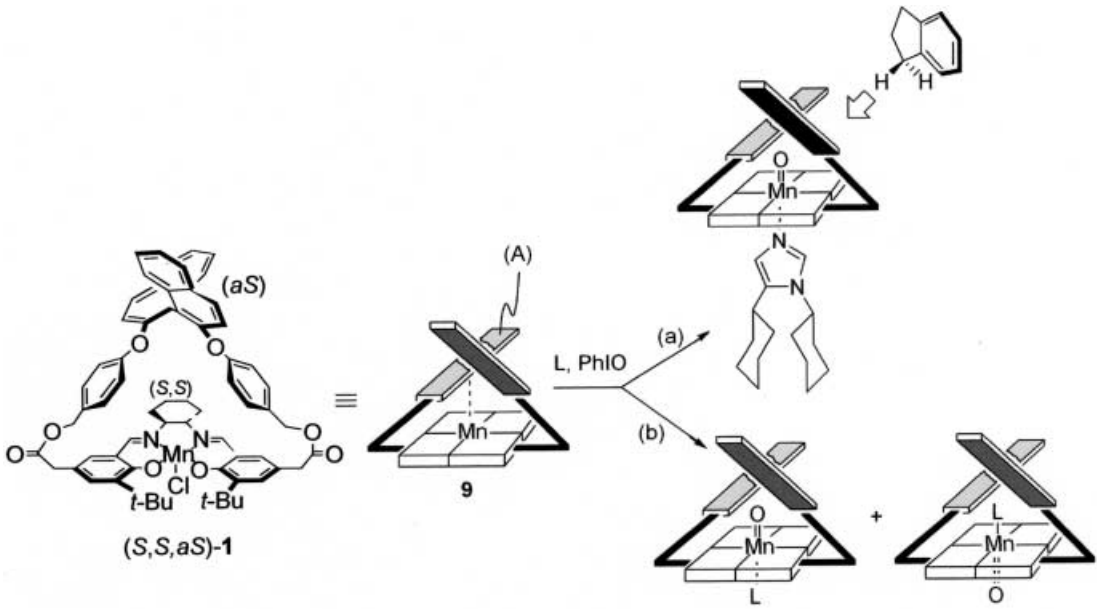


Figure 2. (**a**) L = bulky ligand (1,5-dicyclohexylimidazole). (**b**) L = small ligand (imidazole).

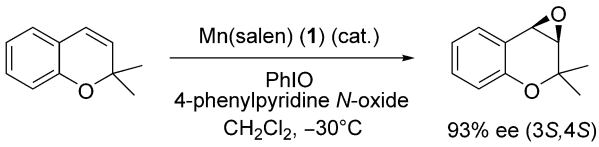
Table 1. Asymmetric hydroxylation of indane using various Mn(salen) complexes.[a]

Entry	Catalyst	Temperature [°C]	Additive	Conversion [%][b]	Alcohol/Ketone	ee [%][c]
1	**1**	0	none	20	1.3	5 (*S*)
2	**1**	0	imidazole	35	4.2	8 (*S*)
3	**1**	0	4-phenylpyridine *N*-oxide	18	5.0	14 (*S*)
4	**1**	0	1,5-dicyclohexylimidazole	41	4.9	25 (*S*)
5	**1**	−30	1,5-dicyclohexylimidazole	25	4.1	34 (*S*)
6	**2**	−30	1,5-dicyclohexylimidazole	24	9.0	15 (*R*)
7	**3**	−30	1,5-dicyclohexylimidazole	24	3.5	15 (*S*)

[a] To a mixture of indane (1 mmol), additive (0.25 mmol), and Mn(salen) complex (0.002 mmol) in CH_2Cl_2 was added PhIO (0.1 mmol). The mixture was stirred for 7 h.
[b] Conversion of indane (total yield of 1-indanol and 1-indanone).
[c] Determined by HPLC analysis using CHIRALCEL OB-H (hexane:2-propanol = 10:1).

corresponding (3*S*,4*S*)-epoxide with 93% ee (50% yield).[13] *cis*-β-Methylstyrene was also oxidized to give the corresponding epoxide with 82% ee.[14] The absolute configuration of the epoxide is the same as that obtained using (*S*,*S*)-**3** and is opposite to that obtained with **4**.

In conclusion, we have synthesized novel manganese complexes (**1** and **2**) bearing a chiral strapping unit, and found that these complexes are effective for the asymmetric hydroxylation of alkanes and asymmetric epoxidation of alkenes. Work is in progress to obtain mechanistic information and design further highly enantioselective procedures for the catalytic oxidation of hydrocarbons.



Scheme 3. Enantioselective oxidation of 2,2-dimethylchromene with Mn(salen) catalyst **1**.

Experimental Section

Mn(salen) (1)-Catalyzed Enantioselective Hydroxylation of Indane with Iodosylbenzene

To a mixture of indane (118 mg, 1.0 mmol), Mn(salen) complex (**1**) (2.2 mg, 0.0020 mmol), 1,5-dicyclohexylimidazole (12 mg, 0.050 mmol), and CH_2Cl_2 (0.5 mL) was added iodosylbenzene (22 mg, 0.10 mmol) at 0 °C under an argon atmosphere. The mixture was stirred at −30 °C for 7 h. After removal of the

solvent, the residue was subject to column chromatography (SiO_2, hexane:ethyl acetate = 10:1) to give 1-indanol as a colorless oil; yield: 27 mg (20%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.84–1.91 (m, 1H, CH_2), 2.38–2.45 (m, 1H, CH_2), 2.47 (br, 1H, OH), 2.74–2.81 (m, 1H, CH_2), 2.97–3.03 (m, 1H, CH_2), 5.15 (d, J = 4.6 Hz, 1H, CH), 7.18–7.25 (m, 3H, ArH), 7.36 (d, J = 6.9 Hz, 1H, ArH). The enantiomeric excess was determined to be 34% ee by HPLC analysis using a chiral column (CHIRALCEL OB−H, hexane:2-propanol = 10:1, 0.5 mL/min).

Mn(salen) (1)-Catalyzed Enantioselective Epoxidation of 2,2-Dimethylchromene with Iodosylbenzene

To a mixture of 2,2-dimethylchromene (16.0 mg, 0.100 mmol), Mn(salen) catalyst (**1**) (1.1 mg, 0.00100 mmol), 4-phenylpyridine *N*-oxide (17.1 mg, 0.100 mmol), and CH_2Cl_2 (1.0 mL) was added iodosylbenzene (22 mg, 0.10 mmol) at −30 °C. The mixture was stirred for 4 h at this temperature. After removal of the solvent, the residue was subject to column chromatography (SiO_2, hexane:ethyl acetate = 30:1) to give 3,4-epoxy-2,2-dimethylchromene as a colorless oil; yield: 8.8 mg (50%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.26 (s, 3H, CH_3), 1.58 (s, 3H, CH_3), 3.50 (d, J = 4.4 Hz, 1H, CH), 4.58 (d, J = 4.6 Hz, 1H, CH), 6.81 (d, J = 8.0 Hz, 1H, ArH), 6.93 (dt, J = 7.5 and 1.1 Hz, 1H, ArH), 7.20–7.26 (m, 1H, ArH), 7.34 (dd, J = 7.3 and 1.6 Hz, 1H, ArH). The enantiomeric excess was determined to be 93% ee by HPLC analysis using a chiral column (CHIRALCEL OB-H, hexane:2-propanol = 10:1, 0.5 mL/min). The absolute configuration was determined by comparison of the retention time of HPLC analysis with literature data.[15]

Acknowledgements

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