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TETRAHEDRON: *ASYMMETRY*

Reaction of tricarbonyl(dienal)iron complexes with *B*-allyldiisopinocampheylborane

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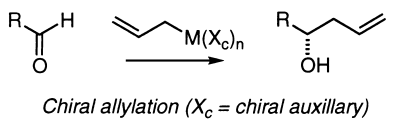
Abstract

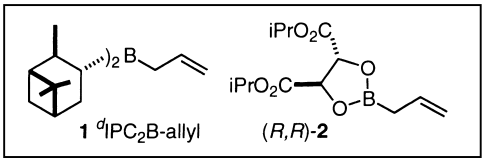
Addition of allyldiisopinocampheylborane to racemic (dienal)iron complexes, followed by oxidation, affords diastereomeric (1,4,6-trien-3-ol)iron complexes with moderate to low enantioselectivity. The high enantioselectivity typically observed for this allylborane reagent is attenuated by steric interaction between the $Fe(CO)_3$ group and the chiral isopinocampheyl groups. Further diminution of the enantioselectivity is observed for dienal complexes in which one rotomer predominates. © 2000 Elsevier Science Ltd. All rights reserved.

1. Introduction

Stereoselective allylation of aldehydes is a powerful method for the generation of optically active homoallylic alcohols (Eq. (1)).[1] The two most widely used reagents, *B*-allyldiisopinocampheylborane **1**[2] and diisopropyl 2-allyl-1,3-dioxa-2-boralane-4,5-dicarboxylate **2**,[3] generally provide products with >90% ee. For aldehyde substrates with α-stereogenic centers this reaction generates diastereomers. The diastereoselectivity of this reaction depends upon the relative strength and direction of the asymmetric directing effect of the chiral allylborane and the *inherent* diastereoselective directing effect of the chiral aldehyde. While chiral auxiliaries present on boron generally dominate the selectivity in this reaction, there are a few examples in which more modest diastereoselectivity is observed due to a mismatch of the directing effects (Eq. (2)).[4]



Chiral allylation (X_c = chiral auxillary)



1 $^{d}IPC_2B$-allyl (*R,R*)-**2**

(1)

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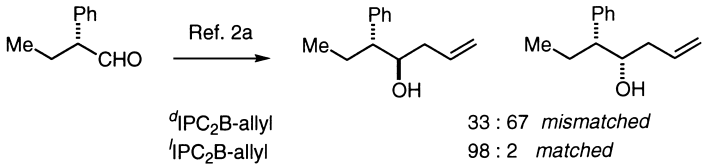
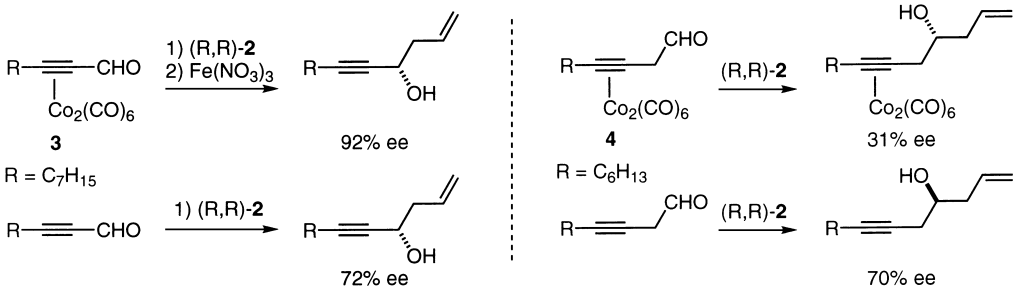


(2)

Ligand complexation to a transition metal frequently alters the reactivity of pendant functional groups.[5] For example, the stereoselective allylation of (2-decynal)$Co_2(CO)_6$ **3** proceeds with greater enantioselectivity than for the free ligand (Scheme 1).[6] In contrast, stereoselective allylation of (3-decynal)$Co_2(CO)_6$ **4** occurs with low enantioselectivity, and with the *opposite* stereochemical outcome from that normally observed.[7] It has been suggested that the geometric relationship between the metal carbonyl unit and the ester substituents on the homochiral dioxaboralane in **2** determines if the enantioselectivity is enhanced, attenuated, or reversed.



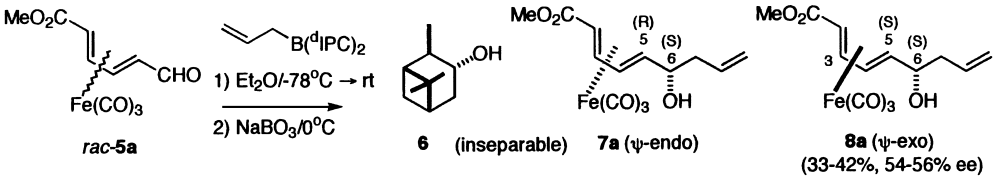
Scheme 1.

Roush and Park have reported on the kinetic resolution of (dienal)$Fe(CO)_3$ complexes using allylboronate **2**.[8] As part of our studies on the synthesis of macrolactin A, we previously reported on the asymmetric allylboration of racemic (methyl 6-oxo-2,4-hexadienoate)$Fe(CO)_3$ **5a** with **1**.[9] We herein report on our detailed study of the asymmetric allylboration of (dienal)$Fe(CO)_3$ complexes **5**.

