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Asymmetric hetero Diels–Alder reaction using chiral cationic metallosalen complexes as catalysts

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Abstract—Chiral cationic (*R*,*S*)- or (*R*,*R*)-(salen)–manganese(III) and –chromium(III) complexes served as the catalysts for asymmetric hetero Diels–Alder reaction of Danishefsky's diene with aldehydes, achieving high enantioselectivity (up to 97% ee at 0°C). The reactions of aldehydes bearing no precoordinating functional group were well effected by using (*R*,*R*)-complexes as catalysts, while those of aldehydes bearing a precoordinating functionality were better effected by using (*R*,*S*)-complexes.

1. Introduction

Chiral Lewis acid-catalyzed asymmetric hetero Diels–Alder (HDA) reaction of Danishefsky's diene (1-methoxy-3-trimethylsilyloxy-1,3-butadiene) and various aldehydes provides versatile building blocks for natural product synthesis.[1] Thus, many chiral Lewis acid catalysts have been applied for this reaction[2] and excellent level of enantioselectivity has been realized with several chiral catalysts.[3]

On the other hand, optically active salen ligands are now recognized as efficient chiral auxiliaries and many metallosalen complexes have been found to serve as excellent catalysts for various asymmetric reactions.[4] For example, (salen)-manganese, –ruthenium, and –cobalt complexes catalyze asymmetric oxene or its isoelectronic nitrene and carbene transfer reactions with high enantioselectivity. Besides, they serve as excellent Lewis acid catalysts. Several years ago, we found that a high valent (salen)-manganese complexes served as the Lewis acid catalyst for asymmetric Diels–Alder reaction even at −78°C.[5] In concurrence with this, (salen)-cobalt and -chromium complexes were found to be excellent Lewis acid catalysts by Jacobsen et al.[6] and more recently we found that (salen)-ruthenium complex was also efficient Lewis acid catalyst.[7] Among them, (salen)-chromium (**1b**)[6a] and -ruthenium[7] complexes have been reported to be good catalysts for asymmetric HDA reaction, showing high enantioselectivity up to 93% ee.[6a] Although high valent (salen)–manganese complex shows potent Lewis acidity, cationic (salen)–manganese(III) complexes also show some Lewis acidity. Furthermore, we recently found that second-generation (salen)–manganese(III) complexes that bear binaphthyl subunit as a chiral auxiliary catalyze a wide range of asymmetric reactions with excellent enantioselectivity[4a] and that some attractive interaction exists between the second-generation salen ligand and substrates.[8a] Based on these findings, we expected that cationic second-generation metallosalen complexes would serve as effective Lewis acid catalysts. Hence, we studied about asymmetric HDA reaction of Danishefsky's diene with cationic second-generation (salen)–manganese(III) and –chromium(III) complexes (hereafter referred to as second-generation Mn- and Cr–salen complexes) as the catalysts.

2. Results and discussion

2.1. Mn–salen catalyzed HDA reaction

We first examined the reaction between benzaldehyde and Danishefsky's diene with cationic Mn–salen complexes **1**–**3** as catalysts (Table 1). Since it had been reported that the apical sites of cationic Mn–salen complexes are ligated by aqua ligands which might show Brønsted-acidity,[8] the reaction was performed in the presence of molecular sieves 3 Å[6a] to favor the coordination of benzaldehyde and to minimize the undesired Brønsted-acid catalysis. Differing from the reported reaction with Cr–salen complex as a catalyst (**1b**, 87% ee, −30°C),[6a] the reaction with the corresponding cationic Mn–salen complex **1a** showed only moderate enantioselectivity (51% ee, 0°C, entry 1). The reaction with second-generation (*R*,*S*)-Mn–salen complex **2a** also showed moderate enantioselectivity (entry 2), but the reaction with its diastereomeric (*R*,*R*)-Mn–salen complex **3** proceeded with good enantioselectivity of 88% ee at 0°C as well as good chemical yield (entry 3). Lowering the reaction temperature enhanced the enantioselectivity

Keywords: cationic metallosalen complex; asymmetric catalysis; hetero Diels–Alder reaction; Danishefsky's diene.

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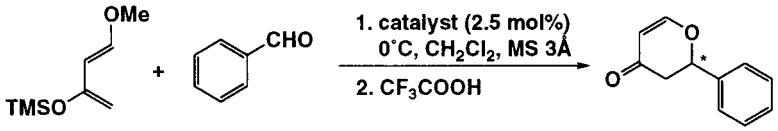
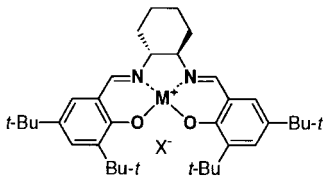
Table 1. Asymmetric HDA reaction with chiral (salen)manganese(III) complexes as catalysts (a solution of aldehyde (0.2 mmol), Danishefsky's diene (0.36 mmol), and catalyst (5 μmol) in dichloromethane (0.5 ml) was stirred in the presence of MS 3 Å for 24 h at 0°C under N_2, unless otherwise mentioned)



