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Synthetic Studies Directed Toward Streptenol D: Enantioselective Preparation of The 3,5-Diacetoxy-6E,8E-Decadiene Segment

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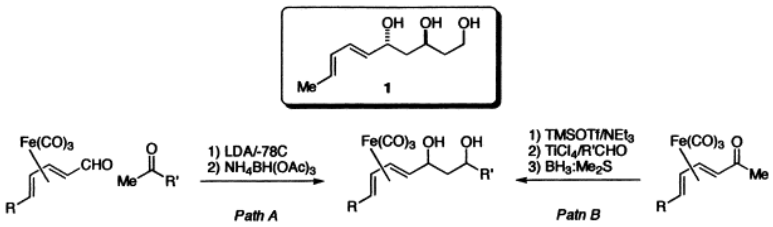
Abstract

The enantioselective preparation of 2-(3'*R*,5'*R*-diacetoxy-6*E*,8*E*-decadienyl)-1,3-dioxane, (+)-**13**, is described. This synthesis of the skeleton of streptenol D utilizes the ability of a diene-complexed (tricarbonyl)iron unit to serve as a protecting and stereodirecting functionality.

1. Introduction

The 4*E*,6*E*-dien-1,3-diol functionality appears in a number of natural products, including macrolactin A, amphotericin B, and streptenol D (**1**). Recently, two groups independently reported the (diene)iron mediated, stereoselective preparation of this type of functionality. Grée et al.[1] reported that the aldol condensation of a

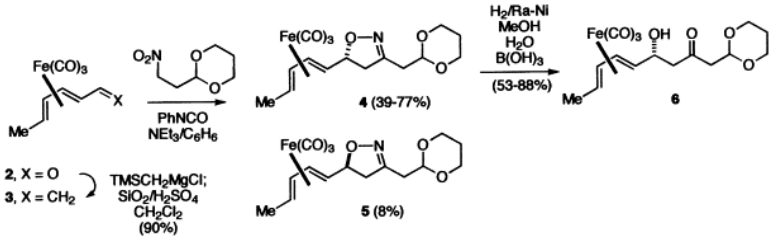
substituted benzophenone with (dienal)$Fe(CO)_3$ proceeded with 43–77% de (Scheme. 1, Path A). Alternatively, the aldol condensation of (3,5-heptadien-2-one)$Fe(CO)_3$ with 3-hydroxypropanal was reported by Franck–Neumann to proceed with 82% de (Scheme. 1, Path B).[2]These accounts prompt us to disclose our own efforts utilizing nitrile oxide–olefin cycloaddition methodology for the preparation of this functionality. In particular, we report on the enantioselective synthesis of the carbon skeleton of streptenol D, a secondary dientriol metabolite isolated from *Streptomyces luteogriseus*.[3]



Scheme. 1.

2. Results and discussion

Our strategy for the preparation of the 4*E*,6*E*-dien-1,3-diol fragment of **1** focused on the ability of the (tricarbonyl)iron group to both direct cyclocondensation reactions in a highly diastereoselective fashion and to act as a protecting group for the complexed diene.[4] For the enantioselective synthesis of **1** this requires the optically active (sorbaldehyde)$Fe(CO)_3$ (**2**) as precursor. Kinetic resolution of *rac*-**2**using baker's yeast (Red Star, Milwaukee, WI) in a fashion similar to the literature procedure,[5] afford (−)-**2**. Complex (−)-**2** prepared in this fashion was determined to be >92% ee by both ^{1}H NMR spectroscopy in the presence of a chiral shift reagent [$Eu(hfc)_3$, $CDCl_3$] and by optical rotation. Peterson olefination of (−)-**2** gave the known[6] triene (+)-**3** (90%, Scheme. 2). Comparison of the rotation of our (+)-**3** ($[\alpha]_D$ +149) with the literature value[6]^b ($[\alpha]_D$ +241) indicates our product to be ca. 62% ee. The reason for the loss of ee in (+)-**3**, compared to that of the precursor (−)-**2**, is not clear.[7], [8], [9]



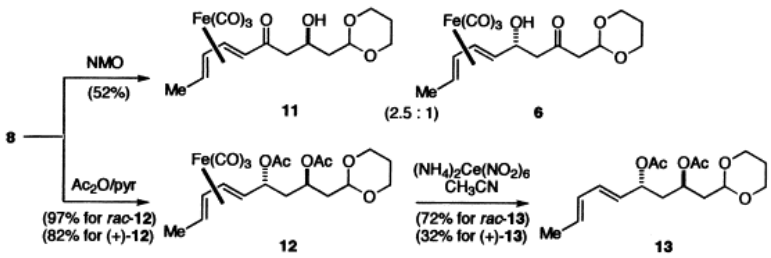
Scheme. 2.