2. Results

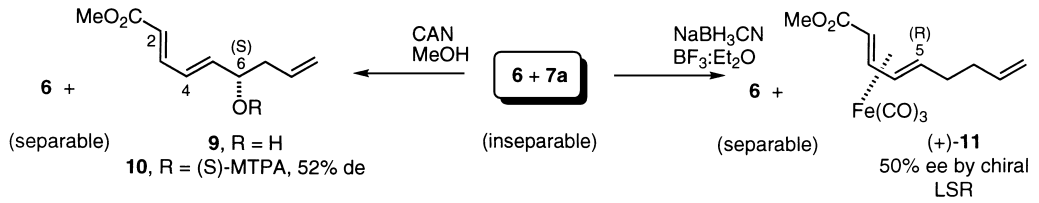
The reaction of *B*-allyldiisopinocampheylborane **1** with (methyl 6-oxo-2,4-hexadienoate)-$Fe(CO)_3$ *rac*-**5a**, followed by brief oxidative work-up gave a mixture of isopinocampheol **6** and the known[8,10] diastereomeric homoallylic alcohols **7a** and **8a** (Eq. (3)). While (–)-**8a** was readily separable (33–42%), the diastereomeric alcohol **7a** could not be easily separated from **6**. Based on the mass of the **6**/**7a** mixture and integration of its ^{1}H NMR spectrum, the yield of **7a** from **5a** was estimated to be ca. 28%. The *relative* configuration of **7a** and **8a**, ψ-*endo* and ψ-*exo*, respectively, are based on a comparison of their NMR spectral data with the literature values.[10] Analysis of the ^{1}H NMR spectra (C_6D_6) of the (*S*)- and (*R*)-MTPA esters of **8a** indicated separation of the H3 signals (δ 5.37 and 5.26 ppm, respectively); integration of these signals indicated that the Mosher's esters were ca. 54–56% de. For the major enantiomer, assignment of

the absolute configuration at C6 (*S*) is based on the relative chemical shifts for H3 and for H5 of the (*S*)- and (*R*)-MTPA esters; these signals for the (*S*) ester appear downfield of those for the (*R*) ester.[11] Comparison of our specific rotation with the literature value[8] for the (5*R*,6*R*) enantiomer indicated that **8a** prepared by this method was 55% ee.



(3)

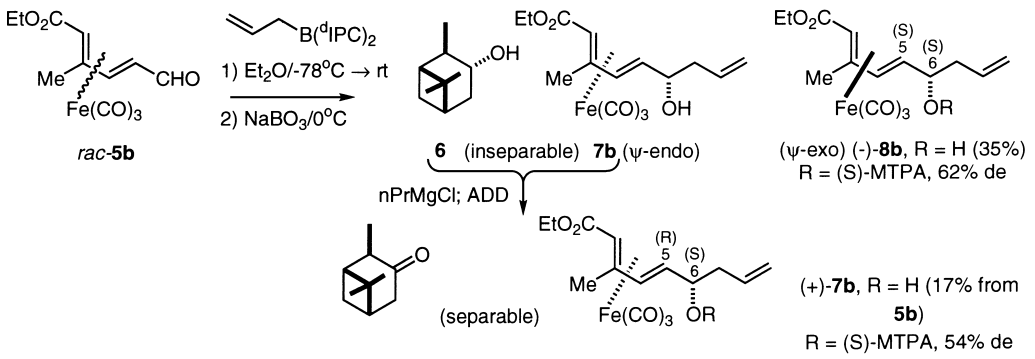
In order to assess the ee of diastereomer **7a**, chemical separation was undertaken. Treatment of the mixture of **6** and **7a** with CAN gave a *separable* mixture of methyl 6-hydroxy-2,4,8-nonatrienoate **9** (26% from **5a**) and **6** (Scheme 2). Analysis of the ^{1}H NMR spectra ($CDCl_3$) of the (*S*)-MTPA ester **10** indicated separation of the H4 signals for the major and minor diastereomers (δ 6.36 and 6.17 ppm, respectively). Integration of these signals indicated **10** to be 52% de. Comparison of the relative chemical shifts for H2, H4, and H5 of the major and minor diastereomers (major downfield of minor) allowed for assignment of (*S*) configuration at C6. Since the stereochemistry at the dienol carbon is not effected by CAN decomplexation,[12] then the configuration of **7a** at C6 must also be (*S*). Selective ionic reduction[13] of the mixture of **7a** and **6** ($NaBH_3CN$/$BF_3{\cdot}Et_2O$) gave a separable mixture of (+)-(methyl 2,4*E*,8-nonatrienoate)$Fe(CO)_3$ (+)-**11** and **6** (Scheme 2). Examination of (+)-**11** by ^{1}H NMR spectroscopy in the presence of Eu(hfc)$_3$ ($CDCl_3$) indicated separation of the methoxycarbonyl signals. By this method, (+)-**11** was determined to be 50% ee. An empirical relationship between the sign of the rotation and absolute configuration has been proposed for acyclic (diene)$Fe(CO)_3$ complexes bearing electron withdrawing groups.[14] On this basis, the absolute configuration of (+)-**11** was assigned as (5*R*). Thus, the homoallylic alcohol precursor **7a** was assigned as (5*R*,6*S*); diastereomeric to **8a**.



Scheme 2.

Reaction of 0.5 equivalents of **1** with *rac*-**5a**, followed by oxidation, gave a similar mixture of **7a**, **8a**, **6**, and recovered starting aldehyde complex **5a**. Examination of recovered **5a** by ^{1}H NMR spectroscopy in the presence of Eu(hfc)$_3$ ($CDCl_3$) indicated only minimal (< 13% ee) kinetic resolution.