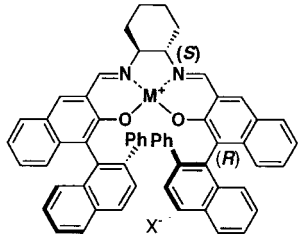
Entry	Catalyst	Temp. (°C)	Yield (%)[a]	% Ee[b]	Confign[c]
1	(*R*)-**1a**	0	50	51	*R*
2	(*R*,*S*)-**2a**	0	88	60	*S*
3	(*R*,*R*)-**3a**	0	95	88	*R*
4[d]	(*R*,*R*)-**3a**	−30	42	92	*R*
5[e]	(*R*,*R*)-**3a**	0	88	76	*R*

[a] Yield was calculated on the basis of the amount of aldehyde used.
[b] Determined by HPLC using Chiralcel OD–H (hexane/*i*-propanol=9:1).
[c] Determined by comparison of the elution order in HPLC analysis (Ref. 6c).
[d] Reaction time was 48 h.
[e] Reaction was carried out in the absence of molecular sieves.

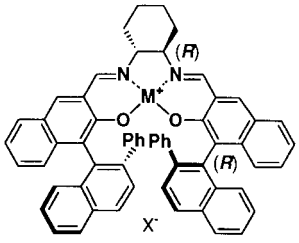
to 92% ee, though the reaction became slow (entry 4). The reaction in the absence of molecular sieves suffered in enantioselectivity and chemical yield (entry 5).



1a: M= Mn, X= PF_6
1b: M= Cr, X= BF_4



2a: M= Mn, X= PF_6
2b: M= Cr, X= BF_4



3a: M= Mn, X= PF_6
3b: M= Cr, X= BF_4

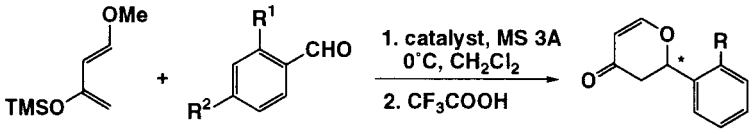
Encouraged by these results, we next examined the reaction of *o*-substituted benzaldehydes by using (*R*,*R*)-Mn–salen complex **3a** as the catalyst (Table 2). Introduction of *o*-substituent, however, generally reduced enantioselectivity of the reactions (entries 5, 6 and 8). In particular, introduction of a polar substituent such as chloro or methoxy group badly reduced enantioselectivity (entries 6 and 8). The adverse effect by the polar groups was considered to be caused by its coordination to the manganese ion which might change the conformation of the salen ligand and affect enantioselectivity. In accord with this consideration, the reaction of *p*-chlorobenzaldehyde showed enantioselectivity as good as that of benzaldehyde (entry 7). We recently revealed that diastereomeric second-generation (*R*,*S*)- and (*R*,*R*)-Mn–salen complexes have the ligand-conformation considerably different to each other[7a] and also proposed that the epoxidation with (*R*,*S*)-Mn–salen complex as a catalyst proceeded through a metallaoxetane intermediate, the ligand of which should adopt *cis*-β-structure.[9] Furthermore, some metallosalen complexes bearing a bidentate counter anion have been reported to take *cis*-β-structure.[10] These results suggested that (*R*,*R*)- and (*R*,*S*)-complexes might change their ligand-conformation in different ways upon coordination of the *o*-polar substituent. Thus, we examined the reaction with (*R*,*S*)-Mn–salen complex **2a** as the catalyst. Although introduction of *o*-methyl substituent only slightly improved enantioselectivity (cf, Table 1, entry 2 and Table 2, entry 1), that of an *o*-coordinating substituent remarkably enhanced enantioselectivity. The reactions of *o*-chloro- and methoxy-benzaldehydes showed high enantioselectivity of 91 and 96% ee, respectively (entries 2 and 4). In contrast to this, the reaction of *p*-chlorobenzaldehyde with **2a** showed only moderate enantioselectivity of 59% ee, suggesting that chelation of the *o*-coordinating substituent with manganese ion is essential for high enantioselection by (*R*,*S*)-**2a** (entry 3).

The above results suggested that (*R*,*R*)-Mn–salen complex **3a** is a catalyst suitable for the reaction of aldehydes bearing no coordinating substituent and small in size, while (*R*,*S*)-Mn–salen complex **2a** for the reaction of substrates bearing a chelating group. On the basis of this knowledge, we examined the reaction of heptanal with complex **3a** as the catalyst. As expected, the reaction at 0°C exhibited high enantioselectivity of 93% ee and the reaction at −40°C showed the enantioselectivity of 98% ee, though the chemical yield suffered (Scheme 1).

