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Kinetic Resolution of Hydroxymethyl-Substituted (Arene)Cr(CO)3 and (Diene)Fe(CO)3 by Lipase

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Abstract: A kinetic resolution of (η^6-arene)chromium complexes and (η^4-diene)iron complexes by lipase has been developed. Racemic tricarbonyl(*o*-substituted benzylalcohol)chromium complexes were kinetically resolved to give (1*R*)-alcohol complexes and the corresponding (1*S*)-acetate complexes, respectively, in high yield and enantioselectivity by transesterification with isopropenyl acetate in the presence of Amano PS or Amano AK. On the other hand, Amano AY recognizes the antipode (1*R*)-alcohol complex. Similarly, hydroxymethyl substituted tricarbonyl(2,4-diene)iron complexes produced optically active alcohol and acetate complexes with high enantioselectivity by lipase catalyzed transacetylation.

Introduction

The use of organometallic transition metal complexes in organic synthesis has developed considerably in recent years; perhaps those which have received most attention are those based on the (arene)$Cr(CO)_3$ and (diene)$Fe(CO)_3$ series. Suitably substituted, these organometallic compounds possess a planar chirality and can be resolved into enantiomerically pure enantiomers. This fact concert with the ability of the tricarbonylchromium or tricarbonyliron functions to effectively block one face of the aromatic or diene moiety, has led to a rapid increase in the use of chiral(arene)chromium and (diene)iron complexes as synthetic intermediates and as catalysts for the asymmetric synthesis.[1,2] The development of simpler, selective methods for the preparation of enantiopure compounds would greatly aid in the application of these chiral transition metal complexes to asymmetric reactions. This planar chirality in the transition metal complexes can be transferred into a new central chirality with a high enantioexcess by means of an appropriate organic reaction, and the transition metal moieties can be easily removed from the products after a transformation reaction to give the metal-free organic compounds with the central chirality. The usual method for the preparation of chiral (arene)chromium and (diene)iron complexes is resolution via recrystallization or column chromatography of the diastereomers derived from racemic complexes and suitable chiral reagents.[3,4] In addition, diastereoselective chromium complexation[5] of the chiral *ortho*-substituted arylaldehyde aminal and diastereoselective *ortho*-lithiation[6] of the chromium complexes of chiral benzaldehyde acetals have been developed for the preparation of (*o*-substituted benzaldehyde)$Cr(CO)_3$. Also, chiral auxiliary directed asymmetric complexation is reported to produce enantiomerically enriched (diene)$Fe(CO)_3$.[7]

Enzyme catalyzed transformations represent an immense potential for the preparation of enantiomerically pure compounds by asymmetrization of the prochiral compounds or kinetic resolution of racemic substrates.

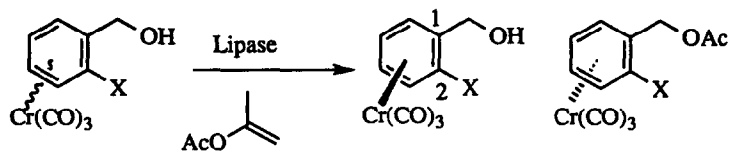
Biotransformation represents an increasingly common methodology for the synthesis of enantiopure organic molecules, and adaptation of this approach for organometallic π-complexes provides a logical extension, despite the difference in type of chirality (planar *vs* carbon-centered), sensitivity to photo-oxidation and general lack of compatibility with aqueous media. Recently, kinetic resolution of organometallic π-complexes, (arene)$Cr(CO)_3$ and (diene)$Fe(CO)_3$, have been achieved by using biocatalysts such as pig liver esterase or baker's yeast in aqueous system.[8] Since the (arene)chromium and (diene)iron complexes are difficult to dissolve in water, a method to deal with these complexes is restricted to those that can cover up the these disadvantages. It is also desirable that a reagent or catalyst can be separated easily from the products after reaction. The use of a lipase as the catalyst for the resolution of enantiomers provides a good method because the lipase works in an organic solvent under an anaerobic atmosphere, and it is easily separated from the reaction products by filtration. As part of our program dealing with the use of planar chirality in organic synthesis, we wish to report here a kinetic resolution of (arene)chromium and (diene)iron complexes by lipase in an organic solvent.[9]

Results and Discussion

Kinetic Resolution of (Arene)chromium Complexes by Lipases.