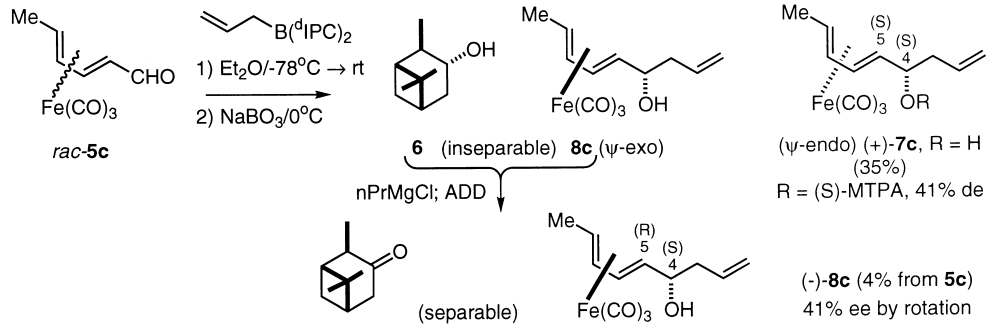
The reaction of *B*-allyldiisopinocampheylborane with (ethyl 3-methyl-6-oxo-2,4-hexadienoate)-$Fe(CO)_3$ *rac*-**5b**, followed by brief oxidative work-up gave a mixture of **6** and diastereomeric homoallylic alcohols **7b** and **8b** (Scheme 3). While (–)-**8b** was readily separable, the diastereomeric



Scheme 3.

alcohol **7b** could not be easily separated from **6**. Based on the mass of the **6**/**7b** mixture and integration of its ^{1}H NMR spectrum, the yield of **7b** from **5b** was estimated to be ca. 30%. Selective oxidation of the mixture of **7b** and **6** under Saigo conditions[15] gave a *separable* mixture of **7b** (18%, from **5b**) and pinocamphone. The *relative* configuration of **7b** and **8b**, at C6 was assigned as ψ-*exo* and ψ-*endo*, respectively, on the basis of their relative chromatographic mobility (**8b** more polar than **7b**) and on the relative chemical shift of their 6-H protons (**8b**, δ 3.56; **7b**, δ 3.64 ppm). It has been empirically found that ψ-*exo* diastereomeric alcohols are in general less mobile than their ψ-*endo* counterparts, and furthermore that the resonance signal for the alcoholic methine proton of ψ-*exo* dienol complexes in general appears upfield of that for the corresponding ψ-*endo* diastereomer.[16] Analysis of the Mosher's esters of **8b** and **7b** indicated separation of the H4 signals; integration of these signals indicated that the Mosher ester of **8b** was 62% de, while the Mosher ester of **7b** was 54% de. For both **8b** and **7b**, assignments of the absolute configurations at C6 (*S*) were based on the relative chemical shifts for H4 of the major and minor diastereomers of the (S)-MTPA esters (major downfield of minor).

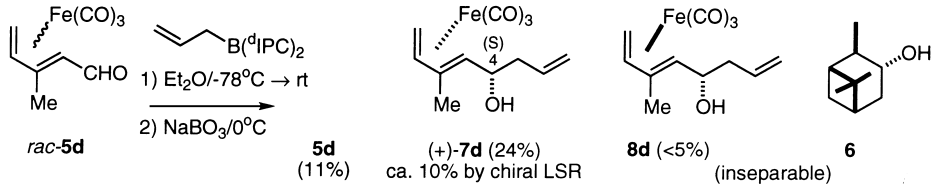
The reaction of *B*-allyldiisopinocampheylborane with (2,4-hexadienal)Fe(CO)$_3$ *rac*-**5c**, followed by brief oxidative work-up gave a mixture of **6** and the known[8,10] diastereomeric homoallylic alcohols **7c** and **8c** (Scheme 4). In this case, (+)-**7c** was readily separable, while the diastereomeric alcohol **8c** co-eluted with **6**. Based on the mass of the **6**/**8c** mixture and integration of its ^{1}H NMR spectrum, the yield of **8c** from **5c** was estimated to be ca. 21%. Oxidation of the mixture of **8c** and **6** under Saigo conditions gave a separable mixture of **8c** (4%, from **5c**) and pinocamphone. The



Scheme 4.

relative configuration of **7c** and **8c**, ψ-*endo* and ψ-*exo*, respectively, are based on comparison of their NMR spectral data with the literature values.[10] The absolute configuration of **7c** (4*S*,5*R*) and **8c** (4*S*,5*S*) and their enantiomeric excesses (40 and 41%, respectively) were determined by comparison of their specific rotations to literature values.[8]

The reaction of *B*-allyldiisopinocampheylborane with (3-methyl-2,4-pentadienal)$Fe(CO)_3$ *rac*-**5d**, followed by brief oxidative work-up gave a mixture of recovered **5d** (11%), isopinocampheol **6** and diastereomeric homoallylic alcohols **7d** (24%) and **8d** (Eq. (4)). Diastereomer **7d** was readily separable by column chromatography, while the diastereomeric alcohol **8d** co-eluted with **6**. Based on the mass of the **6**/**8d** mixture and integration of its ^1H NMR spectrum, the yield of **8d** from **5d** was estimated to be $<5\%$. For this reason, further purification of **8d** was not attempted. The *relative* configuration of **7d** and **8d**, ψ-*endo* and ψ-*exo*, respectively, are based on their relative chromatographic mobility (**8d** more polar than **7d**). Examination of **7d** by ^1H NMR spectroscopy in the presence of $Eu(tfc)_3$ ($CDCl_3$) indicated separation of the H2, H5, and C6-Me signals. By this method, **7d** was determined to be ca. 10% ee. The absolute configuration of **7d** (4*S*) was tentatively assigned on the basis that allylations with $^dIPC_2B$-allyl generally give the (*S*)-homoallylic alcohol as the predominant enantiomer (where the atoms attached to the aldehyde have higher Cahn–Ingold–Prelog sequence priority than the allyl group).

