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Rational Design of Mn-Salen Epoxidation Catalysts: Preliminary Results

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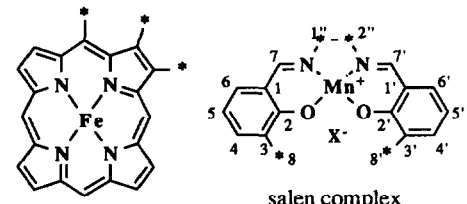
Abstract: (Salen)manganese(III) complex **7** designed on the basis of the new proposal on the olefin's access to metal-oxo bond and complex **10** having axial chirality in salicylaldehyde part were found to be effective catalysts for the epoxidation of unfunctionalized olefins, especially for *cis*-olefins.

Epoxides serve as versatile intermediates in synthetic organic chemistry, because they are readily converted into various useful functional groups in regio- and stereoselective manners. Accordingly, many methodologies for the enantioselective synthesis of epoxides have been reported, since Henbest et al. first reported the epoxidation of styrene with peroxycamphoric acid in 1967.[1] Among them, asymmetric epoxidation using a Ti(OPr-*i*)$_4$/dialkyl tartrate/*t*-butyl hydroperoxide system reported by Sharpless and one of the author (T.K.) is the most useful method for the synthesis of optically active epoxides from the view point of enantioselectivity (>90% ee), mildness of the reaction conditions, and economics.[2] Although the scope of this reaction is very wide, substrates used is limited only to allylic alcohols and simple olefins do not undergo epoxidation under the conditions. In 1983, Davis et al. reported that optically active oxaziridine was an efficient epoxidizing agent of simple olefins. For example, epoxidation of *trans*-β-methylstyrene gave the corresponding epoxide of 66% ee.[3] However, this reaction requires use of stoichiometric amount of expensive oxaziridine. On the other hand, oxidation in *vivo* proceeds enantioselectively with aid of oxidizing enzymes such as cytochrome P-450 that has ironporphyrin complex as an active site. In order to reproduce the catalysis of P-450 in flask, many optically active metalloporphyrins have been synthesized and used for the epoxidation of simple olefins.[4] Epoxidation of mono- and *cis*-disubstituted olefins with these porphyrin complexes generally shows moderate to good level of enantioselectivity but that of *trans*-olefins shows poor selectivity, except for one example.[4b] Difficulty in the construction of effective porphyrin catalyst is partly attributable to its π-conjugated planar structure which does not allow the presence of stereogenic carbons in porphyrin ring. In contrast to porphyrin complex, salen complex that also serves as an oxidation catalyst can contain stereogenic carbons at C1" and C2" and at C8 and C8' carbons (Fig. 1). Since these stereogenic centers are located close to metal center, the higher asymmetric induction can be expected by using this type of optically active salen complexes as catalysts (Fig. 2).[5,6]

Along this line, we synthesized (salen)manganese(III) complexes (**1**-**4**) and examined the epoxidation of

This paper is dedicated to Professor K. Barry Sharpless and Professor Ryoji Noyori.



* = asymmetric carbon

Fig. 1

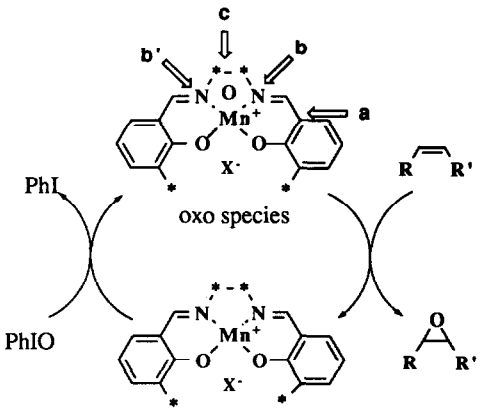
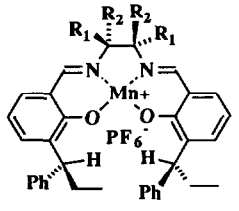
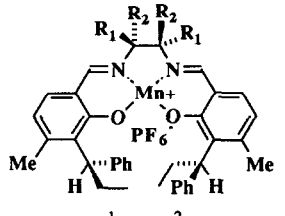


Fig. 2



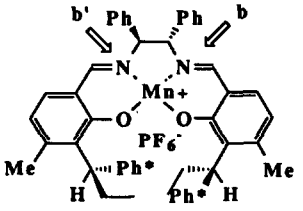
1: R^1=H, R^2=Ph
2: R^1=Ph, R^2=H



3: R^1=Ph, R^2=H
4: R^1=H, R^2=Ph

simple olefins.[5a-d] With **3** among these complexes, moderate to good level of enantioselectivity (up to 82% ee) was realized. Furthermore, this study showed that enantiofacial selection of *cis*-olefins was mainly controlled by the chirality at C1" and C2" and that of *trans*-olefins preferentially by the chirality at C8 and C8'. Although we already proposed that olefins orienting their bulkier vinylic substituents away from C8'-substituent to minimize steric repulsion between them approached metal-oxo bond along nitrogen-manganese bond axis (approach **b**)[7] instead of approaches (**a** and **c**) previously proposed by Jacobsen (Fig. 2),[6] we considered that the above mentioned stereoregulation by salen complex could be explained by further speculating that *trans*-olefins approached from slightly upper side along **b** for steric reason, while *cis*-olefins approached parallel to the plane of salen complex (side-on approach). This speculation partly explained why *trans*-olefins did not show so good enantioselectivity as *cis*-olefins, since the quasi-equatorially oriented C1"-phenyl group would not disturb so strongly the access of *trans*-olefins from **b'** (see the drawing of **5** at the top of the next page). However, we expected that, if we could introduce a bulky group at C8 and C8' which projected toward the oncoming olefins to suppress approach **b'**, enantioselectivity of *trans*-olefins would be improved. Enantioselectivity of *cis*-olefins approaching from **b** was also expected to be improved due to the increased steric repusion between C8(8')-substituents and vinylic substituents.[7] Based on these considerations, we planned to synthesize the salen complexes **5**-**7** having *p*-(*t*-butyl)phenyl group instead of phenyl group, at C8 and C8',[8] in which *t*-butyl group was considered to occupy the appropriate space.