Tricarbonyl(η^6-arene)chromium complexes exist as two enantiomeric forms when the phenyl ring is substituted with different groups at the *ortho*- or *meta*-positions. The preparation of enantiomerically pure (arene)chromium complexes has great potential for the stereoselective transformations and asymmetric synthesis.

In the first attempt, racemic tricarbonyl(*o*-substituted benzylalcohol)chromium (*rac*-**1**) was resolved with isopropenyl acetate in the presence of different lipase. We subjected the $Cr(CO)_3$ complexes of *o*-methyl, *o*-methoxy and *o*-trimethylsilyl (TMS) derivatives of benzylalcohol as the substrates to be resolved and the results are summarized in Table 1. The reaction was terminated after ca. 50% conversion by filtration of the enzyme to give optically active hydroxyl complexes and the corresponding acetate complexes. Transacetylation of *rac* **1** (R = Me) in the presence of a lipase from *Pseudomonas cepacia* (Amano PS) at 25 °C gave the (1*R*,2*S*)-alcohol **2a** in 47% yield with >99% ee along with the corresponding (1*S*,2*R*)-acetate complex **3a** in 48% yield with 98% ee. The absolute configuration of the resolved complexes **2a** and **3a** was determined by comparison of specific rotation values of authentic compounds[1a,3b] derived from resolved tricarbonyl(*o*-methyl benzaldehyde)chromium by Davies procedure.[3i,j,k] For the *o*-methoxy substituted chromium complex **1b**, reaction in the presence of Amano AK from *Pseudomonas sp.* produced the (1*R*,2*S*)-alcohol complex **2b** in 47% yield with 95% ee together with the (1*S*,2*R*)-acetate complex **3b** in 46% yield with 96% ee, respectively. These enzymes recognize and attack selectively the alcohol with the (1*S*,2*R*)-configuration. On the other hand, a lipase Amano AY from *Candida rugosa* reacted with the (1*R*,2*S*)-alcohol, the antipode to that for the reaction with Amano PS and Amano AK, although the enantioselectivity was unsatisfactory (entries 5,8,10). In the case of *o*-trimethylsilyl substituent **1c**, no transesterification with isopropenyl acetate occurred by use of lipase, Amano PS, Amano AK and PPL due to steric hindrance of the Me_3Si group. However, Toyobo A from *Pseudomonas aeruginosa* resolved racemic *o*-TMS complex **1c** to afford the (1*R*,2*S*)-alcohol **2c** in 48% yield with 85% ee and the (1*S*,2*R*)-acetate **3c** in 47% yield with 84% ee though the resolution was slightly decreased (E^{10} = 33, entry 9).



Scheme 1

1 (*racemic*) **2** (1*R*,2*S*) **3** (1*S*,2*R*)

a: X = Me, **b**: X = OMe, **c**: X = $SiMe_3$

Table 1. Kinetic Resolution of Tricarbonyl(*o*-substituted benzyl alcohol)chromium by Lipase