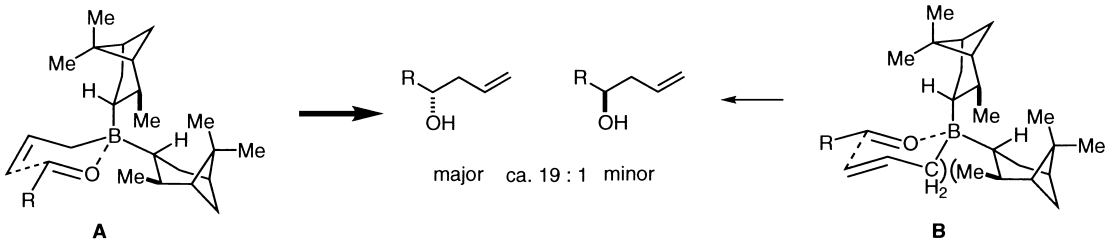


(4)

3. Discussion

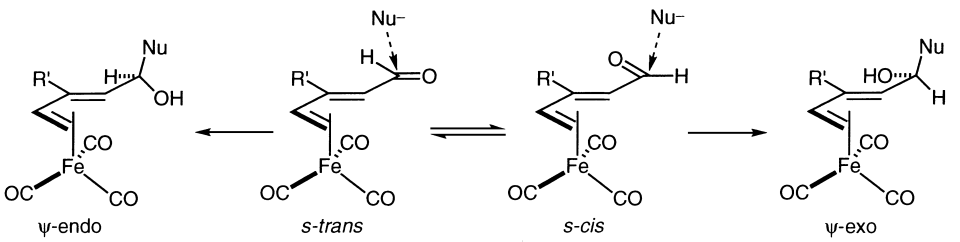
The reaction of allylboranes with aldehydes is believed to proceed via a chair-like transition state in which the aldehyde substituent is oriented in an equatorial fashion.[1,2] For $^dIPC_2B$-allyl, attack on the *re*-face is disfavored due to steric interactions between the isopinocampheyl methyl group and the allylic methylene protons in this transition state (cf. **B**, Scheme 5).[17] For most aldehydes, this difference generally results in $>90\%$ ee (i.e. k_A ca. $19\times k_B$).

Nucleophilic attack at an unsaturated center adjacent to a (diene)$Fe(CO)_3$ affords diastereomeric products. The selectivity for this type of reaction depends: (i) on the steric bulk of the $Fe(CO)_3$ group (reagent approach opposite to iron); and (ii) on the conformation about the diene-to-unsaturated group bond (i.e. *s-cis* versus *s-trans*, Scheme 6).[18] For (sorbaldehyde)$Fe(CO)_3$ *rac*-**5c**,



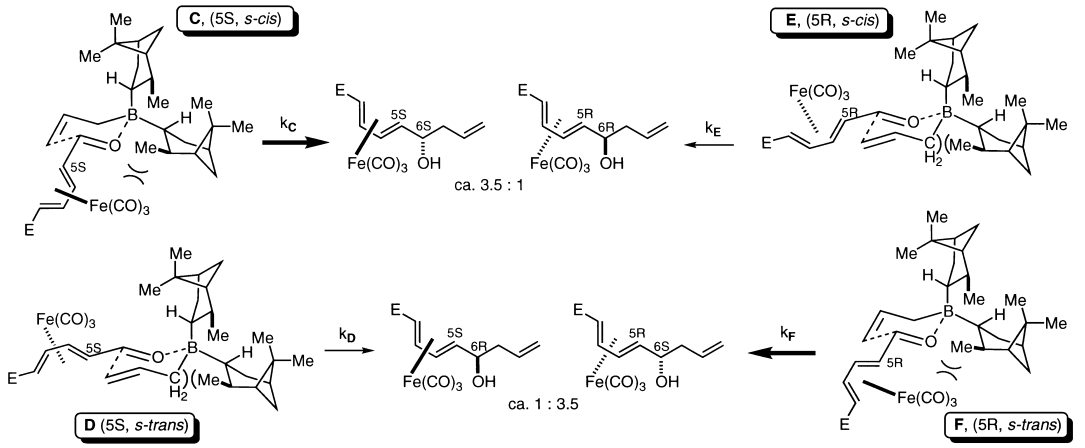
Scheme 5.

low temperature NMR studies by Howell et al.[19] indicate that the proportion of *s-cis*:*s-trans* conformers is nearly 1:1. This analysis is consistent with the experimental results; reaction of (dienal)$Fe(CO)_3$ complex *rac*-**5c** with allyl bromide in the presence of indium gives the ψ-*exo* and ψ-*endo* diastereomeric alcohols (*rac*-**7c**/*rac*-**8c**) in nearly equal amounts.[10]



Scheme 6.

The stereoselective allylation of **5a** with **1** occurs with only modest enantioselectivity (54% ee) and relatively low diastereoselectivity (ψ-*exo*:ψ-*endo*, dr $< 3{:}2$). If it is assumed that stereoselective allylboration occurs only on the face of the aldehyde opposite to the sterically bulky $Fe(CO)_3$ group, and further that only those cyclic transition states in which the aldehyde substituent is equatorial are important, then the observed enantioselectivity depends upon the relative stabilities of the four possible transition states **C**, **D**, **E**, and **F** (Scheme 7). Since only minimal kinetic resolution of the aldehyde was observed in the present studies, then the relative rates of reactivity of each enantiomer of **5** with **1** *must be nearly equal* (i.e. $k_C+k_D \approx k_E+k_F$). It therefore follows that the rate of reactivity of (5*S*)-**5a** in its *s-cis* conformer (**C**) is ca. 3.5 times greater than for the *s-trans* conformer (**D**), while for (5*R*)-**5a** the rate of reactivity of the *s-trans* conformer (**F**) must be ca. 3.5 times greater than that of the *s-cis* conformer (**E**). The attenuated enantioselectivity for stereoselective allylation of **5a** (compared to that reported for achiral alkyl or aryl aldehydes[2]) indicates that the diastereomeric transition states (i.e. **C** versus **D**) must be somewhat close in energy. For transition state **C**, steric interaction between the isopinocampheyl methyl group and the $Fe(CO)_3$ adjunct should contribute to increasing the energy of this transition state so that there is less of a difference in energy between **C** and **D**. The case is similar for transition state **F** relative to **E**.



Scheme 7.