2.2. Cr–salen catalyzed HDA reaction

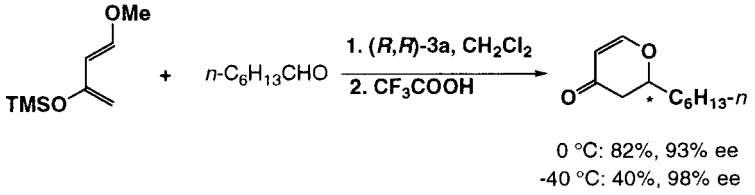
As described in the beginning of this paper, asymmetric catalysis of cationic Cr(III)–salen complex has been reported by Jacobsen et al.[6a] Since chromium and manganese ions show similar catalytic activity in many respects,[11] we also examined HDA reaction with second-generation cationic Cr(III)–salen complexes as the catalyst (Table 3). Likewise the reaction with Mn(III)–salen complexes, Cr(III)–salen complexes also showed an interesting substrate-specificity. The reaction of benzaldehyde with (*R*,*R*)-complex **3b** showed high enantioselectivity of 93% ee even at 0°C (entry 3) which is better than that observed with (*R*,*R*)-Mn-complex **3a**, while the same reaction with (*R*,*S*)-complex **2b** exhibited moderate enantioselectivity of

Table 2. Asymmetric HDA reaction of various aldehydes with Mn–salen complexes as catalysts (a solution of aldehyde (0.2 mmol), Danishefsky's diene (0.36 mmol), and catalyst (5 μmol) in dichloromethane (0.5 ml) was stirred in the presence of MS 3 Å for 24 h at 0°C under N_2. Yield was calculated on the basis of the amount of aldehyde used)



Entry	Catalyst	Aldehyde		Yield (%)	% Ee[a]
		R^1	R^2		
1	(*R*,*S*)-**2a**	Me	H	61	−66
2	(*R*,*S*)-**2a**	Cl	H	99	−91[b]
3	(*R*,*S*)-**2a**	H	Cl	95	−59
4	(*R*,*S*)-**2a**	MeO	H	98	−96[b]
5	(*R*,*R*)-**3a**	Me	H	60	82
6	(*R*,*R*)-**3a**	Cl	H	99	41[b]
7	(*R*,*R*)-**3a**	H	Cl	97	88
8	(*R*,*R*)-**3a**	MeO	H	97	68[b]

[a] Determined by HPLC analysis using Chiralcel OD–H (hexane/*i*-propanol=9:1), unless otherwise mentioned. Configuration of the products obtained with **2a** was opposite to that obtained with **3a**.
[b] Determined by HPLC analysis using Chiralcel OJ (hexane/*i*-propanol=9:1).



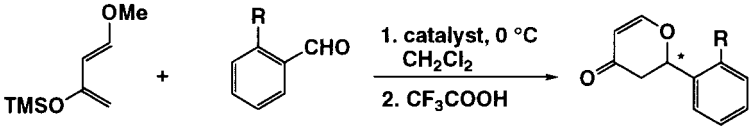
Scheme 1.

78% ee (entry 1). In contrast to this, the reaction of *o*-methoxybenzaldehyde with complex **3b** was moderately enantioselective (entry 5) but the reaction of *o*-methoxybenzaldehyde with **2b** showed excellent enantioselectivity of 96% ee (entry 2). It is noteworthy that addition of molecular sieves did not affect enantioselectivity and chemical yield, when Cr–salen complexes were used as catalysts (cf entries 3 and 4). Thus, all the Cr–salen catalyzed reactions were performed in the absence of molecular sieves.

Based on these results, (*R*,*R*)-Cr–salen complex **3b** was expected to be the most suitable catalyst for the HDA reaction of aliphatic aldehydes (Table 4). Actually, the reaction of cyclohexanecarbaldehyde proceeded with enantioselectivity of 96% ee and that of heptanal with enantioselectivity of 97% ee at 0°C as well as good chemical yields. HDA reaction of α,β-unsaturated aldehyde was also effected with a slightly diminished enantioselectivity (entry 3).

It is worth while to note that, in all the reactions examined, (*R*,*S*)- and (*R*,*R*)-complexes showed opposite sense of enantioselectivity (see, Tables 1–3), suggesting that ligand-conformation of complexes which was dictated by the chirality of the ethylenediamine unit[8a] plays an

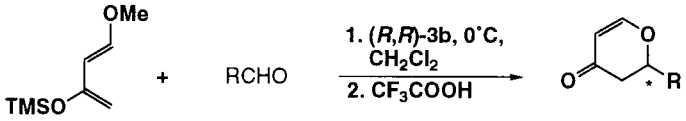
Table 3. Asymmetric HDA reaction with Cr–salen complexes as catalysts (a solution of aldehyde (0.2 mmol), Danishefsky's diene (0.36 mmol), and catalyst (5 μmol) in dichloromethane (0.5 ml) was stirred for 24 h at 0°C under N_2. Yield was calculated on the basis of the amount of aldehyde used)



Entry	Catalyst	Aldehyde (*R*)	Yield (%)	% Ee[a]
1	(*R*,*S*)-**2b**	H	96	−78
2	(*R*,*S*)-**2b**	MeO	88	−96[b]
3	(*R*,*R*)-**3b**	H	93	93
4[c]	(*R*,*R*)-**3b**	H	92	93
5	(*R*,*R*)-**3b**	MeO	90	63[b]

[a] Determined by HPLC using Chiralcel OD–H (hexane/*i*-propanol=9:1), unless otherwise mentioned.
[b] Determined by HPLC using Chiralcel OJ (hexane/*i*-propanol=9:1).
[c] Reaction was carried out in the presence of molecular sieves 4A.