On the other hand, it was also found from the above preliminary experiment that asymmetric induction by (salen)manganese(III) catalysts often varied with the substrates used, as shown in Scheme 1.[5c,e] The small



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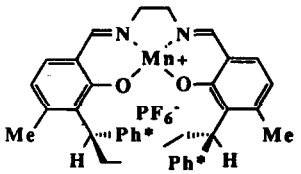

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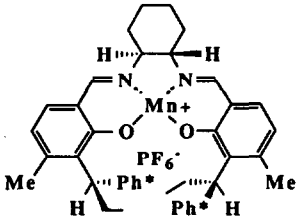

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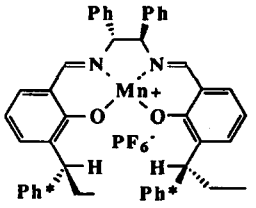

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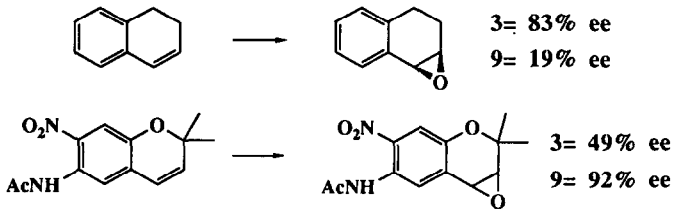
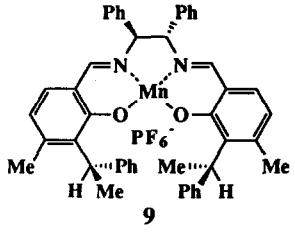
Ph* = 4-(*t*-butyl)phenyl

difference in size of C3- and C3'-substituents gave a strong influence on enantioselectivity. This dependence of asymmetric induction on the substrate was considered to be partly attributable to the conformational inflexibility of C3- and C3'-substituents that were forced to take a hydrogen atom-in-aromatic plane conformation in order to minimize the steric repulsion between C3(3') and C4(4') substituents. We, therefore, expected that high and constant enantioselectivity would be realized in the epoxidation of wider range of substrates, if C3- and C3'-substituents were replaced by more flexible chiral groups. According to this idea, we also synthesized salen complexes (**10a** and **11**) bearing binaphthyl groups of axial chirality[9] instead of central chirality and explored the epoxidation using them as catalysts.[8]





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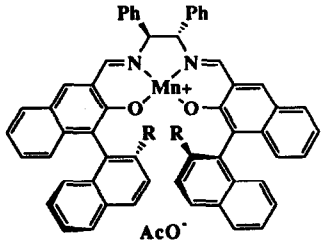
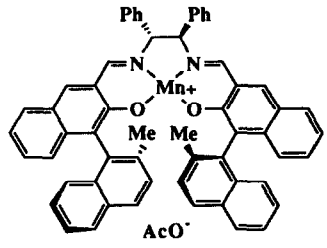
Scheme 1

Synthesis of (Salen)manganese(III) Complexes (5-7) Bearing *p*-(*t*-Butyl)phenyl Group at C8 and C8'

The requisite 3-[1-(*p*-*t*-butylphenyl)propyl]-4-methylsalicylaldehyde (**18**) for the synthesis of **5-7** was prepared from *p*-*t*-butylbenzoic acid (**12**) (Scheme 2). Compound **12** was first converted into methyl *p*-(*t*-butyl)cinnamate (**13**) in a conventional manner. Diisobutylaluminum hydride (DIBAH) reduction of **13** and subsequent treatment of the resulting allylic alcohol with Br_2-PPh_3 gave bromide **14**, which was further treated



10a: R= Me
10b: R= Ph



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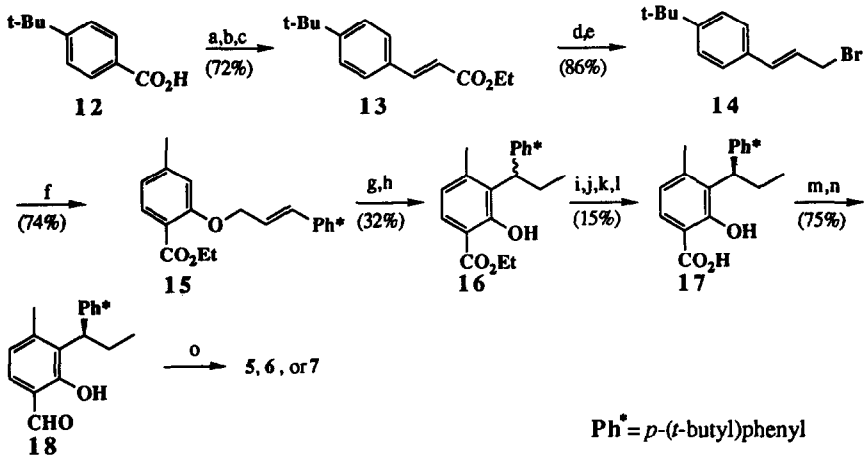
with ethyl 4-methylsalicylate in the presence of NaH giving ether **15**. Heating **15** at 170-180 °C followed by hydrogenation gave *dl*-salicylate **16**. Compound **16** was hydrolyzed and resolved with aid of (-)-brucine. (*R*)-(+)-Salicylic acid **17** was converted into (*R*)-(-)-aldehyde **18** by lithium aluminum hydride (LAH) reduction and subsequent 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) oxidation. Aldehyde **18** thus obtained was converted into salen complexes (**5**, **6**, and **7**) according to the reported procedure.[5d]