Allylation of (dienal)$Fe(CO)_3$ complex **5d** with **1** occurs with good diastereoselectivity (ψ-*endo*:ψ-*exo*, dr >5:1) but only *negligable* enantioselectivity (ca. 10% ee). This may be rationalized on the basis that the dienal complex **5d** exists predominantly in the *s-trans* isomer due to steric interaction between the aldehyde oxygen and the C3 methyl group in the *s-cis* conformer (cf. Scheme 6, R' = Me). Furthermore, the 2*S* and 2*R* enantiomers of **5d** react with **1** at nearly the same rate.

In summary, the addition of allyldiisopinocampheylborane to *racemic* (dienal)iron complexes, followed by oxidation, affords diastereomeric (1,4,6-trien-3-ol)iron complexes with moderate to low enantioselectivity. In these cases, the high enantioselectivity typically observed for this allylborane reagent is attenuated by steric interaction between the $Fe(CO)_3$ group and the chiral isopinocampheyl groups. Further diminution of the enantioselectivity is observed for dienal complexes in which one rotomer predominates.

4. Experimental

4.1. General data

Spectrograde solvents were used without purification with the exception of dry ether and dry THF which were distilled from sodium benzophenone ketyl. Column chromatography was performed on silica gel 60 (60–200 mesh, Aldrich). Specific rotations were recorded on a Perkin–Elmer 341 optical polarimeter. All ^1H NMR and ^{13}C NMR spectra were recorded on a GE Omega GN-300 instrument at 300 and 75 MHz, respectively. High resolution mass spectra (EI) were obtained from the Washington University Resource for Biomedical and Bioorganic Mass Spectrometry. Dienal complexes **5a**,[12] **5b**,[20] **5c**,[21] and **5d**[20] were prepared by literature procedures.

4.2. General procedure for allylation with B-allyldiisopinocampheylborane (–78°C)

To a solution of *B*-diisopinocampheylmethoxyborane in anhydrous ether (ca. 0.1 to 0.2 M) at –78°C was added dropwise a solution of allylmagnesium bromide in ether (1 equiv). The reaction mixture was stirred at –78°C for 15 min and then allowed to warm to 23°C and stir for ca. 1 h, during which time the formation of magnesium salts was evident. The allylborane solution was cooled to –78°C, and a solution of the aldehyde (1 equiv.) dissolved in the minimum amount of ether was added dropwise. The reaction mixture was stirred at –78°C for 1 h, and then warmed to 23°C for the indicated amount of time. The reaction mixture was cooled in an ice bath and solid $NaBO_3 \cdot 4H_2O$ (1 equiv.) was added in small portions. The mixture was diluted with ether, washed with water, followed by brine, dried ($MgSO_4$) and concentrated.

4.3. General procedure for preparation of Mosher's esters

To a solution of the homoallylic alcohol (ca. 0.2 mmol) in dry THF (5 mL) was added (*R*)- or (*S*)-methoxytrifluoromethylphenylacetic acid (ca. 0.6 mmol), DCC (130 mg) and DMAP (15 mg). The reaction mixture was stirred at rt for 2 h, and then water (2 mL) was added. The mixture was extracted with ether, and the combined ethereal extracts washed with 3% aqueous HCl, water, and brine, dried ($MgSO_4$) and evaporated. The residue was purified by column chromatography (hexane:ethyl acetate, 9:1) to give a mixture of diastereomers.

4.4. Asymmetric allylation of tricarbonyl(methyl 6-oxo-2,4-hexadienoate)iron

Dienal complex **5a** (5.65 g, 20.2 mmol) was added, with stirring, to *B*-allyldiisopinocampheylborane at –78°C for 1 h, and the mixture was further stirred at 23°C for 1 h, followed by oxidative work-up. Purification of the residue by column chromatography (hexanes:ethyl acetate, 9:1) gave a mixture of **7a** and isopinocampheol (4.76 g). Further elution (hexanes:ethyl acetate, 9:1) gave **8a** as a yellow oil (2.58 g, 45%): ψ-*exo*: $[\alpha]_D$ –101 (*c* 0.6, $CHCl_3$) [lit.[8] (5*R*,6*R*) $[\alpha]_D$ +186 (*c* 0.6, $CHCl_3$)]; ^{1}H NMR ($CDCl_3$) δ 5.85 (m, 2H), 5.51 (dd, *J* = 5.1, 8.7 Hz, 1H), 5.20 (m, 2H), 3.67 (s, 3H), 3.60 (m, 1H), 2.49 (m, 1H), 2.28 (td, *J* = 7.1, 14.1 Hz, 1H), 1.58 (br s, OH), 1.28 (dd, *J* = 6.9, 8.1 Hz, 1H), 1.05 (dd, *J* = 1.2, 8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 172.4, 133.4, 119.6, 85.2, 84.1, 71.8, 65.4, 51.7, 46.1, 43.3. The ^{1}H NMR spectral data for this compound in C_6D_6 were identical with the literature values.[10]

The Mosher ester of **8a** with (*S*)-MTPA was prepared by the above general procedure (96%). Integration of the major and minor diastereomeric signals for H2 and H4 indicated a ratio of 78:22 (56% de); signals for the major diastereomer: ^{1}H NMR (C_6D_6) δ 7.66–7.63 (m, 2H), 7.15–7.04 (m, 3H), 5.53 (dddd, *J* = 6.6, 7.2, 10.2, 17.1 Hz, 1H), 5.37 (ddd, *J* = 1.2, 5.1, 8.4 Hz, 1H), 5.03 (ddd, *J* = 0.9, 5.1, 8.4 Hz, 1H), 5.00–4.83 (m, 3H), 3.42 (s, 3H), 3.29 (s, 3H), 2.24 (m, 1H), 1.20 (m, 1H), 0.89 (dd, *J* = 0.9, 8.4 Hz, 1H), 0.77 (t, *J* = 9.3 Hz, 1H).