Table 4. Asymmetric HDA reaction of aliphatic and α,β-unsaturated aldehydes with (*R*,*R*)-Cr–salen complex **3b** as the catalyst (a solution of aldehyde (0.2 mmol), Danishefsky's diene (0.36 mmol), and catalyst (5 μmol) in dichloromethane (0.5 ml) was stirred for 24 h at 0°C under N_2. Yield was calculated on the basis of the amount of aldehyde used)



Entry	Aldehyde (*R*)	Yield (%)	% Ee[a]
1	*c*-C_6H_{11}	92	96
2	*n*-C_6H_{13}	98	97
3	(*E*)-$C_6H_5CH{=}CH$	Quantitative (75%)[b]	91 (98% ee)[b,c]

[a] Determined by HPLC using Chiralcel OD–H (hexane/ *i*-propanol= 9:1), unless otherwise mentioned.
[b] Number in the parentheses is the value after recrystallization.
[c] Determined by HPLC using Chiralcel OD (hexane/*i*-propanol=9:1).

important role in asymmetric induction by the complexes, though the detailed mechanism of asymmetric induction is unclear at present. Despite the ambiguity of the mechanism of asymmetric induction, the present reaction is considered to proceed via [4+2] cycloaddition pathway for the following reasons: ^{1}H NMR analysis of HDA reaction of benzaldehyde in CD_2Cl_2 showed that the primary product was the corresponding silylated cycloaduct and neither the trimethylsilyloxy dienone (Mukaiyama aldol condensation adduct) nor the desilylated compound was detected. Furthermore, the Mukaiyama aldol condensation adduct which was separately synthesized according to the literature,[12] was not converted to the cyclic compound under the present reaction conditions. We also examined HDA reaction with (*R*,*S*)- and (*R*,*R*)-(salen)titanium dichloride complexes.[13] Although Ti-complexes show the same substrate specificity as described above, enantioselectivity and chemical yield were inferior to those by Mn– and Cr–salen complexes. For example, HDA reaction of benzaldehyde with (*R*,*R*)-(salen)titanium dichloride complex at 0°C provided the corresponding product of 80% ee in 36%.

In conclusion, we were able to disclose that second-generation cationic Mn(III)– and Cr(III)–salen complexes are efficient Lewis acid catalysts for asymmetric HDA reaction. Further studies on the mechanism of their asymmetric induction of the present reactions and their application to natural product synthesis are now proceeding in our laboratory.

3. Experimental

3.1. General procedures

^{1}H NMR spectra were recorded at 400 MHz on a BRUKER DPX-400. 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 SHIMADZU FTIR-8600 instrument. Optical rotations were measured with a JASCO P-1020 polarimeter. Column chromatography was conducted on silica gel BW-820MH, 70–200 mesh ASTM, available from FUJI SILYSIA CHEMICAL LTD. Preparative thin layer chromatography was performed on 0.5 mm×20 cm×20 cm E. Merck silica gel plate (60 F-254). Enantiomeric excesses were determined by HPLC analysis using SHIMADZU LC-10AT-VP equipped with an appropriate optically active column as described in the footnotes of the corresponding Tables. Reagents and solvents were used as received unless otherwise mentioned below. Commercially available methanol-free dichloromethane was dried and distilled over calcium hydride before use. Tetrahydrofuran (THF) was dried and deoxygenated by treatment with sodium benzophenone–ketyl and distilled shortly before use. Heptanal, *o*-tolualdehyde, and *o*-chlorobenzaldehyde (Tokyo Kasei Kogyo Co., Ltd), benzaldehyde, *o*-methoxybenzaldehyde, and *p*-chlorobenzaldehyde (Nacalai Tesque, Inc.), and cyclohexanecarbaldehyde and 1-methoxy-3-trimethylsilyloxy-1,3-butadiene (Danishefsky's diene) (Aldrich) were also purified by distillation prior to use. Chiral Mn(III)–salen complexes **1a**,[14] **2a**,[15] and **3a**[15] were prepared as previously reported. Reactions were carried out under an atmosphere of nitrogen if necessary. All the products were fully analyzed but only the spectroscopic data are given here for known compounds.