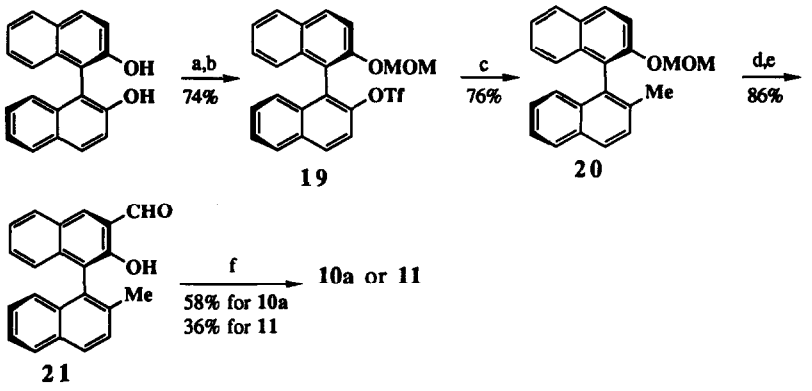


a) LAH; b) MnO_2; c) $(EtO)_2P(O)CH_2CO_2Et$, NaH; d) DIBAH; e) PPh_3, Br_2;
f) NaH, ethyl 4-methylsalicylate; g)180 °C; h) H_2-Pd /C; i) 5N NaOH, j) 1N HCl;
k) (-)-brucine; l) six repeated recrystallization from acetone; m) LAH; n) DDQ;
o) i) diamine [(1*S*,2*S*)-diphenylethylenediamine for **5**, ethylenediamine for **6**, (1*S*,2*S*)-cyclohexanediamine for **7**], $Mn(OAc)_2{\cdot}4H_2O$; ii) Cp_2FePF_6

Scheme 2

Synthesis of (Salen)manganese(III) Complexes Bearing Binaphthyl Groups

Complexes (**10a** and **11**) were prepared from (a*R*)-binaphthol, which was triflated and subsequently protected as a MOM ether to give triflate **19**. Treatment of **19** with methylmagnesium bromide in the presence of a nickel catalyst gave **20**. Compound **20** was treated with *t*-butyllithium and dimethylformamide successively and the resulting aldehyde was deprotected with trimethylsilyl bromide to give **21** which was



a) Tf_2NPh, collidine, CH_2Cl_2, reflux; b) MOMCl, $(i\text{-}Pr)_2NEt$, CH_2Cl_2, RT; c) MeMgBr, $NiCl_2(PPh_3)_2$, Et_2O, reflux; d) i: *t*-BuLi, THF, -78 °C, ii: DMF, RT; e) TMSBr, CH_2Cl_2, 0 °C; f) i: (1*S*,2*S*)-(-)- and (1*R*,2*R*)-(+)-diphenylethylenediamine (for **10a** and **11**, respectively), EtOH, ii: $Mn(OAc)_2 \cdot 4H_2O$, CH_3CN, O_2

Scheme 3

further converted into (salen)manganese(III) complexes **10a** and **11** according to the literature procedure.[5d]

Epoxidations with (Salen)manganese Complexes (5, 6, 7, and 8)

With complexes **5**, **6**, and **7** in hand, we first examined the epoxidation of *trans*-stilbene with iodosylbenzene as a terminal oxidant and the results are shown in Table 1 (entries 1-4). Epoxidation with **5** showed the enhanced enantioselectivity (56% ee) as compared with the reported value (48% ee) using **3** as a catalyst.[5b] Since the enantiofacial selection of *trans*-olefins is mainly dictated by the chirality of C3 substituent (*vide supra*), we next examined the reaction with salen complex **6** which have no chirality in ethylenediamine part and found that enantioselectivity was further improved to 61% ee. Replacement of ethylenediamine in **6** with (1*S*,2*S*)-cyclohexanediamine did not give much difference in enantioselectivity (62% ee, entry 3).[10,11] We also examined the epoxidation of *trans*-β-methylstyrene with **7** but only poor selectivity was observed (entry 7). Since complex **1** was a better catalyst for the epoxidation of this olefin than complex **3** in a preliminary experiment,[5a] we synthesized complex **8** and examined the epoxidation. However, **1** and **8** showed the similar level of asymmetric induction (entries 5 and 6). This is considered to be attributable to the conformation of C3- and C3'-substituents in **1** and **8**.[12] Contrary to the epoxidation of *trans*-olefins, the epoxidation of *cis*-olefins with **7** all showed good to excellent level of asymmetric induction up to 96% ee (entries 8-11). It is noteworthy that presence of functional groups such as amide, nitro, and *N*-oxide did not affect asymmetric induction (entries 10 and 11). Although the substrates used are limited, we could first show the salen complex that exhibited the moderate to good level of asymmetric induction in the epoxidation of both *cis*- and *trans*-olefins.

Epoxidations with (Salen)manganese Complexes (10 and 11)

To know the asymmetry-inducing ability of complexes **10a** and **11**, we first examined the epoxidation of dihydronaphthalene (Table 2) and found that **10a** showed higher asymmetric induction than **11**, though insufficient level (entries 1 and 2). Since we had found that addition of donor ligand to salen-catalyzed reaction system often improved asymmetric induction,[5c] we next examined epoxidation with **10a** in the presence of

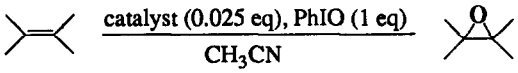
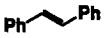
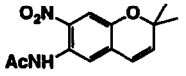
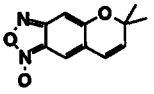


Table 1. Asymmetric epoxidation of various olefins using (salen)manganese(III) complexes (**5-8**)[a)]

Entry	Substrate	Catalyst	Time (h)	Yield (%)	% e.e.	Abs. confign.
1		**5**	24	70	56	1*R*,2*R*
2	"	**6**	24	64	61	1*R*,2*R*
3	"	**7**	22	65	62	1*R*,2*R*
4	"	**3**	12	95	48	1*R*,2*R*
5		**8**	24	26	55[b)]	1*R*,2*R*
6	"	**1**	58	32	56[b,c)]	1*R*,2*R*
7	"	**7**	24	61	9	1*R*,2*R*
8		**7**	24	32[d)]	86[e)]	1*S*,2*R*
9		**7**	24	38	91[f)]	1*S*,2*R*
10		**7**	24	78	96	-[g)]
11	 **22**	**7**	24	63	94	-[g)]

a) Reactions were carried out in acetonitrile at room temperature with a molar ratio of substrate: catalyst: iodosylbenzene =1: 0.025: 1.
b) Reaction was carried out in dichloromethane in the presence of 10 eq. of 2-methylimidazole.
c) 2 eq. of iodosylbenzene were used.
d) A 8.1:1 mixture of the corresponding *cis*- and *trans*-epoxides was produced. E.e. of the *trans*-isomer was 55% ee.
e) The reaction was carried out in dichloromethane and aqueous sodium hypochlorite (5%) was used as a terminal oxidant.
f) The reaction was carried out in dichloromethane in the presence of 10 eq. of 4-dimethylaminopyridine *N*-oxide.
g) Absolute configuration was not determined.