The Mosher ester of **8a** with (*R*)-MTPA was prepared by the above general procedure (96%). Integration of the major and minor diastereomeric signals for H2 and H4 indicated a ratio of 77:23 (54% de); signals for the major diastereomer: ^{1}H NMR (C_6D_6) δ 7.67–7.63 (m, 2H), 7.15–7.05 (m, 3H), 5.49 (m, 1H), 5.26 (ddd, *J* = 1.1, 5.1, 8.1 Hz, 1H), 5.07 (dd, *J* = 5.1, 8.4 Hz, 1H), 5.00–4.76 (m, 3H), 3.33 (s, 3H), 3.18 (s, 3H), 2.29–2.06 (m, 2H), 0.73 (d, *J* = 8.4 Hz, 1H), 0.55 (t, *J* = 9.0 Hz, 1H).

4.5. Decomplexation of ψ-endo homoallylic alcohol 7a

To a solution of ψ-*endo* homoallylic alcohol **7a** and isopinocampheol (5.4 g) in methanol (125 mL) was added, in small portions, ceric ammonium nitrate (36.8 g). The reaction mixture was stirred for 1 h, diluted with water (125 mL) and extracted with ether. The combined ethereal extracts were dried ($MgSO_4$) and concentrated. Purification of the residue by column chromatography (SiO_2, 5→20% ethyl acetate/hexanes) gave **9** as a colorless oil (0.85 g): ^{1}H NMR ($CDCl_3$) δ 7.28 (dd, *J* = 11.4, 15.3 Hz, 1H), 6.40 (dd, *J* = 11.4, 15.3 Hz, 1H), 6.13 (dd, *J* = 5.4, 15.3 Hz, 1H), 5.90 (d, *J* = 15.3 Hz, 1H), 5.79 (m, 1H), 5.20–5.13 (m, 2H), 4.31 (br q, *J* = 5.7 Hz, 1H), 3.74 (s, 3H), 2.45–2.25 (m, 2H), 1.89 (br s, OH).

The (*S*)-Mosher ester **10** was prepared by the above general procedure (41%). Integration of the major and minor diastereomeric signals for H4 indicated a ratio of 76:24 (52% de); signals for the major diastereomer: ^{1}H NMR ($CDCl_3$) δ 7.58–7.35 (m, 5H), 7.23 (ddd, *J* = 0.9, 11.1, 15.3 Hz, 1H), 6.36 (dd, *J* = 11.1, 15.3 Hz, 1H), 6.03 (dd, *J* = 6.9, 15.3 Hz, 1H), 5.91 (d, *J* = 15.6 Hz, 1H), 5.68–5.55 (m, 2H), 5.18–5.01 (m, 2H), 3.75 (s, 3H), 3.51 (q, *J* = 1.2 Hz, 3H), 2.53–2.42 (m, 2H).

4.6. Ionic reduction of tricarbonyl(methyl 6-hydroxy-2,4,8-nonatrienoate)iron

To a solution of **7a** and **6** (468 mg) in THF (10 mL) at –78°C was added $NaBH_3CN$ (903 mg) followed by $BF_3{\cdot}Et_2O$ (1.8 mL). The reaction mixture was stirred at –78°C for 1 h, warmed to rt and stirred for 18 h. The reaction mixture was cooled to 0°C and water (1 mL) was cautiously

added. The reaction mixture was concentrated, and extracted with ether. The combined ethereal extracts were washed with saturated aqueous $NaHCO_3$, followed by H_2O, and brine, dried ($MgSO_4$) and concentrated. Purification of the residue by column chromatography (hexane:ethyl acetate, 9:1) gave (+)-**11** as a yellow oil (46.7 mg): $[\alpha]_D$ +132 (*c* 0.934, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 5.86–5.73 (m, 2H), 5.24 (dd, $J=5.3$, 8.6 Hz, 1H), 5.07 (qd, $J=1.6$, 17.4 Hz, 1H), 5.02 (m, 1H), 3.65 (s, 3H), 2.27–2.12 (m, 2H), 1.82 (dtd, $J=6.5$, 7.2, 14.7 Hz, 1H), 1.70 (dtd, $J=6.8$, 7.3, 14.7 Hz, 1H), 1.36 (dq, $J=1.0$, 6.9 Hz, 1H), 0.97 (dd, $J=1.0$, 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 172.6, 137.3, 116.0, 87.5, 83.4, 64.8, 51.8, 45.9, 36.0, 33.6; FAB-HRMS *m*/*z* 306.0191 (calcd for $C_{13}H_{14}O_5Fe$ *m*/*z* 306.0190). Analysis by ^1H NMR spectroscopy in the presence of a chiral shift reagent (Eu[hfc]$_3$, $CDCl_3$) indicated that the product was 50% ee.

4.7. Asymmetric allylation of tricarbonyl(ethyl 3-methyl-6-oxo-2,4-hexadienoate)iron

Dienal complex **5b** (1.00 g, 3.25 mmol) was added, with stirring, to *B*-allyldiisopinocampheylborane at –78°C for 1 h, and the mixture was further stirred at 23°C for 18 h, followed by oxidative work-up. Purification of the residue by column chromatography (hexanes:ethyl acetate, 13:1) gave a mixture of **7b** and isopinocampheol (0.69 g). Further elution (hexanes:ethyl acetate, 17:3) gave **8b** as a yellow oil (0.400 g, 35%): ψ-*exo*: $[\alpha]_D$ –66.6 (*c* 1.00, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 5.85 (tdd, $J=6.3$, 11.1, 17.1 Hz, 1H), 5.32 (d, $J=8.4$ Hz, 1H), 5.21 (m, 2H), 4.12 (m, 2H), 3.56 (sept, $J=3.9$ Hz, 1H), 2.51 (s) and 2.54–2.47 (m, total 4H), 2.29 (dt, $J=13.8$, 8.1 Hz, 1H), 1.90 (d, $J=3.6$ Hz, OH), 1.26 (t, $J=7.0$ Hz, 3H), 1.16 (t, $J=7.8$ Hz, 1H), 0.79 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 171.7, 133.6, 119.3, 101.7, 86.9, 72.3, 62.3, 60.2, 48.2, 43.3, 18.5, 14.1; EI-HRMS *m*/*z* 350.0455 (calcd for $C_{15}H_{18}O_6Fe$ *m*/*z* 350.0453).