Condensation of 2-(2-nitroethyl)-1,3-dioxane with *rac*-**3** (PhNCO/NEt_3)[10] gave a mixture of diastereomeric isoxazolines **4** and **5** (7.5:1, 76% de, Scheme. 2) from which the major diastereomer could be cleanly separated by column chromatography (36–77% yield of isolated **4**). The major product was assigned the indicated stereochemistry by analogy to literature precedent.[6], [11] This diastereoselectivity results from the approach of the nitrile oxide to the complexed triene in the *S-trans*conformer on the face opposite to the bulky (tricarbonyl)iron group. Similar cyclocondensation of (+)-**3**gave (−)-**4** (39%).
Notably, *intermolecular* cyclocondensations of nitrile oxides with 3-substituted-1-alkenes are generally less diastereoselective (ca. 0–54% de).[12] Reductive hydrolysis[13] of *rac*-**4** gave the hydroxyketone *rac*-**6** (53–88%). In a similar fashion, (−)-**4** gave (+)-**6** (72%, based on consumed starting material). The relative configuration of **6** was tentatively assigned on the basis of the stereochemical assignment for the precursor **4**. Thus, over these two steps (cyclocondensation/reductive hydrolysis), the (tricarbonyl)iron adjunct serves as a stereodirecting and protecting group.

Hydride reduction of *rac*-**6** with $NaBH(OAc)_3$ in acetic acid (23°C) proceeded with low diastereoselectivity to give a mixture of **7** and **8** (2:3, Eq. (1)). Lowering the reaction temperature in a mixture of acetic acid–acetonitrile (−25°C) increased the diastereoselectivity (1:10).[14] Vapor diffusion recrystallization[15] (pentane into ethyl acetate) gave pure **8** (55–83%). In contrast, reduction of *rac*-**6**with $NaBH_3CN$ gave a mixture of **7** and **8** predominating in the *syn* diastereomer (10:1). The relative stereochemistries of **7** and **8** were assigned by comparison of the ^{13}C NMR chemical shifts of the diol methine carbons with those of the known[11][a] *anti* and *syn* isomers of (5,7-nonadien-2,4-diol)$Fe(CO)_3$, **9**and **10**, for which the structure of **10** was determined by X-ray diffraction analysis.[11][b] In particular, the signals for **7** (δ 72.1 and 66.5 ppm) more closely match those of **9** (δ 72.4 and 65.8 ppm), while the signals for **8** (δ 74.7 and 69.3 ppm) more closely match those of **10** (δ 75.5 and 69.1 ppm). This correlation corroborates the initial ψ-*exo* stereochemical assignment for **4**. Reduction of (+)-**6** with $NaBH(OAc)_3$ (−23°C) afforded (+)-**8** (60%).

With the relative stereochemistries of the diol in place, removal of the $Fe(CO)_3$ group was attempted. Oxidative complexation of (diene)$Fe(CO)_3$ complexes with amine oxides has been documented.[16]However, in our hands, attempted decomplexation of *rac*-**7** with NMO instead gave an inseparable mixture of hydroxyketones **6** and **11** (1:2.5, Scheme. 3). Complex **6** was identified by comparison of its ^1H NMR spectral data with that of an authentic sample, while the structure of **11** was assigned by comparison of its ^1H NMR spectral data with that of a similar hydroxyketone reported by Franck–Neumann et al.[2][a] We have recently reported on this unusual NMO oxidation of (dienol)iron complexes.[17] Attempted decomplexation of *rac*-**7** with CAN gave a complex mixture of unidentified products in low yield. For this reason, acylation of the diol was performed prior to decomplexation. Reaction of *rac*-**7** with acetic anhydride/pyridine gave *rac*-**12** (97%) while (+)-**7** gave (−)-**12** (82%). Treatment of *rac*-**12** with CAN (CH_3CN/H_2O, 0°C) gave *rac*-**13** (72%) as a colorless oil which solidified in the freezer. The ^1H NMR spectral data for the diendiol fragment of *rac*-**13** match well with those of streptenol D triacetate.[3][a] In a similar fashion, decomplexation of (−)-**12** gave (+)-**13**. Examination of *rac*-**13** by ^1H NMR spectroscopy in the presence of $Eu(hfc)_3$ ($CDCl_3$) indicated a clean separation of the acetal methine signals. By this method, (+)-**13** was determined to be 58% ee. Unfortunately, due to the high stability of the 1,3-dioxane ring, attempts at hydrolysis resulted in complex product mixtures. Nonetheless, the stereodirecting and diene protecting abilities of the $Fe(CO)_3$ group have been demonstrated in this synthesis of the 3,5-diacetoxy-6*E*,8*E*-decadiene segment of streptenol D.