various donor ligands and found that addition of pyridine *N*-oxide remarkably enhanced asymmetric induction as well as chemical yield (entries 3-5). Other olefins were also submitted to the epoxidation under the same conditions. Reaction of *cis*-olefins proceeded with constant and high selectivity of 86~91% ee (entries 5, 7-9) as expected, differing from the epoxidation with **3** and **9** as catalysts (Scheme 1). In contrast, epoxidation of *trans*-olefins showed only poor selectivity (entries 11 and 12). This low enantioselectivity is partly attributable to the conformation of the binaphthyl moiety wherein the methyl groups are not directed toward the metal center and can not suppress the *trans*-olefin's approach along **b'** (Fig. 2). The above results and speculation suggested that higher enantioselectivity would be realized in the epoxidation of *cis*-olefins if we could replace the methyl group (**R** in **10a**) with more bulky substituent such as phenyl (**10b**) or *t*-butyl group. Although preliminary results, epoxidation of dihydronaphthalene and chromene derivative **22** with **10b** actually showed the improved enantioselectivity of 92 and 98% ee, respectively (entries 6 and 10).[13)]

The results described in this paper shows a good prospect of (salen)manganese(III) complexes having stereogenic centers at C1", C2", C8, and C8' carbons as a catalyst of epoxidation of simple olefins. Further

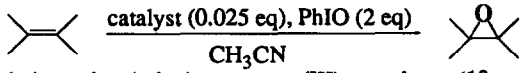
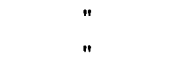
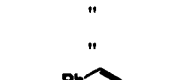


Table 2. Asymmetric epoxidation using (salen)manganese(III) complexes (**10** and **11**)

Entry	Substrate	Salen complex	Additive	Time (h)	Yield (%)	% e.e.	Abs. confign.
1		**10a**	-	24	41	68	1*S*,2*R*
2	"	**11**	-	24	52	38	1*R*,2*S*
3	"	**10a**	2-methylimidazole	24	67	51	1*S*,2*R*
4	"	**10a**	DMAP-*N*-oxide[a]	24	71	86	1*S*,2*R*
5	"	**10a**	Pyr-*N*-oxide[b]	24	77	86	1*S*,2*R*
6	"	**10b**	Pyr-*N*-oxide[b]	24	96	92	1*S*,2*R*
7		**10a**	Pyr-*N*-oxide[b]	24	48[c]	89[d]	1*S*,2*R*
8		**10a**	Pyr-*N*-oxide[b]	24	99	89	-[e]
9	 **22**	**10a**	Pyr-*N*-oxide[b]	24	52	91	-[e]
10	"	**10b**	Pyr-*N*-oxide[b]	24	69	98	-[e]
11		**10a**	Pyr-*N*-oxide[b]	24	68	28	1*S*,2*S*
12		**10a**	Pyr-*N*-oxide[b]	24	52	0	-

a) DMAP-*N*-oxide = 4-dimethylaminopyridine *N*-oxide.
b) Pyr-*N*-oxide = pyridine *N*-oxide.
c) The reaction gave a 3.3:1 mixture of the corresponding *cis*- and *trans*-epoxides.
d) The number is the % ee for the *cis*-epoxide. The optical purity of the *trans*-epoxide is 83%.
e) Absolute configuration was not determined.

study is continuing in our laboratory to invent a more effective salen catalyst on the basis of new hypotheses on the olefin's access to metal-oxo bond and to clarify the asymmetric induction mechanism in salen-catalyzed epoxidation.

Experimental

NMR spectra were recorded at 400 MHz on a JEOL GX-400 or at 90 MHz on a JEOL FX-90Q instrument. All signals were expressed as ppm down field from tetramethylsilane used as an internal standard (δ-value in $CDCl_3$). IR spectra were obtained with a JASCO IR-700 instrument. Optical rotation was measured with a JASCO DIP-360 automatic digital polarimeter. Column chromatography was conducted on Silica Gel 60, 70-230 mesh ASTM, available from E. Merck. Preparative thin layer chromatography was performed on 0.5 mm x 20 cm x 20 cm E. Merck silica gel plate (60 F-254). Solvents were dried and distilled shortly before use. Reactions were carried out under an atmosphere of nitrogen if necessary.

Ethyl *p*-*t*-butylcinnamate (13). To a solution of **12** (45.32 g, 0.254 mol) in THF (350 ml) was added LAH (14.67 g, 0.366 mol) by portions over 20 min at 0 °C, and then the mixture was stirred for 3 h at rt and another 2 h at 50-60 °C. The reaction mixture was quenched with 3 N HCl (200 ml), extracted with ether, dried over $MgSO_4$, and concentrated to give the corresponding alcohol (40.13 g, 96%). To a solution of the alcohol (20.92 g, 0.127 mol) in ether (330 ml) was added γ-MnO_2 (102 g, 1.17 mol). After stirring 1 d at rt, the mixture was filtered through a pad of Celite and concentrated to give the corresponding aldehyde (18.5 g, 89%).

To a suspension of NaH (4.91 g of a 60% dispersion in mineral oil, 0.123 mol) in THF (250 ml) was added a solution of triethylphosphonoacetate (22.8 g, 0.102 mol) in THF (50 ml) dropwise over 20 min at 0 °C and the mixture was stirred for 2 h at rt and cooled to 0 °C. To this solution, the aldehyde (16.5 g, 0.102 mmol) in THF (50 ml) was added dropwise over 10 min and the whole mixture was stirred for 12 h at rt. The mixture was treated with sat. NH_4Cl (100 ml) and extracted with ether (100 ml x 2). The organic layer was washed with brine, dried over $MgSO_4$, and chromatographed on silica gel (hexane-ethyl acetate = 19:1) to give **13** (21.0 g, 88%) as an oil. **13**; IR (neat): 2963, 2905, 2870, 1715, 1636, 1609, 1514, 1313, 1267, 1211, 1171, 984, 829 cm^{-1}. ^1H NMR (400 MHz): 7.67 (d, J = 16.12 Hz, 1H), 7.47 (dd, J = 6.35, 1.96 Hz, 2H), 7.41 (dd, J = 6.35, 1.96 Hz, 2H), 6.90 (d, J = 16.12 Hz, 1H), 4.26 (q, J = 7.34 Hz, 2H), 1.34 (t, J = 7.34 Hz, 3H), 1.33 (s, 9H). Calcd. for $C_{15}H_{24}O_2$: C, 77.54; H, 8.68%. Found: C, 77.75; H, 8.60%.