3.1.1. (*R*,*R*)-(Salen)chromium(III) tetrafluoroborate 3b. The parent (*R*,*R*)-salen ligand was prepared from a 2:1 mixture of its chiral (*R*)-salycilaldehyde[16] and (*R*,*R*)-diamine units in ethanol as described in Ref. 15a. Without further purification, the ligand (397 mg, 0.48 mmol) was added to a solution of anhydrous $Cr(II)Cl_2$ (67 mg, 0.55 mmol) in dry, deoxygenated THF (15 ml) under nitrogen atmosphere. The resulting brown solution was stirred for 3 h and then exposed to air. Stirring was continued over night to give a dark brown solution, which was diluted with CH_2Cl_2 (60 ml) followed by washing with sat. NH_4Cl (3×50 ml) and aq. NaCl (3×50 ml). The organic phase was dried over Na_2SO_4 and concentrated under reduced pressure to afford the corresponding (*R*,*R*)-(salen)chromium(III) chloride as a brown solid (356 mg, 74%). IR (KBr): 3487 (br), 3051, 2934, 2858, 1632, 1612, 1582, 1551, 1493, 1448, 1425, 1394, 1350, 1331, 1294, 1271, 1246, 1227, 1190, 1146, 1123, 1026, 953, 912, 864, 762, 746, 702, 579, 548, 536 cm^{-1}. Anal. Calcd for $C_{60}H_{44}N_2O_2CrClH_2O$THF: C, 76.67; H, 5.43; N, 2.79%. Found: C, 76.63; H, 5.47; N, 3.11%. Without further purification, a part of this complex (104 mg, 0.10 mmol) was dissolved in dry CH_2Cl_2 (2.0 ml) and $AgBF_4$ (22.1 mg, 0.11 mmol) was added to the solution in the dark. After 5.5 h of stirring at room temperature, the mixture was filtered through a pad of Celite and washed with CH_2Cl_2. Concentration of the combined filtrate gave the titled complex as a brown solid (98.9 mg, 94%). IR

(KBr): 3487 (br), 3051, 2936, 2860, 1632, 1612, 1582, 1555, 1493, 1448, 1425, 1394, 1352, 1329, 1294, 1271, 1246, 1226, 1190, 1146, 1122, ca. 1050 (br), 1026, 953, 866, 822, 764, 748, 702, 581, 534, 527 cm^{-1}. Anal. Calcd for $C_{60}H_{44}N_2O_2CrBF_4H_2OTHF$: C, 72.94; H, 5.16; N, 2.66%. Found: C, 72.95; H, 5.26; N, 2.93%. The complex thus obtained was used as the catalyst in this study without further purification.

3.1.2. (*R*,*S*)-(Salen)chromium(III) tetrafluoroborate 2b. The corresponding (*R*,*S*)-(salen)chromium(III) chloride was synthesized as a brown solid (511 mg, 73%) from the parent (*R*,*S*)-salen ligand[15b] (538 mg, 0.65 mmol) and anhydrous Cr(II)Cl_2 (88 mg, 0.72 mmol) under the same conditions as descried for complex **3b**. IR (KBr): 3485 (br), 3049, 2932, 2856, 1632, 1612, 1582, 1551, 1491, 1448, 1425, 1393, 1350, 1329, 1294, 1263, 1246, 1225, 1188, 1146, 1123, 1026, 951, 912, 866, 759, 746, 702, 577, 550, 536 cm^{-1}. Anal. Calcd for $C_{60}H_{44}N_2O_2CrClH_2O2THF$: C, 76.00; H, 5.81; N, 2.61%. Found: C, 75.84; H, 5.81; N, 2.61%. Without further purification, a part of this complex (93 mg, 0.087 mmol) was dissolved in THF (2.0 ml) and $AgBF_4$ (19 mg, 0.11 mmol) was added to the solution in the dark. After being stirred at room temperature overnight, the mixture was filtered through a pad of Celite and washed with THF. Concentration of the combined filtrate gave the titled complex as a brown solid (92 mg, quantitative). IR (KBr): 3474 (br), 3049, 2961, 2932, 2856, 1634, 1614, 1582, 1553, 1491, 1448, 1425, 1394, 1348, 1329, 1294, 1261, 1227, 1190, 1146, 1123, ca. 1070 (br), 1043, 1028, 951, 914, 866, 818, 799, 760, 702, 611, 579, 550, 521 cm^{-1}. Anal. Calcd for $C_{60}H_{44}N_2O_2CrBF_4H_2OTHF$: C, 72.94; H, 5.16; N, 2.66%. Found: C, 72.86; H, 5.40; N, 2.69%. The complex thus obtained was used as the catalyst in this study without further purification.

3.2. Typical experimental procedure of the asymmetric hetero Diels–Alder reaction catalyzed by Mn(III)–salen complex

To a suspension of Mn–salen complex (5.1 mg, 5 μmol) and freshly dried powdered 3 Å molecular sieves (50 mg) in dry dichloromethane (0.5 ml) were successively added aldehyde and 1-methoxy-3-trimethylsilyloxy-1,3-butadiene (70 μl, 0.36 mmol) at 0°C under nitrogen atmosphere. After stirring for 24 h at the temperature, the mixture was treated with a drop of trifluoroacetic acid and stirred for another 5 min. The mixture was concentrated in vacuo and the residue was chromatographed on silica gel (hexane/ethyl acetate=8/2) to give the corresponding 2,3-dihydropyran-4-one derivative. The enantiomeric excess of the product was determined by HPLC analysis using optically active column as described below.

3.3. Typical experimental procedure of the asymmetric hetero Diels–Alder reaction catalyzed by Cr(III)–salen complex

To a solution of (*R*,*R*)-Cr(III)–salen complex (4.8 mg, 5 μmol) in dry dichloromethane (0.5 ml) were successively added aldehyde (0.2 mmol) and 1-methoxy-3-trimethylsilyloxy-1,3-butadiene (70 μl, 0.36 mmol) at 0°C under nitrogen atmosphere. After stirring for 24 h at the temperature, the reaction mixture was treated with a drop of trifluoroacetic acid and further stirred for another 5 min. The mixture was concentrated in vacuo and the residue was chromatographed on silica gel (hexane/ethyl acetate=8/2) to give the corresponding 2,3-dihydropyran-4-one derivative. The enantiomeric excess of the product was determined by HPLC analysis using optically active column as described below.