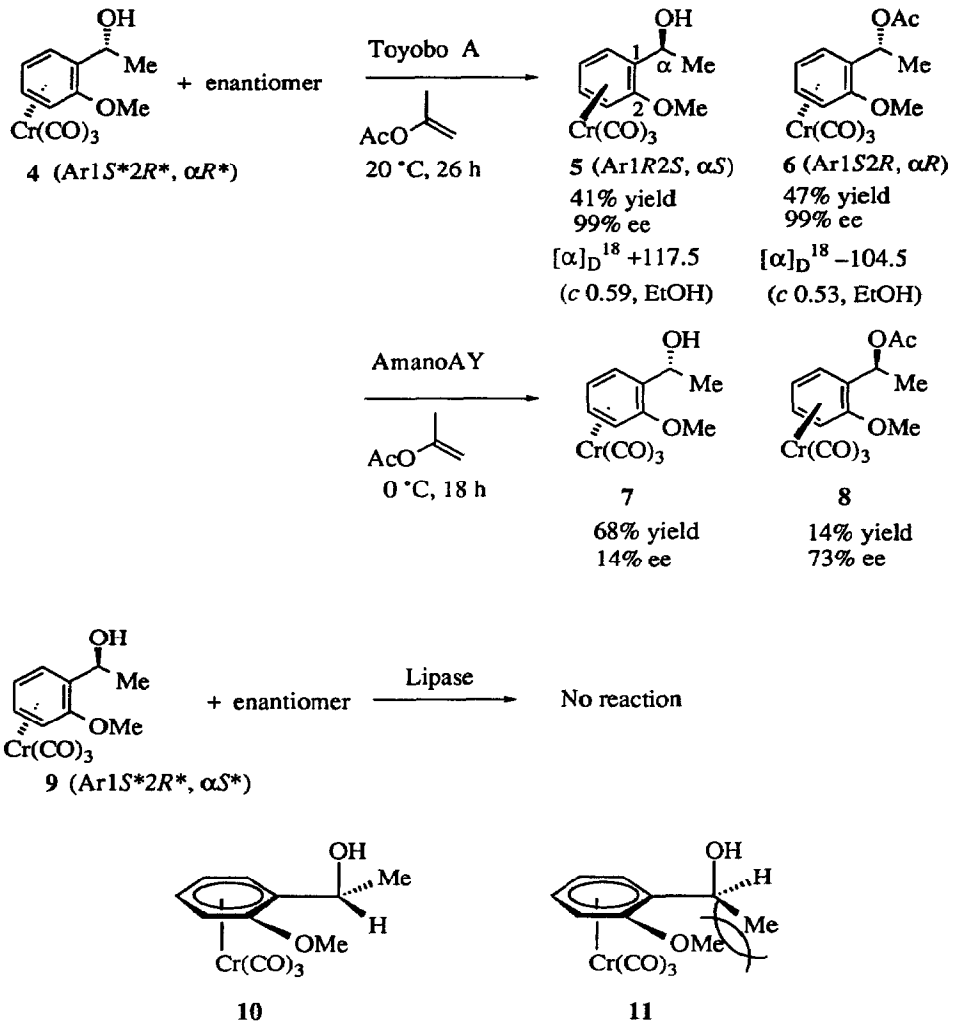
entry	X	enzyme	conditions °C, hrs	(1*R*,2*S*)-OH **2** yield (%), % ee	(1*S*,2*R*)-OAc **3** yield (%), % ee	E
1	Me	Amano AK	25, 3.4	47, 91	48, 92[a]	76
2	Me	Amano AK	40, 1.3	47, 90	47, 92	74
2	Me	Amano PS	25, 3.0	47, >99	48, 98	>500
4	Me	Toyobo A	25, 5.2	49, 84	49, 86	35
5	Me	Amano AY	20, 0.3	46, 42 (1*S*)	46, 47 (1*R*)	4
6	OMe	Amano AK	25, 7.5	47, 95	46, 96[b]	183
7	OMe	Amano PS	25, 6.0	48, 92	45, 93	91
8	OMe	Amano AY	25, 0.3	46, 42 (1*S*)	46, 47 (1*R*)	4
9	$SiMe_3$	Toyobo A	40, 14	47, 84	48, 85[a]	33
10	$SiMe_3$	Amano AY	40, 14	47, 19 (1*S*)	48, 28 (1*R*)	2

a; ee was determined by ^{1}H-NMR in the presence of Pr[hfc]$_3$. *b*; determined by HPLC with Chiralcel OF (10% 2-propanol in hexane).

We next turned our attention to the enzyme catalyzed kinetic resolution of diastereomeric arene chromium complexes having a stereogenic center at the benzylic position (Scheme 2). These arene chromium compounds have both planar and central chiralities, and are attractive for the asymmetric reactions. Reaction of a racemic mixture of two enantiomers (Ar1*S**2*R**, α*R**)-4[11,12] with isopropenyl acetate in the presence of Toyobo A produced the transesterification product (Ar1*S*2*R*, α*R*)-**6** in 47% yield with >99% ee remaining the (Ar1*R*2*S*, α*S*)-alcohol complex **5** in 41% yield with >99% ee. A previous report[13] shows that the resolution of central chirality of racemic α-phenyl ethylalcohol without the $Cr(CO)_3$ group is achieved by Amano PS giving (*R*)-α-phenyl ethylacetate with >95% ee. Extremely high resolution of **4** in good yields is based on a matched combination of both planar and central chiralities, since the lipase from the same origin resulted in efficient resolutions of (*o*-substituted benzylalcohol)chromium complexes as mentioned above. The absolute configuration was determined by comparison of specific rotation values with authentic samples.[14] On the other hand, Amano AY reacted with the antipode hydroxyl complex to afford the (Ar1*R*2*S*, α*S*)-acetate complex **8** with same results of *o*-substituted benzylalcohol complexes as discussed above. In contrast to the above results, no transesterification was observed for diastereomeric chromium complexes (Ar1*S**2*R**, α*S**)-**9**.[11,12] No reaction for these complexes is attributed to a conformation **11**, in which a severe steric interaction between methyl and *o*-methoxyl substituents exists in an *exo*-hydroxyl conformation.[15] In an *endo*-hydroxyl conformation, the lipase can not attack the hydroxyl due to the steric hindrance of $Cr(CO)_3$ group. Easy transesterification of diastereomeric (Ar1*S**2*R**,α*R**)-chromium complex **4** is based on the *exo*-hydroxyl