(1)



Scheme. 3.

3. Experimental section

3.1. General data

Spectrograde solvents were used without purification with the exception of dry ether (which was distilled from sodium benzophenone ketyl) and dichloromethane (which was distilled from P_2O_5 and then stored over molecular seives). Column chromatography was performed on silica gel 60 (60–200 mesh, Aldrich). Thin layer chromatography was performed on Kodak Chromagram (silica gel without fluorescent indicator) and

visualization was effected by I_2 vapor. Melting points were obtained on a Mel-Temp melting point apparatus and are uncorrected. Specific rotations were recorded on a Perkin–Elmer 341 optical polarimeter. Infrared spectra were recorded on a Mattson 4020 FT-IR instrument. All ^{1}H NMR and ^{13}C NMR spectra were recorded on a GE Omega GN-300 instrument at 300 and 75 MHz, respectively. Elemental analyses were obtained from Midwest Microlabs, Indianapolis, IN and high resolution mass spectra (EI) were obtained from the Washington University Resource for Biomedical and Bioorganic Mass Spectrometry. Tricarbonyl(sorbaldehyde)iron (**2**) was prepared by literature methods.[18] 2-(2-Nitroethyl)-1,3-dioxane was prepared by the reaction of 2-(2-bromoethyl)-1,3-dioxane with $NaNO_2$ (DMF) in a fashion similar to the literature preparation of 2-(2-nitroethyl)-1,3-dioxolane.[19]

3.2. Kinetic resolution of tricarbonyl[η^4-2,4-hexadienal]iron 2

To degassed water (280 ml) was added Red Star yeast (28.0 g) and glucose (7.00 g). After stirring at rt for 30 min, a solution of *rac*-**2** (0.800 g, 3.39 mmol) in ethanol (5 ml) was added and the mixture was stirred for 1.5 h. The mixture was extracted with ether (5×100 ml), dried ($MgSO_4$) and concentrated. Purification by column chromatography (hexane:ethyl acetate (17:3)) gave (−)-**2** as a red oil (0.152 g, 19%; $[\alpha]_D$ −106 (c=1.00, $CHCl_3$); lit.[5] $[\alpha]_D$ −112 (c=1.00, $CHCl_3$); lit.[6]^b $[\alpha]_D$ −79 (c=0.8, MeOH)) followed by (2,4-hexadien-1-ol)$Fe(CO)_3$ as a red oil (0.420, 52%). The spectral data for (−)-**2** and the alcohol were identical with their racemic counterparts. Analysis of (−)-**2** by ^{1}H NMR spectroscopy in the presence of a chiral shift reagent (Eu[hfc]$_3$, $CDCl_3$) indicated it to be >92% ee.

3.3. (+)-Tricarbonyl[3-6 η^4-1,3,5-heptatriene]iron (+)-3

The preparation of (+)-**3** from (−)-**2** (1.50 g, 6.35 mmol) was accomplished by the literature procedure6, 11 for the preparation of *rac*-**3** (1.36 g, 90%); $[\alpha]_D$ +149 (c=1.00, $CHCl_3$); lit.[6]^b $[\alpha]_D$ +241 (c=1.0, MeOH). All spectral data were identical with those of *rac*-**3**.