3.3.1. (*R*)-2,3-Dihydro-2-phenyl-4*H*-pyran-4-one. (Table 3, entry 3) Colorless oil. 93% ee [Chiralcel OD–H, hexane: *i*-propanol=9:1, 0.5 mL/min, t_R (major) 24.0 min, t_R (minor) 28.8 min]. $[\alpha]_D^{24}=-88.9°$ (*c* 1.07, $CHCl_3$) [Lit.[17] $[\alpha]_D^{23}=-96.3°$ (*c* 0.87, $CHCl_3$) for optically pure material]. ^1H NMR (400 MHz): δ 7.49 (d, *J*=6.4 Hz, 1H), 7.46–7.36 (m, 5H), 5.54 (dd, *J*=1.5, 6.4 Hz, 1H), 5.44 (dd, *J*=3.4, 14.7 Hz, 1H), 2.92 (dd, *J*=14.7, 16.5 Hz, 1H), 2.67 (ddd, *J*=1.5, 3.4, 16.5 Hz, 1H). IR (KBr): 1678, 1595, 1497, 1454, 1404, 1369, 1271, 1229, 1209, 1173, 1040, 989, 934, 797, 758, 698, 638, 611, 476, 446 cm^{-1}. The absolute configuration was determined to be (*R*) based on comparison of the measured specific rotation with the literature value.[17]

3.3.2. 2,3-Dihydro-2-(*o*-tolyl)-4*H*-pyran-4-one. (Table 2, entry 5) Colorless oil. 82% ee [Chiralcel OD, hexane: *i*-propanol=9:1, 0.5 mL/min, t_R (major) 22.0 min, t_R (minor) 32.2 min]. $[\alpha]_D^{25}=-58°$ (*c* 0.13, $CHCl_3$). ^1H NMR (400 MHz): δ 7.51 (d, *J*=5.9 Hz, 1H), 7.45 (m, 1H), 7.31–7.27 (m, 2H), 7.22 (m, 1H), 5.64 (dd, *J*=2.9, 14.7 Hz, 1H), 5.54 (dd, *J*=1.5, 5.9 Hz, 1H), 2.90 (dd, *J*=14.1, 17.1 Hz, 1H), 2.61 (ddd, *J*=1.5, 2.9, 17.1 Hz, 1H), 2.37 (s, 3H). IR (KBr): 3063, 3028 2966, 2924, 1678, 1593, 1494, 1462, 1404, 1367, 1271, 1223, 1188, 1040, 989, 932, 868, 795, 760, 727, 484 cm^{-1}. HRFABMS. Calcd for $C_{12}H_{13}O_2$ $[M+H]^+$: 189.0915. Found: 189.0920. The absolute configuration has not been determined.

3.3.3. 2-(*o*-Chlorophenyl)-2,3-dihydro-4*H*-pyran-4-one. (Table 2, entry 2) Colorless oil. 91% ee [Chiralcel OJ, hexane:*i*-propanol=9:1, 0.5 mL/min, t_R (major) 28.7 min, t_R (minor) 35.6 min]. $[\alpha]_D^{25}=-140°$ (*c* 0.82, $CHCl_3$). ^1H NMR (400 MHz): δ 7.60 (dd, *J*=1.5, 7.5 Hz, 1H), 7.52 (d, *J*=6.0 Hz, 1H), 7.41 (dd, *J*=2.0, 7.5 Hz, 1H), 7.37 (ddd, *J*=2.0, 7.5, 7.5 Hz, 1H), 7.32 (ddd, *J*=2.0, 7.5, 7.5 Hz, 1H), 5.83 (dd, *J*=4.0, 14.1 Hz, 1H), 5.56 (dd, *J*=1.0, 6.0 Hz, 1H), 2.81 (ddd, *J*=1.0, 4.0, 17.1 Hz, 1H), 2.72 (dd, *J*=14.1, 17.1 Hz, 1H). IR (KBr): 3094, 3083, 3032, 2966, 2907, 1668, 1587, 1483, 1441, 1414, 1364, 1340, 1283, 1229, 1173, 1128, 1045, 997, 966, 934, 870, 826, 799, 770, 746, 723, 692, 638, 611, 550, 509, 486, 473, 448, 421 cm^{-1}. Anal. Calcd for $C_{11}H_9O_2Cl$: C, 63.32; H, 4.35%. Found: C, 63.43; H, 4.40%. The absolute configuration has not been determined.