conformation **10** with minimized such steric interaction. In general, lipase catalyzed transesterification of racemic *o*-substituted benzylalcohol chromium complexes provides a useful method for the preparation of optically active arene chromium complexes.

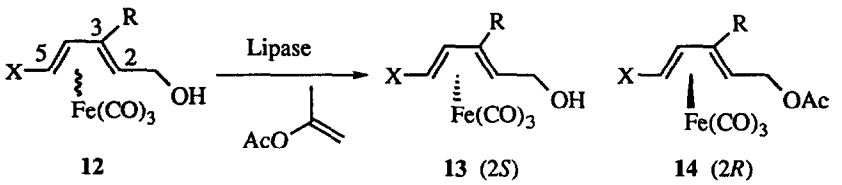
Scheme 2



Kinetic Resolution of (Diene)iron Complexes by Lipases

Planar chiral (diene)$Fe(CO)_3$ complexes have continued to attract attention as the chiral synthons in asymmetric reactions and have been applied to the preparation of complex natural products. Enantiopure formyl substituted (diene)$Fe(CO)_3$ complexes are usually prepared by a resolution procedure of the corresponding diastereomers.[4] The kinetic resolution of racemic (diene)$Fe(CO)_3$ complexes by lipase in organic solvent was also studied as follows (Scheme 3).

Reaction of racemic tricarbonyl(2,4-hexadiene-1-ol)iron (**12a**) with isopropenyl acetate in the presence of Amano PS at 20 °C gave (2*S*)-alcohol **13a** in 22% yield with 97% ee together with the corresponding (2*R*)-acetate **14a** in 73% yield with 35% ee. Although the selectivity of enzymatic reaction at 20 °C is moderate (E = 7.4), transesterification at a lower temperature (at 0 °C) proceeded with increased selectivity (entry 2, E = 15). This enzyme recognizes (diene)$Fe(CO)_3$ complexes with the (2*R*)-configuration at the position having the hydroxymethyl group, whereas Amano AY reacts the (2*S*)-configuration complex as well as the (arene)$Cr(CO)_3$ complexes (entry 3). However, the resolution of these iron complexes **12a, 12b** was not so high selective. This low selectivity would be attributed to lack a substituent at the C-3 position in hydroxymethyl substituted (2,4-diene)iron complexes, whereas (*o*-substituted benzylalcohol)chromium complexes resulted in high enantioselectivity by lipase catalyzed transesterification as discussed above. Therefore, introduction of a functional group at the C-3 position would be expected to lead to high selectivity, since such a structural feature of (diene)$Fe(CO)_3$ complexes is similar to that of the (*o*-substituted benzylalcohol)chromium complexes. Thus, transesterification of racemic 3-methyl-5-phenyl-derivative **12d** with Amano PS gave the (2*R*)-acetate **14d** in 51% yield with 93% ee together with the (2*S*)-alcohol **13d** in 48% yield with 99% ee (entry 9, E = 145). Similarly, 5-butyl substituted diene complex **12c** resulted in high selectivity by lipase catalyzed transesterification.