***p*-*t*-Butylcinnamyl bromide (14).** To a solution of **13** (10.3 g, 44.3 mmol) in dichloromethane (100 ml) was added DIBAH (110 ml, a 0.93 M solution in hexane) dropwise over 15 min at -78 °C, and the mixture was stirred for 16 h at rt. The reaction mixture was quenched with water (40 ml) and 6 N HCl (80 ml), extracted with ether (160 ml), washed successively with sat. aqueous $NaHCO_3$ and with brine, dried over $MgSO_4$, and chromatographed on silica gel (hexane-ethyl acetate = 9:1 ~ 4:1) to give the corresponding alcohol (8.09 g, 96%). A solution of PPh_3 (10.58 g, 40.3 mmol) in CH_3CN (53 ml) was treated with bromine (ca. 2 ml) at 0 °C until the solution turned into pale brown in color. When the addition was completed, the mixture was warmed to 60 °C to give the clear solution and then allowed to cool to rt with stirring. To this solution, was added the above alcohol (7.65 g, 40.2 mmol) in CH_3CN (75 ml) dropwise over 5 min and the mixture was stirred for 22 h at rt. The mixture was concentrated *in vacuo* to dryness, triturated with hexane, and filtered. Concentration of the filtrate afforded **14** (9.77 g, 96%) as colorless crystallines, which was directly used in the next step. **14**; Mp 45.5-46.5 °C. IR (KBr): 2961, 2903, 2868, 1638, 1609, 1508, 1464, 1408, 1364, 1198, 1109, 966, 822, 802, 583, 540 cm^{-1}. ^1H NMR (400 MHz): 7.38-7.31 (m, 4H), 6.63 (d, J = 15.62 Hz, 1H), 6.36 (dt, J = 15.62, 7.81 Hz, 1H), 4.16 (d, J = 7.81 Hz, 2H), 1.31 (s, 9H). Calcd. for $C_{13}H_{17}Br$: C, 61.67; H, 6.77%. Found: C, 61.67; H, 6.76%.

Ethyl 4-methyl-*O*-(*p*-*t*-butylcinnamyl)salicylate (15). To a suspension of NaH (1.85 g, a 60% dispersion in mineral oil, 46.3 mmol) in DMF (25 ml) was added a solution of ethyl 4-methylsalicylate (6.99 g, 38.8 mmol) in DMF (5 ml) dropwise over 10 min at 0 °C, and the mixture was allowed to warm to rt with stirring. To this solution was added a solution of **14** (9.77 g, 38.6 mmol) in DMF (10 ml) and the resulting mixture was stirred overnight at rt. After quenching with aqueous H_3PO_4 (5%, 15 ml), the reaction mixture was partitioned between ethyl acetate (75 ml) and water (40 ml). The organic layer was separated, washed with sat. aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and chromatographed on silica gel (hexane-ethyl acetate = 20:1 ~ 4:1) to give **15** (9.80 g, 74 %) as colorless crystallines. **15**; Mp 54.0-55.0 °C. IR (KBr): 1722, 1609, 1506, 1385, 1292, 1236, 1178, 1146, 1082, 1018, 980, 851, 773, 554 cm^{-1}. ^1H NMR (400 MHz): 7.73 (d, J = 6.81 Hz, 1H), 7.35 (br s, 4H), 6.82 (s, 1H), 6.80 (d, J = 7.73 Hz, 1H), 6.77 (dt, J = 16.11, 1.46 Hz, 1H), 6.39 (dt, J = 16.11, 5.37 Hz, 1H), 4.77 (dd, J = 5.37, 1.46 Hz, 1H), 4.36 (q, J = 7.33, 2H), 2.36 (s, 3H), 1.38 (t, J = 7.33 Hz, 3H), 1.32 (s,. 9H). Calcd. for $C_{23}H_{28}O_3$: C, 77.54; H, 8.68%. Found: C, 77.75; H, 8.60%.

(*RS*)-Ethyl 4-methyl-3-[1-(*p*-*t*-butylphenyl)propyl]salicylate (16). A mixture of **15** (4.18 g, 11.9 mmol) and $CaCO_3$ (1.19 g) was heated to 180 °C for 15h with stirring and then cooled to rt. The mixture was diluted with ethyl acetate (24 ml) and filtered. To the filtrate was added a 10% palladium charcoal (9.9 mg) and the mixture was stirred for 3 h under hydrogen atmosphere. The resulting mixture was filtered through a pad of Celite, concentrated, and chromatographed on silica gel (hexane-CH_2Cl_2 = 19:1) to give **16** (1.38 g, 33%) as an oil. **16**; IR (neat): 3422, 3090, 2963, 2872, 1666, 1616, 1508, 1456, 1398, 1371, 1296, 1242, 1207, 1157, 1022, 781, 756 cm^{-1}. ^1H NMR (400 MHz): 11.21 (1H, OH), 7.63 (d, J = 7.81 Hz), 7.27-7.20

(m, 4H), 6.67 (d, J = 7.63 Hz, 1H), 4.41 (br s, 1H), 4.36 (q, J = 7.33 Hz, 2H), 2.47-2.17 (m, 5H), 1.39 (t, J = 7.33 Hz, 3H), 1.28 (s, 9H), 0.88 (t, J = 7.27 Hz, 3H). Calcd. for $C_{23}H_{30}O_3$: C, 77.93; H, 8.53%. Found: C, 77.85; H, 8.66%.