3.3.4. 2-(*p*-Chlorophenyl)-2,3-dihydro-4*H*-pyran-4-one. (Table 2, entry 7) Colorless oil. 88% ee [Chiralcel OD–H, hexane:*i*-propanol=9:1, 0.5 mL/min, t_R (major) 26.5 min, t_R (minor) 32.9 min]. $[\alpha]_D^{25}=-76.3°$ (*c* 1.17, $CHCl_3$). ^1H NMR (400 MHz): δ 7.47 (d, *J*=5.9 Hz, 1H), 7.40 and 7.34 (psuedo ABq, J_{AB}=8.6 Hz, 4H), 5.54 (dd, *J*=1.0, 6.4 Hz, 1H), 5.41 (dd, *J*=3.9, 14.2 Hz, 1H), 2.86 (dd, *J*=14.2, 16.6 Hz, 1H), 2.65 (ddd, *J*=1.0, 3.4, 16.6 Hz, 1H). IR

(KBr): 3081, 3058, 3036, 1666, 1595, 1491, 1402, 1362, 1308, 1265, 1227, 1209, 1171, 1088, 1057, 1038, 1015, 988, 984, 953, 862, 839, 816, 791, 746, 718, 675, 642, 544, 527, 480, 457 cm^{-1}. Anal. Calcd for $C_{11}H_9O_2Cl$: C, 63.32; H, 4.35%. Found: C, 63.62; H, 4.53%. The absolute configuration has not been determined.

3.3.5. 2,3-Dihydro-2-(*o*-methoxyphenyl)-4*H*-pyran-4-one. (Table 2, entry 4) Colorless oil. 96% ee [Chiralcel OJ, hexane:*i*-propanol=9:1, 0.5 mL/min, t_R (major) 32.8 min, t_R (minor) 38.7 min]. $[\alpha]_D^{25}=-63°$ (*c* 0.45, $CHCl_3$). ^1H NMR (400 MHz): δ 7.54 (d, *J*=5.5 Hz, 1H), 7.46 (dd, *J*=1.5, 7.5 Hz, 1H), 7.34 (ddd, *J*=1.5, 8.0, 9.5 Hz, 1H), 7.03 (pseudo t, *J*=7.5 Hz, 1H), 6.92 (pseudo d, *J*=8.0 Hz, 1H), 5.81 (dd, *J*=5.5, 12.0 Hz, 1H), 5.54 (d, *J*=5.5 Hz, 1H), 3.84 (s, 3H), 2.81–2.69 (m, 2H). IR (KBr): 3072, 3007, 2964, 2941, 2907, 2839, 1680, 1603, 1589, 1497, 1464, 1441, 1404, 1367, 1273, 1250, 1225, 1202, 1181, 1165, 1111, 1040, 1026, 991, 934, 870, 827, 787, 756, 638, 613, 577, 559, 519, 480, 449, 434 cm^{-1}. HRFABMS. Calcd for $C_{13}H_{13}O_3$ $[M+H]^+$: 205.0865. Found: 205.0868. The absolute configuration has not been determined.

3.3.6. 2-Hexyl-2,3-dihydro-4*H*-pyran-4-one. (Table 4, entry 2) Colorless oil. 99% ee [Chiralcel OD–H, hexane: *i*-propanol=9:1, 0.5 mL/min, t_R (minor) 11.0 min, t_R (major) 11.8 min]. $[\alpha]_D^{25}=-172°$ (*c* 0.192, $CHCl_3$). ^1H NMR (400 MHz): δ 7.36 (d, *J*=6.0 Hz, 1H), 5.40 (dd, *J*=1.0, 6.0 Hz, 1H), 4.40 (ddt, *J*=4.0, 7.5, 9.0 Hz, 1H), 2.52 (dd, *J*=13.1, 16.6 Hz, 1H), 2.43 (ddd, *J*=1.0, 4.0, 16.6 Hz, 1H), 1.82 (m, 1H), 1.65 (m, 1H), 1.52–1.26 (m, 8H), 0.91–0.87 (m 3H). IR (KBr): 2959, 2926, 2856, 1722, 1682, 1597, 1464, 1406, 1379, 1275, 1229, 1198, 1121, 1040, 905, 791 725, 488, 438 cm^{-1}. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.52; H, 10.09%. The absolute configuration has not been determined.

3.3.7. (*R*)-2-Cyclohexyl-2,3-dihydro-4*H*-pyran-4-one. (Table 4, entry 1) Colorless oil. 96% ee [Chiralcel OD–H, hexane:*i*-propanol=9:1, 0.5 mL/min, t_R (minor) 12.2 min, t_R (major) 13.5 min]. $[\alpha]_D^{25}=-164°$ (*c* 1.13, $CHCl_3$) [Lit. $[\alpha]_D^{23}=-159°$ for 76% ee material (*c* 0.5, $CHCl_3$)[3j]; $[\alpha]_D^{26}=-157°$ for 93% ee material (*c* 1.03, CH_2Cl_2)[6a]]. ^1H NMR (400 MHz): δ 7.38 (d, *J*=5.9 Hz, 1H), 5.39 (dd, *J*=1.0, 5.9 Hz, 1H), 4.17 (ddd, *J*=3.4, 5.4, 8.8 Hz, 1H), 2.56 (dd, *J*=14.2, 16.6 Hz, 1H), 2.39 (ddd, *J*=1.0, 3.4, 16.6 Hz, 1H), 1.91–1.62 (m, 5H), 1.34–1.01 (m, 6H). IR (neat): 3049, 2930, 2855, 1680, 1595, 1450, 1406, 1279, 1240, 1217, 1188, 1038, 993, 910, 889, 876, 837, 797, 750, 640, 525, 488, 463 cm^{-1}. The absolute configuration was determined to be (*R*) based on comparison of the measured specific rotation with the literature value.[3j]