The Mosher ester of **8b** with (*S*)-MTPA was prepared by the above general procedure (71%). Integration of the major and minor diastereomeric doublet signals for H4 indicated a ratio of 81:19 (62% de); signals for major diastereomer: ^1H NMR (C_6D_6) δ 7.70–7.61 (m, 2H), 7.10–6.95 (m, 3H), 5.58 (tdd, $J=7.5$, 10.2, 17.4 Hz, 1H), 5.19 (d, $J=8.1$ Hz, 1H), 5.03–4.89 (m, 3H), 3.99–3.81 (m, 2H), 3.43 (s, 3H), 2.38 (m, 1H), 2.30 (s, 1H), 2.11 (s, 3H), 0.96 (t, $J=7.1$ Hz, 3H), 0.85 (m, 1H), 0.80 (s, 1H).

The Mosher ester of **8b** with (*R*)-MTPA was prepared by the above general procedure (62%). Integration of the major and minor diastereomeric signals for H4 indicated a ratio of 81:19 (62% de); signals for major diastereomer: ^1H NMR (C_6D_6) δ 7.69–7.61 (m, 2H), 7.10–6.95 (m, 3H), 5.63 (dddd, $J=6.0$, 7.8, 10.2, 16.2 Hz, 1H), 5.23 (d, $J=8.1$ Hz, 1H), 5.07–4.92 (m, 3H), 3.97–3.77 (m, 2H), 3.38 (s, 3H), 2.37 (m, 1H), 2.29 (m, 1H), 2.15 (s, 3H), 0.93 (t, $J=7.2$ Hz, 3H), 0.69 (s, 1H), 0.63 (dd, $J=8.1$, 9.6 Hz, 1H).

To a solution of ψ-*endo* homoallylic alcohol **7b** and **6** (200 mg) in dry THF (4 mL) at rt was added a solution of *n*-propylmagnesium chloride (0.43 mL, 2.0 M in ether, 0.86 mmol). After stirring for 5 min, solid 1,1′-(azodicarbonyl)dipiperidine (218 mg, 0.862 mmol) was added. The reaction mixture was stirred at rt for 1 h, quenched with brine, and extracted with ether. The ethereal layers were washed with brine, dried ($MgSO_4$) and concentrated. Purification of the residue by column chromatography (hexanes:ethyl acetate, 9:1) gave **7b** as a yellow oil (58 mg): ψ-*endo*: $[\alpha]_D$ +39.0 (*c* 1.16, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 5.83 (dddd, $J=6.4$, 8.3, 11.3, 15.6 Hz, 1H), 5.25–5.20 (m, 2H), 5.16 (br d, $J=6.0$ Hz, 1H), 4.21–4.02 (m, 2H), 3.64 (m, 1H), 2.52 (s, 3H), 2.43 (m, 1H), 2.26 (dt, $J=14.0$, 8.1 Hz, 1H), 1.78 (d, $J=3.3$ Hz, OH), 1.25 (t, $J=7.1$ Hz, 3H), 1.21 (m, 1H), 0.69 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 171.8, 133.7, 119.2, 100.4, 85.6, 72.0, 65.7, 60.1, 47.9, 44.9, 18.6, 14.2; EI-HRMS *m*/*z* 350.0461 (calcd for $C_{15}H_{18}O_6Fe$ *m*/*z* 350.0453).

The Mosher ester of **7b** with (*S*)-MTPA was prepared by the above general procedure (37%). Integration of the major and minor diastereomeric signals for H4 indicated a ratio of 77:23 (54% de); signals for major diastereomer: ^{1}H NMR (C_6D_6) δ 7.81–7.72 (m, 2H), 7.15–7.00 (m, 3H), 5.43 (tdd, $J=7.1$, 10.0, 16.9 Hz, 1H), 4.99–4.82 (m, 2H), 4.74 (td, $J=6.0$, 8.0 Hz, 1H), 4.39 (d, $J=7.8$ Hz, 1H), 4.00–3.82 (m, 2H), 3.49 (s, 3H), 2.33 (m, 1H), 2.24 (s, 3H), 2.15 (m, 1H), 0.96 (t, $J=7.1$ Hz, 3H), 0.71 (t, $J=8.4$ Hz, 1H), 0.60 (s, 1H).

4.8. Asymmetric allylation of tricarbonyl(2,4-hexadienal)iron

Dienal complex **5c** (1.00 g, 4.24 mmol) was added, with stirring, to *B*-allyldiisopinocampheylborane at –78°C for 1 h, and the mixture was further stirred at 23°C for 18 h, followed by oxidative work-up. Purification of the residue by column chromatography (hexanes:ethyl acetate, 39:1) gave **7c** as a yellow oil (0.410 g, 35%). Further elution (hexanes:ethyl acetate, 19:1) gave a mixture of **8c** and isopinocampheol (0.90 g). Compound **7c**: ψ-*endo*: $[\alpha]_D$ +10.1 (*c* 3.36, $CHCl_3$) [lit.[8] (4*R*,5*R*) $[\alpha]_D$ –24.7 (*c* 0.74, $CHCl_3$)]; ^{1}H NMR ($CDCl_3$) δ 5.81 (dddd, $J=6.3$, 7.8, 9.3, 17.4 Hz, 1H), 5.19–5.10 (m, 3H), 5.06 (dd, $J=4.9$, 8.5 Hz, 1H), 3.53 (m, 1H), 2.39–2.22 (m, 2H), 1.58 (br s, OH), 1.41 (d, $J=6.3$ Hz, 3H), 1.12 (m, 1H), 1.00 (t, $J=7.8$ Hz, 1H); ^{1}H NMR (C_6D_6) δ 5.50 (ddt, $J=6.9$, 10.2, 17.1 Hz, 1H), 4.90 (m, 2H), 4.61 (dd, $J=5.1$, 8.7 Hz, 1H), 4.32 (dd, $J=4.8$, 8.7 Hz, 1H), 3.21 (m, 1H), 2.05–1.95 (m, 2H), 1.16 (d, $J=3.0$ Hz, OH), 0.99 (d, $J=6.3$ Hz, 3H), 0.65 (t, $J=7.8$ Hz, 1H), 0.57 (m, 1H); EI-HRMS *m*/*z* 278.0236 (calcd for $C_{12}H_{14}O_4Fe$ *m*/*z* 278.0241).