(*R*)-4-Methyl-3-[1-(*p*-*t*-butylphenyl)propyl]salicylic acid (17). *dl*-Salicylate **16** (4.42 g, 12.5 mmol) was dissolved in the mixture of EtOH (28 ml) and 5 N NaOH (13 ml). After stirring for 27 h at rt and another 30 min at 60 °C, the mixture was acidified with 4N HCl (28 ml) and extracted with ethyl acetate (200 ml). The aqueous layer was reextracted with ethyl acetate (50 ml). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated to give carboxylic acid (*RS*)-**17** (3.87 g, 95 %) as colorless crystallines. (*RS*)-**17** (3.87 g, 11.9 mmol) and (-)-brucine•$2H_2O$ (4.86 g, 12.3 mmol) were dissolved in hot acetone (80 ml), filtered, and cooled to rt. The mixture was left overnight at rt. The crystalline precipitate was collected by filtration and recrystallized six times from acetone. The salt thus obtained was decomposed by adding 1N HCl and extracted with ethyl acetate. The extract was washed with brine, dried over anhydrous $MgSO_4$, and concentrated to give optically pure carboxylic acid (*R*)-**17** (637 mg, 16% from **16**). The optical purity of **17** was determined by HPLC analysis (DAICEL CHIRALCEL OD, hexane, flow rate 0.4 ml/min) of the corresponding methyl ester. The absolute configuration of **17** was determined to be *R* by chemical correlation.[14] **17**; $[\alpha]_D^{24}$ +8.12° (c 0.686, EtOH). Mp 187.1-188.1 °C. IR (KBr): 3450, 2966, 2872, 1649, 1612, 1497, 1456, 1302, 1238, 889, 785, 712 cm^{-1}. ^1H NMR (400 MHz): 10.83 (1H, O<u>H</u>), 7.68 (d, J = 8.30 Hz, 1H), 7.24 (ABq, J = 8.30, 4H), 6.72 (d, J = 8.30, 1H), 4.42 (br s, 1H), 2.46-2.19 (m, 5H), 1.29 (s, 9H), 0.89 (t, J = 7.33 Hz, 3H). Calcd. for $C_{21}H_{26}O_3$: C, 77.27; H, 8.03%. Found: C, 77.00; H, 7.99%.

(*R*)-4-Methyl-3-[1-(*p*-*t*-butylphenyl)propyl]salicylaldehyde (18). LAH (156 mg, 4.03 mmol) was added to a solution of **17** (615 mg, 1.96 mmol) in THF (10 ml) at 0 °C. The mixture was warmed to 60 °C and stirred for 1 h. After being cooled to rt, the reaction mixture was quenched with methanol (1 ml) and 1 N HCl (30 ml) and extracted with ethyl acetate (40 ml). The extract was washed with brine, dried over $MgSO_4$, and concentrated to give the corresponding alcohol (575 mg, 98%). A solution of the alcohol (555 mg, 1.8 mmol) in ethyl acetate (4 ml) was added dropwise over 10 min to a solution of DDQ (453 mg, 2.0 mmol) at 0 °C. After stirring for 31 h at rt, hexane (2 ml) was added to the reaction mixture and the resulting precipitates was filtered off. The filtrate was concentrated and chromotographed on silica gel (hexane-ethyl acetate = 20:1) to give **18** (355 mg, 64%) as an oil. **18**; $[\alpha]_D^{29}$ -28.3° (c 1.45, EtOH). IR (neat): 2963, 2870, 1649, 1618, 1508, 1456, 1223, 802 cm^{-1}. ^1H NMR (400 MHz): 11.45 (1H, O<u>H</u>), 9.79 (s, 1H), 7.30 (d, J = 7.81 Hz, 1H), 7.25 (ABq, J = 8.55, 4H), 6.81 (d, J = 7.81 Hz, 1H), 4.40 (br s, 1H), 2.45-2.20 (m, 5H), 1.28 (s, 9H), 0.89 (t, J = 7.33 Hz, 3H). Calcd. for $C_{21}H_{26}O_2$: C, 81.25; H, 8.44%. Found: C, 81.10; H, 8.50%.

(Salen)manganese complex (7). Aldehyde **18** (41.6 mg, 134 mmol) and (1*S*,2*S*)-cyclohexanediamine (7.6 mg, 67 mmol) were dissolved in EtOH (2 ml), stirred for 7 h at rt (yellow crystalline may precipitate) and concentrated *in vacuo* to dryness. To the residue were successively added $Mn(OAc)_2$•$4H_2O$ (16.4 mg, 67 mmol) and deairated CH_3CN (2 ml) under argon atmosphere and the mixture was stirred for 2 h at rt. A solution of ferricenium hexafluorophosphate (22.1 mg, 67 mmol) in deairated CH_3CN (2 ml) was added and the whole mixture was further stirred for 32 h at rt. The mixture was concentrated to dryness, washed with hexane to remove the side product, ferrocene, and crystallized from hexane-dichloromethane to give **7** (44.6 mg, 74%). **7**; IR (KBr):2961, 2868, 1616, 1531, 1452, 1383, 1315, 1223, 1107, 1026, 953, 849, 777, 706, 559 cm^{-1}. Calcd. for $C_{48}H_{60}N_2O_2MnPF_6$•$0.5CH_2Cl_2$: C, 61.88; H, 6.53; N, 2.98%. Found: C, 61.79; H, 6.58; N, 3.04%.

Salen complexes **5** and **6** were synthesized with (1*S*,2*S*)-diphenylethylenediamine and ethylenediamine,

respectively, according to the same procedure as described for **7**.

5; IR (KBr): 2963, 2870, 1612, 1589, 1529, 1454, 1385, 1298, 837, 775, 705, 557 cm^{-1}. Calcd. for $C_{56}H_{62}N_2O_2MnPF_6 \cdot 1.4H_2O$: C, 65.93; H, 6.40; N, 2.75%. Found: C, 65.99; H, 6.37; N, 2.70%.

6; IR (KBr): 2963, 2870, 1618, 1591, 1529, 1447, 1387, 1294, 847, 557 cm^{-1}. Calcd. for $C_{44}H_{54}N_2O_2MnPF_6 \cdot 0.5C_6H_{14}$: C, 63.79; H, 6.95; N, 3.17%. Found: C, 64.09; H, 6.81; N, 3.43%.