3.3.8. (*R*)-2,3-Dihydro-2-[(*E*)-styryl]-4*H*-pyran-4-one. (Table 4, entry 3) The isolated material was recrystallized from a minimum amount of a 5:1 mixture of Et_2O and hexane to give colorless needlelike crystals (75%) in 98% ee [Chiralcel OD, hexane:*i*-propanol=9:1, 0.5 mL/min, t_R (minor) 30.3 min, t_R (major) 63.0 min]. $[\alpha]_D^{24}=-213°$ (*c* 0.38, $CHCl_3$) [Lit. $[\alpha]_D^{26}=-215°$ for 99% ee material (*c* 0.36, CH_2Cl_2)[6a]]. Mp 55–56°C. ^1H NMR (400 MHz): δ 7.42–7.39 (m, 3H), 7.37–7.27 (m, 3H), 6.72 (d, *J*=16.1 Hz, 1H), 6.33 (dd, *J*=6.5, 16.1 Hz, 1H), 5.47 (dd, *J*=1.0, 5.9 Hz, 1H), 5.07 (ddd, *J*=4.2, 6.5, 13.2 Hz, 1H), 2.74 (dd, *J*=13.2, 16.6 Hz, 1H), 2.62 (ddd, *J*=1.0, 4.2, 16.6 Hz, 1H). IR (KBr): 3063, 3024, 2964, 2907, 1678, 1593, 1493, 1450, 1414, 1377, 1306, 1273, 1250, 1221, 1171, 1126, 1057, 1043, 989, 974, 897, 864, 841, 827, 802, 746, 692, 529, 488, 446 cm^{-1}. The absolute configuration has not been determined.

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13. Ti(IV)–salen complexes were synthesized by treatment of the corresponding salen ligands with equimolar titanium(IV) tetrachloride in dichloromethane at room temperature and purified by recrystallization from dichloromethane and acetonitrile. (*R*,*R*)-Ti–salen complex. ^{1}H NMR (400 MHz): δ 8.36 (s, 1H), 8.20 (d, J=8.8 Hz, 1H), 8.08 (s, 1H), 7.98 (d, J=8.3 Hz, 1H), 7.86–7.81 (m, 1H), 7.58 (d, J=8.3 Hz, 1H), 7.45–7.41 (m, 1H), 7.36–7.31 (m, 2H), 7.28–7.23 (m, 2H), 7.05 (d, J=8.3 Hz, 1H), 6.72 (dt, J=2.4, 6.8 Hz, 1H), 6.37–6.31 (m, 4H), 4.03–3.95 (m, 1H), 2.46 (br d, J=11.7 Hz, 1H), 2.04 (br d, J=8.8 Hz, 1H), 1.53–1.46 (br m, 1H), 1.42–1.30 (br m, 1H). IR (KBr): 3447, 3051, 2936, 2856, 1609, 1583, 1493, 1445, 1425, 1393, 1352, 1292, 1265, 1246, 1221, 1188, 1171, 1151, 1123, 1072, 1045, 1024, 957, 910, 891, 862, 818, 797, 789, 770, 758, 708, 694, 648, 619, 598, 554, 496, 473, 459, 422 cm^{-1}. Anal. Calcd for $C_{60}H_{44}N_2O_2Cl_2Ti\cdot0.5\ H_2O$: C, 75.63; H, 4.76; N, 2.94%. Found: C, 75.61; H, 4.71; N, 2.92%. (*R*,*S*)-Ti–salen complex. ^{1}H NMR (400 MHz): δ 8.29 (s, 1H), 8.10 (d, J=8.8 Hz, 1H), 7.96–7.94 (m, 2H), 7.78–7.72 (m 1H), 7.76–7.73 (m, 1H), 7.41–7.37 (m, 2H), 7.31–7.28 (m, 8H), 6.82 (t, J=7.3 Hz, 1H), 6.61 (t, J=7.3 Hz, 1H), 6.38 (d, J=7.3 Hz, 1H), 4.07–4.00 (m, 1H), 2.49 (br d, J=11.2 Hz, 1H), 2.00 (br d, J=10.3 Hz, 1H), 1.53–1.46 (br m, 1H), 1.40–1.29 (br m, 1H). IR (KBr): 3452, 3051, 2934, 2856, 1609, 1583, 1493, 1445, 1425, 1393, 1352, 1292, 1267, 1246, 1221, 1188, 1171, 1151, 1123, 1072, 1043, 1024, 959, 910, 889, 862, 818, 797, 789, 770, 756, 708, 694, 648, 619, 598, 554, 496, 473, 459, 422 cm^{-1}. Anal. Calcd for $C_{60}H_{44}N_2O_2Cl_2Ti\cdot1.5\ H_2O$: C, 74.23; H, 4.88; N, 2.89%. Found: C, 74.10; H, 4.70; N, 2.99%.
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