The Mosher ester of **7c** with (*S*)-MTPA was prepared by the above general procedure (75%). Integration of the major and minor diastereomeric signals for the OMe groups indicated a ratio of 70:30 (41% de); signals for major diastereomer: ^{1}H NMR (C_6D_6) δ 7.85–7.77 (m, 2H), 7.21–6.97 (m, 3H), 5.47 (tdd, $J=7.0$, 10.1, 17.0 Hz, 1H), 5.01–4.82 (m, 2H), 4.70 (ddd, $J=5.1$, 6.5, 8.7 Hz, 1H), 4.37–4.22 (m, 2H), 3.52 (s, 3H), 2.37 (m, 1H), 2.22 (m, 1H), 0.98 (d, $J=5.8$ Hz, 3H), 0.55 (t, $J=7.8$ Hz, 1H), 0.49 (qd, $J=6.3$, 8.0 Hz, 1H).

To a solution of ψ-*exo* homoallylic alcohol **8c** and **6** (0.45 mg) in dry THF (3 mL) at rt was added a solution of *n*-propylmagnesium chloride (0.24 mL, 2.0 M in ether, 0.48 mmol). After stirring for 5 min, solid 1,1′-(azodicarbonyl)dipiperidine (122 mg, 0.485 mmol) was added. The reaction mixture was stirred at rt for 1 h, quenched with brine, and extracted with ether. The ethereal layers were washed with brine, dried ($MgSO_4$) and concentrated. Purification of the residue by column chromatography (hexanes:ethyl acetate, 4:1) gave **8c** as a yellow oil (26 mg): ψ-*exo*: $[\alpha]_D$ –17.3 (*c* 0.52, $CHCl_3$) [lit.[8] (4*R*,5*S*) $[\alpha]_D$ +43.3 (*c* 1.2, $CHCl_3$)]; ^{1}H NMR ($CDCl_3$) δ 5.85 (dtd, $J=6.3$, 8.3, 9.8, 17.7 Hz, 1H), 5.25 (dd, $J=4.9$, 8.3 Hz, 1H), 5.22–5.16 (m, 2H), 5.08 (dd, $J=4.9$, 8.7 Hz, 1H), 3.46 (m, 1H), 2.53–2.45 (m, 1H), 2.25 (td, $J=8.0$, 14.1 Hz, 1H), 1.82 (d, $J=3.7$ Hz, OH), 1.42 (d, $J=5.9$ Hz, 3H), 1.25 (m, 1H), 0.95 (t, $J=8.3$ Hz, 1H); EI-HRMS *m*/*z* 278.0248 (calcd for $C_{12}H_{14}O_4Fe$ *m*/*z* 278.0241).

4.9. Asymmetric allylation of tricarbonyl(3-methyl-2,4-pentadienal)iron

Dienal complex **5d** (0.350 g, 1.48 mmol) was added, with stirring, to *B*-allyldiisopinocampheylborane at –78°C for 1 h, and the mixture was further stirred at 23°C for 1 h, followed by oxidative work-up. Purification of the residue by column chromatography gave three fractions. The first fraction (hexane:ethyl acetate, 49:1) gave the ψ-*endo* alcohol **7d** as a yellow oil (100 mg, 24%), the second fraction (hexane:ethyl acetate, 19:1) consisted of unreacted **5d** (40 mg, 11%), while the third fraction (hexane:ethyl acetate, 13:1) afforded a mixture of the ψ-*exo* alcohol **8d**

and isopinocampheol (ca. 1:10, 250 mg). On the basis of the ^{1}H NMR integration of this latter fraction, the amount of **8d** produced was $< 5\%$.

Compound **7d**: $[\alpha]_D$ +13 (*c* 0.86, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 5.86 (dddd, $J = 6.6$, 8.1, 9.9, 17.7 Hz, 1H), 5.18–5.10 (m, 3H), 3.75 (tt, $J = 3.3$, 8.6 Hz, 1H), 2.46–2.37 (m, 1H), 2.27 (td, $J = 7.8$, 13.8 Hz, 1H), 2.17 (s, 3H), 1.67 (m, 2H), 0.87 (d, $J = 8.7$ Hz, 1H), 0.18 (dd, $J = 2.7$, 9.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 134.1, 118.5, 100.9, 82.8, 70.8, 69.3, 42.8, 37.5, 19.1; EI-HRMS *m*/*z* 222.0335 (calcd for $C_{10}H_{14}O_2Fe$ (M–2CO) *m*/*z* 222.0343). Examination of this sample by ^{1}H NMR spectroscopy in the presence of a chiral shift reagent (Eu[tfc]$_3$, $CDCl_3$) evidenced separation of the H2, H5 and C6-Me signals for the two enantiomers. Integration of these signals indicated that the product was ca. 10% ee.

Compound **8d**: ^{1}H NMR (300 MHz, $CDCl_3$, partial) δ 5.87 (m, 1H), 5.48 (d, $J = 8.4$ Hz), 5.27–5.11 (m), 3.72 (m), 2.46–2.37 (m, 1H).

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