12 **13** (2*S*) **14** (2*R*) Scheme 3

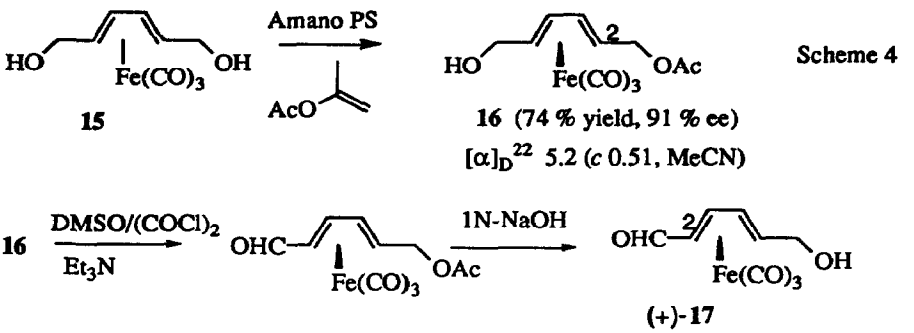
a: X = Me, R = H; **b**: X = Ph, R = H; **c**: X = Bu^n, R = Me; **d**: X = Ph, R = Me

Table 2. Kinetic Resolution of $Fe(CO)_3$ Complexes by Lipase

entry	complex	lipase	conditions °C, hrs	(2*S*)-OH **13** yield %, ee %	(2*R*)-OAc **14** yield %, ee %	E
1	**12a**	Amano PS	20, 4	22, 97[a]	73, 35[b]	7.4
2	**12a**	Amano PS	0, 6	64, 35	28, 83	15.0
3	**12a**	Amano AY	0, 0.5	53, 35 (*R*)	46, 36 (*S*)	2.9
4	**12b**	Amano PS	15, 16	36, 96[a]	60, 58[a]	14.0
5	**12b**	Amano AK	20, 30	45, 56	44, 62	7.4
6	**12b**	Amano AY	0, 1	18, 99 (*R*)	78, 24 (*S*)	6.5
7	**12c**	Amano PS	0, 4	47, 92[c]	46, 90[c]	62.0
8	**12c**	Amano AK	20, 47	51, 71	46, 77	16.0
9	**12d**	Amano PS	20, 20	48, 99[d]	51, 93[d]	145.0
10	**12d**	Amano AK	20, 47	46, 99	51, 88	82.0

a; determined by HPLC with Chiralcel OD. *b*; determined by HPLC with Chiralcel OD in the alcohol complex prepared by reduction. *c*: determined by HPLC with Chiralcel OJ in the corresponding benzoate complex. *d*; determined by HPLC with Chiralcel OJ.

A chiral monoacetate from the *meso* diol iron complex **15** was also prepared from by the same method (Scheme 4). Reaction of **15** with Amano PS afforded the (2*R*)-mono acetate **16** in 74% yield with 91% ee and the corresponding diacetate complex in 5% yield. The selectivity of biocatalyzed transacetylation of *meso* diol **15** proceeds stereospecifically at the pro-*R* hydroxymethyl group as well as the hydroxymethyl substituted (arene)chromium complexes and (diene)iron complexes as described above. The absolute configuration of **16** was determined by transformation to stereodefined (+)-tricarbonyl(5-hydroxymethyl-2,4-pentadienal)iron[8e] (**17**) by oxidation and following hydrolysis.



Scheme 4

In conclusion, hydroxymethyl substituted (arene)chromium and (diene)iron complexes with planar chirality can be easily resolved by lipase catalyzed transesterification to produce the corresponding optically active complexes with high enantioselectivity.

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Experimental section

All manipulations involving organometallics were carried out under an atmosphere of argon or nitrogen and using an inert gas/vacuum double-manifold techniques. All melting points were determined by a Yanagimoto MPJ-2 micromelting point apparatus and are uncorrected. ^{1}H-NMR spectra were measured on a Hitachi R-90, a Varian VXR-200 or a JEOL GX-400 and all NMR spectra were recorded in $CDCl_3$ solvent with tetramethylsilane as an internal reference. IR spectra were measured on a JASCO A-100 spectrometer. Optical rotations were obtained on a JASCO DIP-370 automatic polarimeter at wavelength 589 nm (sodium D line) using a 1.0-dm cell with a total volume of 3 mL. The optical purity of compounds **3a** and **3c** was determined by peak area of acetoxy methyl proton in NMR in the presence of chiral shift reagent Pr(hfc)$_3$, and ee of the remaining hydroxyl complexes **2a** and **2b** was determined by same method after conversion to the corresponding acetate complexes. The enantiomeric excess of chromium complexes **3b**, **6** and **8** was determined by HPLC using a Chiralcel OF column eluted with 10% 2-propanol in hexane. For the (diene)iron complexes, the optical purity of compounds **13a**, **13b** , **14b** and the corresponding benzoate compounds derived from **16** was determined by HPLC using a Chiralcel OD column. The enantiomeric excess of

compounds **13d, 14d** and the corresponding benzoate complexes derived from **13c** and **14c** was determined by HPLC using a Chiralcel OJ column.