(a*R*)-2-Methoxymethoxy-2'-trifluormethanesulfonyloxy-1,1'-binaphthyl (19). To a solution of (a*R*)-(+)-2,2'-dihydroxy-1,1'-binaphthyl (286 mg 1.0 mmol) in dichloromethane (4 ml) were successively added 2,4,6-collidine (132 ml, 1.0 mmol), 4-dimethylaminopyridine (15 mg, 0.12 mmol), and *N*-phenyltrifluoromethanesulfonimide (357 mg, 1.0 mmol). After stirring for 13 h at 45 °C, the mixture was concentrated *in vacuo* and chromatographed on silica gel (toluene and then ethyl acetate) to give the corresponding monotriflate (378 mg, 90%). To a solution of the monotriflate (219 mg, 0.52 mmol) in dichloromethane (2 ml) were added *N,N*-diisopropylethylamine (181 µl, 1.0 mmol) and chloromethyl methyl ether (79 µl, 1.0 mmol). After stirring for 21 h at rt, the reaction mixture was quenched with water and extracted with dichloromethane. The organic layer was dried over Na_2SO_4, concentrated, and chromatographed on silica gel (toluene-hexane = 1:1~1:0) to give **19** (224 mg, 92%) and the unreacted monotriflate (15.4 mg, 7%). **19**; Mp 85-86 °C. $[\alpha]_D^{25}$ -30.2° (c 0.669, $CHCl_3$). IR (KBr): 3061, 2959, 2903, 1624, 1595, 1508, 1475, 1418, 1335, 1310, 1246, 1202, 1144, 1086,1069, 1032, 1009, 957, 941, 924, 901, 856, 839, 814, 758, 708, 685, 623, 581, 498 cm^{-1}. ^1H NMR (400 MHz): 8.05 (d, J = 9.28 Hz, 1H), 8.02 (d, J = 9.28 Hz, 1H), 7.98 (d, J = 8.30 Hz, 1H), 7.76 (d, J = 7.89 Hz, 1H), 7.63 (d, J = 9.28 Hz, 1H), 7.57 (d, J = 9.28 Hz, 1H), 7.54 (ddd, J = 8.30, 5.86, 1.96 Hz, 1H), 7.39-7.32 (m, 3H), 7.26 (dt, J = 7.83, 1.46 Hz, 1H), 7.03 (d, J = 9.28 Hz, 1H), 5.11 (ABq, J = 7.08 Hz, 2H), 3.22 (s, 3H). Calcd. for $C_{23}H_{17}O_5F_3S$: C, 59.74; H, 3.71%. Found: C, 59.82; H, 3.77%.

(a*S*)-2-Methoxymethoxy-2'-methyl-1,1'-binaphthyl (20). To a solution of **19** (224 mg, 0.48 mmol) in ether (2 ml) were added $NiCl_2(PPh_3)_2$ (6.3 mg, 0.012 mmol) and ethereal methylmagnesium bromide (3 M, 320 µl, 0.96 mmol). After stirring for 3 h at 40 °C, the reaction mixture was quenched with water, extracted with ether, washed with brine, dried over Na_2SO_4, and concentrated to give practically pure **20** (122 mg, 76%), which was directly used in the next step. **20**; $[\alpha]_D^{25}$ +12.5° (c 0.878, $CHCl_3$). IR (KBr); 2964, 2905, 1620, 1589, 1506, 1466, 1238, 1148, 1080, 1032, 1009, 918, 895, 812, 756 cm^{-1}. ^1H NMR (400 MHz): 7.96 (d, J = 9.28 Hz, 1H), 7.90-7.86 (m, 3H), 7.57 (d, J = 8.78 Hz, 1H), 7.51 (d, J = 8.79 Hz, 1H), 7.40-7.33 (m, 2H), 7.24-7.19 (m, 2H), 7.15 (d, J = 8.30 Hz, 1H), 7.03 (d, J = 8.30 Hz, 1H), 5.02 (ABq, J = 7.14 Hz, 2H), 3.12 (s, 3H), 2.11 (s, 3H). Calcd. for $C_{23}H_{20}O_2$: C, 84.12; H, 6.14%. Found: C, 83.91; H, 6.16%.

(a*S*)-3-Formyl-2-hydroxy-2'-methyl-1,1'-binaphthyl (21). To a solution of **20** (122 mg, 0.37 mmol) was added *t*-butyllithium (1.7 M in pentane, 480 µl) at -78 °C and the mixture was stirred for 3 h at the same temperature. DMF (143 µl, 1.85 mmol) was then added and the mixture was allowed to warm to rt. After stirring for 3 h, the reaction mixture was quenched with sat. aqueous NH_4Cl, extracted with ether, washed with sat. aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, concentrated, and chromatographed on silica gel (toluene-hexane = 1:1 ~ 1:0) to give the corresponding aldehyde (124 mg, 93%) and the unreacted **20** (11 mg 7%). A solution of the aldehyde (124 mg, 0.35 mmol) in dichloromethane (1.4 ml) was treated with trimethylsilyl bromide (185 µl, 1.4 mmol) at 0° C in the presence of MS 4Å and stirred for 6 h at the temperature. The reaction mixture was quenched with sat. aqueous $NaHCO_3$, extracted with dichloromethane, dried over $MgSO_4$, and concentrated to give practically pure **21** (122 mg, 76%) as yellow crystallines, which was directly used in

the next step. **21**; $[\alpha]_D^{24}$ -2.74° (c 0.510, EtOH). Mp 187-188 °C. IR(KBr); 2363, 1653, 1506, 1339, 1312, 1115, 812, 779, 752, 706 cm^{-1}. ^1H NMR (400 MHz): 10.40 (1H, OH), 10.21 (s, 1H), 8.33 (s, 1H), 8.01-7.99 (m, 1H), 7.91 (d, J = 8.30 Hz, 1H), 7.90 (d, J = 8.30 Hz, 1H), 7.53 (d, J = 8.79, 1H), 7.42-7.37 (m, 3H), 7.28-7.22 (m, 1H), 7.14-7.12 (m, 1H), 7.07-7.05 (m, 1H), 2.14 (s, 3H). Calcd. for $C_{22}H_{16}O_2$: C, 84.59; H, 5.16%. Found: C, 84.45; H, 5.20%.