Preparation of racemic (arene)chromium and (diene)iron complexes. Racemic tricarbonyl(*o*-substituted benzylalcohol)chromium complexes **1** were prepared from the corresponding arene compounds with $Cr(CO)_6$ in butyl ether and THF (10/1) under usual thermal conditions.[16] The diastereomeric chromium complexes of α-(*o*-methoxyphenyl)-ethylalcohol **4** and **9** was prepared by reduction of (*o*-methoxy acetophenone)chromium with $LiAlH_4$ and methylation of (*o*-anisaldehyde)chromium with MeLi, respectively.[12] The (diene)iron complexes **12** were obtained by complexation with $Fe_3(CO)_{12}$ in benzene under usual conditions.[17] *Meso* iron complex **15** was synthesized by the literature method.[8g]

Lipase catalyzed acylation of (arene)chromium complexes. A mixture of racemic tricarbonyl(*o*-methylbenzyl alcohol)chromium **1a** (52 mg, 0.2 mmol) and lipase Amano PS (100 mg) in isopropenyl acetate (350 μL) was stirred at room temperature (25° C) for 6 h under nitrogen. Methylene chloride (3 mL) was added to the reaction mixture and the resulting mixture was filtered through a short column of silica gel to remove the lipase. The filtrate was evaporated under reduced pressure and the residue was purified by silica gel chromatography (20% ether in hexane) to give 28.1 mg (47%) of the resolved acetate **3a** (X = Me) and 25.2 mg (47%) of alcohol complex **2a** (X = Me). Physical data are as follows: **2a** (X = Me); ^{1}H-NMR δ 1.75 (1H, t, *J* = 5.8 Hz), 2.22 (3H, s), 4.47 (2H, dd, *J* = 4.8, 6.6 Hz), 5.18 (1H, d, *J* = 6.4 Hz), 5.21 (1H, t, *J* = 6.2 Hz), 5.35 (1H, t, *J* = 6.4 Hz), 5.62 (1H, d, *J* = 6.2 Hz); $[\alpha]_D^{25}$ –5.2 (*c* 0.56, $CHCl_3$); Anal. Calcd for $C_{11}H_{10}O_4Cr$: C, 51.17, H, 3.90; Found: C, 50.90; H, 3.86. **3a** (X = Me); ^{1}H-NMR δ 2.10 (3H, s), 2.24 (3H, s), 4.76 (1H, d, *J* = 12.6 Hz), 4.90 (1H, d, *J* = 12.6 Hz), 5.13 (1H, d, *J* = 6.2 Hz), 5.16 (1H, t, *J* = 5.2 Hz), 5.40 (1H, t, *J* = 6.6 Hz), 5.55 (1H, d, *J* = 1.2 Hz); $[\alpha]_D^{25}$ +38.9 (*c* 0.61, $CHCl_3$); Anal. Calcd for $C_{13}H_{12}O_5Cr$: C, 51.96, H, 4.04; Found: C, 52.01, H, 4.03.

(Ar1*R*2*S*)-Tricarbonyl(*o*-methoxybenzyl alcohol)chromium (2b): $[\alpha]_D^{20}$ 241 (*c* 0.50, $CHCl_3$); 95% ee. **(Ar1*S*2*R*)-Tricarbonyl(*o*-methoxybenzyl acetate)chromium (3b)**: $[\alpha]_D^{20}$ –137 (*c* 0.52, $CHCl_3$); 96% ee; The enantiomeric excess of the acetate of **2b** and the corresponding antipode **3b** was determined by HPLC with Chiralcel OF (10% of 2-propanol in hexane); retention time; 26.83 min for acetate of **2b**. 30.50 min for **3b**.

(Ar1*R*2*S*, α*S*)-Tricarbonyl[α-(*o*-methoxyphenyl)-ethylalcohol]chromium (5); mp 68°C, $[\alpha]_D^{20}$ +117.5 (*c* 0.59, EtOH), ^{1}H-NMR ($CDCl_3$) δ 1.51 (3H, d, *J* = 7 Hz), 2.40 (1H, d, *J* = 4 Hz), 3.77 (3H, s), 4.75–5.07 (3H, m), 5.52 (1H, dt, *J* = 7, 1 Hz), 5.75 (1H, dd, *J* = 7, 1 Hz); IR ($CHCl_3$) 3600, 1960, 1880 cm^{-1}. Anal. Calcd for $C_{12}H_{12}O_5Cr$: C, 50.01, H, 4.20; Found: C, 50.10. H, 4.29. Enantiomeric excess was determined by HPLC with Chiralcel OF after conversion of **5** to the corresponding acetate complex.

(Ar1*S*2*R* α*R*)-Tricarbonyl[α-(*o*-methoxyphenyl)-ethylacetate]chromium (6); mp 75°C; ^{1}H-NMR ($CDCl_3$) δ 1.56 (3H, d, *J* = 6), 2.06 (3H, s), 4.80 (1H, t, *J* = 7 Hz), 4.96 (1H, t, *J* = 7 Hz), 5.55 (1H, dd, *J* = 7, 1 Hz), 5.79 (1H, dd, *J* = 7, 1 Hz), 5.93 (1H, q, *J* = 6 Hz); IR ($CHCl_3$) 1960, 1880, 1720 cm^{-1}. Anal. Calcd for $C_{14}H_{14}O_5Cr$: C, 50.92, H, 4.27; Found: C, 50.93, H, 4.27. $[\alpha]_D^{20}$ –104.5 (*c* 0.53, EtOH). The enantiomeric excesses of **6** and the antipode acetate derived from **5** was determined by HPLC with Chiralcel OF (eluted with 10% 2-propanol in hexane; flow rate 0.5 mL/min; UV detector 254 nm); Retention time 25.45 min for acetate of (Ar1*R*2*S*, α*S*)-**5**; 30.47 min for (Ar1*S*2*R* α*R*)-**6**.

Resolution of racemic tricarbonyl(3-methyl-5-phenyl-2,4-pentadiene-1-ol)iron (12d); Using the same procedure with (arene)chromium complexes, tricarbonyl(dienol)iron complexes were resolved to optically active complexes by lipase catalyzed transesterification; (2*S*)-Tricarbonyl(3-methyl-5-phenyl-2,4-pentadiene-1-ol)iron (**13d**); $[\alpha]_D^{23}$ –268.6 (*c* 0.73, EtOH); 99% ee; Retention times on HPLC with Chiralcel OJ-H (eluted with 10% 2-propanol in hexane, flow rate 0.5 mL/min; detector UV 254 nm); 16.62 min for (2*R*)-isomer, 24.43 min for (2*S*)-isomer. (2*R*)-Tricarbonyl(3-methyl-5-phenyl-2,4-pentadienyl-1-acetate)iron (**14d**); ^{1}H-NMR δ 1.15–1.35 (1H, m), 1.90–2.10 (1H, m), 2.10 (3H, s), 2.29 (3H, s), 4.33 (2H, dd, *J* = 6.3, 3.5 Hz), 5.71 (1H, d, *J* = 9.2 Hz), 7.15-7.22 (5H, m); IR($CHCl_3$) 2025, 1980, 1730, 1220 cm^{-1}; MS (relative intensity) *m/e* 356 (M^+, 5), 328 (10), 300 (28). HRMS calcd for $C_{17}H_{16}O_5Fe$ 356.0348. found 356.0369. $[\alpha]_D^{23}$ +196.9 (*c* 0.87, EtOH). 93% ee; Retention times on HPLC with Chiralcel OJ-H (eluted with 10% 2-propanol in hexane, flow rate 0.5 mL/min; detector UV 254 nm); 16.33 min for (2*S*)-isomer, 27.74 min for (2*R*)-isomer.