(Salen)manganese complex (10a). (1*S*,2*S*)-(+)-Diphenylethylenediamine (10.6 mg, 0.05 mmol) was added to a solution of **21** (31.2 mg, 0.1 mmol) in ethanol (2 ml) and the mixture was stirred for 10 h at rt. After concentration *in vacuo* to dryness, the residue was dissolved in CH_3CN. To the solution was then added $Mn(OAc)_2 \cdot 4H_2O$ (12.3 mg, 0.05 mmol) and the mixture was stirred for 17h at rt in air. After concentration to dryness, the resulting dark brown mass was crystallized from dichloromethane-hexane to give **10a** (26.6 mg, 58%). **10a**; IR (KBr): 3053, 2922, 2853, 1609, 1555, 1508, 1454, 1423, 1387, 1344, 1327, 1300, 1227, 1188, 1148, 810,746, 702 cm^{-1}. Calcd. for $C_{60}H_{45}N_2O_4Mn$: C, 78.94; H, 4.97; N, 3.07%. Found: C, 79.80; H, 5.32; N, 3.07%.

(Salen)manganese complex (11). Salen complex **11** was synthesized from **21** and (1*R*,2*R*)-(-)-diphenylethylenediamine by the same way as described for **10a**. **11**; IR (KBr): 3051, 2920, 1605, 1555, 1508, 1454, 1389, 1344, 1327, 1300, 1221, 1188, 1150, 1126, 810, 770, 704, 687 cm^{-1}. Calcd. for $C_{60}H_{45}N_2O_4Mn \cdot 1.5H_2O$: C, 76.67; H, 5.15; N, 2.98%. Found: C, 76.50; H, 5.22; N, 3.06%

Typical experimental procedure is described for the epoxidation of 6-acetamido-2,2-dimethyl-7-nitrochromene with **7**.

Epoxidation of 6-acetamido-2,2-dimethyl-7-nitrochromene catalyzed by 7 (Table 1, entry 10). Iodosylbenzene (16.9 mg, 77 μmol) was added at once to a solution of 6-acetamido-2,2-dimethyl-7-nitrochromene (20.1 mg, 77 μmol) and **7** (1.7 mg, 1.9 μmol) in CH_3CN (1.4 ml) under nitrogen atomosphere. After stirring for 24 h at rt, the mixture was carefully concentrated *in vacuo*. The residue was chromatographed on silica gel (hexane-ethyl acetate = 4:1 ~ 1:1) to give 6-acetamido-3,4-epoxy-2,2-dimethyl-7-nitrochromene as yellow crystallines (16.7 mg, 65%). The optical purity of this sample was determined to be 96% ee by HPLC (DAICEL CHIRALCEL OJ, hexane- 2-propanol = 1:1, flow rate 0.5 ml/min).

6-Acetamido-3,4-epoxy-2,2-dimethyl-7-nitrochromene; Mp 141 °C (decompose). $[\alpha]_D^{25}$ -44.1° (96% ee, c 0.368, EtOH). IR (KBr): 3254, 1670, 1545, 1512, 1400, 1371, 1346, 1298, 1261, 1207, 1175, 1159, 881, 691 cm^{-1}. ^1H NMR (400 MHz): 10.09 (s, 1H), 8.79 (s, 1H), 7.64 (s, 1H), 3.97 (d, J = 4.40 Hz, 1H), 3.55 (d, J = 4.40 Hz, 1H), 1.59 (s, 3H), 1.27 (s, 3H). Calcd. for $C_{13}H_{14}N_2O_5$: C, 56.11; H, 5.07; N, 10.07%. Found: C, 56.09; H, 5.07; N, 9.95%.

4,5-Epoxy-6,6-dimethyl-chromano[c]furazan-2-oxide; Mp 123-124 °C. $[\alpha]_D^{25}$ -185° (94% ee, c 0.250, $CHCl_3$). IR (KBr): 1630, 1595, 1533, 1491, 1475, 1393, 1371, 1340, 1321, 1263, 1190, 1161, 1130, 1015, 951, 924, 885, 864, 847, 824, 785, 756, 654, 577 cm^{-1}. ^1H NMR (400 MHz): 7.50 (br s, 1H), 6.81 (br s, 1H), 4.00 (d, J = 4.15 Hz, 1H), 3.55 (d, J = 4.15 Hz, 1H), 1.61 (s, 3H), 1.33 (s, 3H). Calcd. for $C_{11}H_{10}N_2O_4$: C, 56.41; H, 4.30; N, 11.96%. Found: C, 56.55; H, 4.34; N, 11.88%.

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9) The flexibility of binaphthyl-type structure has already been discussed by Noyori: Noyori, R. *Kagaku Zoukan*, **1982**, *97*, 57.

10) The complex bearing (1*R*,2*R*)-cyclohexanediamine as ethylenediamine part showed poor asymmetric induction of 18.6% ee.

11) (Salen)manganese(III) complex bearing only cyclohexanediamine as a chiral source, has already been reported to be a good catalyst for the epoxidation of *cis*-olefins. However, no epoxidation of *trans*-olefins using the complex has been reported (reference 6c).

12) Although we have no certain information about the conformation of C3- and C3'-substituents, inspection of **1** and **8** with CPK model suggests that the conformation wherein aryl groups are directed away from the metal center is preferential. Accordingly, the change from phenyl group (**1**) to 4-*t*-butylphenyl group (**8**) is considered to give almost no influence on enantioselectivity.

13) Sasaki, H.; Irie, R.; Katsuki, T. to be published elsewhere. Complex **10b** was synthesized in a similar manner to that described for **10a**.

14) (*S*)-Ethyl 4-methyl-3-(1-phenylpropyl)salicylate[5c] was converted into acid (*S*)-**17** by the sequence: i) FeCl3, t-butyl chloride, ii) NaOH. Chiroptical comparison of (*S*)-**17** and the acid **17** obtained by the resolution with (-)-brucine showed the configuration of the acid **17** to be *R*.

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