Resolution of tricarbonyl(3-methyl-2,4-nonadiene-1-ol)iron (**12c**) was achieved by Amano PS by the same procedure. **(2*S*)-Tricarbonyl(3-methyl-2,4-nonadiene-1-ol)iron (13c)**; 46% yield; ^{1}H-NMR δ 0.83-1.79 (12H, m), 2.19 (3H, s), 3.81 (2H, d, *J* = 7.1 Hz), 5.00 (1H, d, *J* = 8.6 Hz); IR ($CHCl_3$) 2870, 2025, 1960, 1390 cm^{-1}; MS (relative intensity)*m/e* 294 (M^+, 18), 266 (25), 238 (40), 210 (68); HRMS calcd for $C_{13}H_{18}O_4Fe$: 294.0547. found 294.0555. $[\alpha]_D^{19}$ –2.0 (*c* 0.85, MeOH). 92% ee; Retention times on HPLC with Chiralcel OJ after conversion to the corresponding benzoate complex (eluted with 10% 2-propanol in hexane, flow rate 0.2 mL/min; detector UV 254 nm); 21.96 min for (2*S*)-isomer. 24.20 min for (2*R*)-isomer. (2*R*)-Tricarbonyl(3-methyl-2,4-nonadienyl-1-acetate)iron (**14c**); $[\alpha]_D^{19}$ +2.7 (*c* 1.0, MeOH), 90% ee.

Reaction of tricarbonyl(2,4-hexadiene-1,6-diol)iron (**15**) with isopropenyl acetate catalyzed by Amano PS gave (2*R*)-tricarbonyl(6-hydroxyl-2,4-hexadienyl-1-acetate)iron (**16**). 74% yield; ^{1}H-NMR δ 0.41 (1H, dd, *J* = 9.2, 1.8 Hz), 0.85 (1H, t, *J* = 8.2 Hz), 1.84 (1H, dt, *J* = 6.7, 1.8 Hz), 2.12 (3H, s), 3.65-3.73 (1H, m), 4.04 (1H, dd, *J* = 11.6, 7.2 Hz), 4.23 (1H, dd, *J* = 11.6, 3.0 Hz), 5.28-5.36 (1H, m), 5.47 (1H, dd, *J* = 8.1, 4.6 Hz); IR ($CDCl_3$) 2030, 1965, 1720, 1370 cm^{-1}; MS (relative intensity) *m/e* 268 (M^+–CO, 18), 240 (65), 212 (100). $[\alpha]_D^{22}$ +5.2 (*c* 0.51, MeCN). The enantiomeric excess of **16** was determined after transformation to the corresponding benzoate complex by HPLC with Chiralcel OD (hexane/2-propanol 20/1, 0.2 mL/min). Retention times; 67.30 min for (2*S*)-isomer, 71.7 min for (2*R*)-isomer.

Preparation of 17. To a mixture of oxalyl chloride (11 mg, 0.083 mmol), DMSO (13 mg, 0.17 mmol) in dry CH_2Cl_2 (5 mL) was added a solution of **16** (16 mg, 0.055 mmol) at –78° C under nitrogen. The reaction mixture was stirred for 15 min at the same temperature, and triethylamine (16 mg, 0.055 mmol) was added to the mixture. The resulting mixture was slowly warmed to 0 °C, and extracted with methylene chloride. The extract was washed with brine, dried over $MgSO_4$ and evaporated *in vacuo*. The residue was used for next hydrolysis without purification. A mixture of formyl complex (9.3 mg, 0.032 mmol) obtained by above oxidation in MeOH (2 mL) in aqueous 1N-NaOH (1.0 mL) was stirred at 0° C for 10 min under nitrogen. After stirring for 10 min, the mixture was quenched with water and extracted with ether. The extract was washed with brine, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified by SiO_2 chromatography to give **17**. ^{1}H-NMR δ 1.20-1.45 (1H, m), 1.50-1.85 (2H, m), 3.90 (2H, d, *J* = 6.0 Hz), 5.50 (1H, dd, *J* = 8.5, 7.5 Hz), 5.85 (1H, dd, *J* = 8.5, 7.5 Hz), 9.35 (1H, s); $[\alpha]_D^{17}$ +52.9 (*c* 0.20, MeCN). lit.[8e,g], $[\alpha]_D$ –28 (MeCN) for (2*R*)-Tricarbonyl(5-hydroxymethyl-2,4-pentadienal)iron .

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