3.4. Preparation of isoxazoline *rac*-4

To a solution of 2-(2-nitroethyl)-1,3-dioxane (1.00 g, 6.00 mmol) in benzene (10 ml) was added phenyl isocyanate (0.700 g, 6.00 mmol), *rac*-**3** (0.720 g, 3.00 mmol) and triethylamine (0.600 g, 6.00 mmol). The mixture was stirred for 24 h at rt, after which water (15 ml) was added and the mixture was extracted with ether. The organic layer was washed with water followed by brine, then dried ($MgSO_4$) and concentrated. The white crystalline by-product formed was washed with hexanes to extract the product. Purification by column chromatography (hexane:ethyl acetate (7:3)) gave **5** (0.090 g, 8%) followed by **4** (0.680 g, 60%), both as yellow oils. **5**: ^{1}H NMR ($CDCl_3$) δ 5.28 (ddd, *J*=1.2, 5.1, 8.7 Hz, 1H), 5.03 (dd, *J*=5.1, 8.7 Hz, 1H), 4.77 (t, *J*=4.8 Hz, 1H), 4.18–4.08 (m, 3H), 3.82–3.71 (m, 2H), 2.81 (dd, *J*=4.5, 14.4 Hz, 1H), 2.62 (d, *J*=2.1 Hz, 1H), 2.44 (dd, *J*=5.4, 14.4 Hz, 1H), 2.07 (m, 1H), 1.41 (d, *J*=6.3 Hz, 3H), 1.40 (m, 1H), 1.25–1.16 (m, 2H), 1.06 (dt, *J*=1.2, 8.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 157.5, 100.0, 86.5, 85.5, 82.2, 66.8, 63.1, 58.5, 48.0, 33.8, 25.5, 19.0. **4**: IR ($CDCl_3$) 2976, 2860, 2046, 1977 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.21 (ddd, *J*=0.9, 4.8, 8.1 Hz, 1H), 5.08 (dd, *J*=5.1, 8.7 Hz, 1H), 4.74 (t, *J*=4.8 Hz, 1H), 4.24 (q, *J*=9.9 Hz, 1H), 4.10 (m, 2H), 3.76 (td, *J*=2.4, 9.9 Hz, 2H), 3.18 (dd, *J*=9.9, 17.4 Hz, 1H), 2.85 (dd, *J*=8.7, 17.1 Hz, 1H), 2.63 (m, 2H), 2.14–1.93 (broad m, 1H), 1.42 (d, *J*=6.0 Hz, 3H), 1.34 (m, 2H), 1.01 (dt, *J*=0.9, 9.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 155.1, 99.4, 87.4, 83.6, 83.0, 66.8, 59.4, 59.1, 45.0, 33.6, 25.4, 19.1; EI-HRMS *m/z* 378.0630 (calcd for $C_{16}H_{19}NO_6Fe$ $(M+H)^+$ 378.0640).

3.5. Preparation of isoxazoline (−)-4

The preparation of (−)-**4** from (+)-**3** (1.53 g, 6.50 mmol) was carried out in the same fashion as for the preparation of *rac*-**4**. The bulk sample was isolated as a yellow oil (0.96 g, 39%); $[\alpha]_{546}$ −6.0 (c=1.00, $CHCl_3$); diffusion controlled recrystallization (ethyl acetate:pentane) gave (−)-**4** as golden yellow crystals; $[\alpha]_{546}$ −11.1

(c=1.00, $CHCl_3$); mp 71–74°C. Anal. calcd for $C_{16}H_{19}NO_6Fe$: C, 50.95; H, 5.08. Found C, 51.27; H, 5.08. All spectral data were identical to those of *rac*-**4**.

3.6. Tricarbonyl[η^4-2-(5′-hydroxy-3′-oxo-6,8-decadienyl)-1,3-dioxane]iron *rac*-6

To a solution of **4** (0.200 g; 0.530 mmol) in MeOH:H_2O (15:1, 40 ml) in a three-necked flask was added Raney nickel (1 ml slurry in H_2O) and $B(OH)_3$ (0.20 g). The flask was fitted with a balloon, the flask purged twice with H_2, and then inflated with H_2 gas. The reaction mixture was stirred for 24 h at rt and then the mixture was filtered through filter-aid and extracted with ether. The combined ether extracts were concentrated and the residue was purified by column chromatography (hexanes:ethyl acetate (7:3)) to give *rac*-**6** as a light yellow solid (0.180 g, 88%); mp 108–110°C; IR ($CDCl_3$) 3381, 2976, 2040, 1955, 1724 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.26 (dd, *J*=4.8, 8.1 Hz, 1H), 5.06 (dd, *J*=5.1, 8.7 Hz, 1H), 4.92 (t, *J*=5.1 Hz, 1H), 4.12 (m, 2H), 3.77 (m, 3H), 3.51 (OH), 2.88 (dd, *J*=2.4, 17.7 Hz, 1H), 2.73 (m, 3H), 2.17–1.98 (broad m, 1H), 1.40 (d, *J*=6.3 Hz, 3H), 1.36–1.20 (m, 2H), 0.91 (t, *J*=8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 208.2, 98.5, 86.6, 82.6, 70.2, 66.9, 62.0, 58.6, 51.3, 48.8, 25.4, 19.1. Anal. calcd for $C_{16}H_{20}O_7Fe$: C, 50.55; H, 5.30. Found C, 50.60; H, 5.39.

3.7. Preparation of (+)-6

The preparation of (+)-**6** from (−)-**4** (0.940 g, 2.49 mmol) was carried out in the same fashion as for the preparation of *rac*-**6**. Purification by column chromatography gave recovered starting material (0.310 g, 41%) followed by (+)-**6** (0.410 g, 43%; $[\alpha]_D$ +31.9 (c=1.00, $CHCl_3$)). All spectral data were identical with those of *rac*-**6**.

3.8. Tricarbonyl[η^4-2-(3′,5′-dihydroxy-6,8-decadienyl)-1,3-dioxane]iron (*rac*-8)

To a solution of *rac*-**6** (0.100 g, 0.260 mmol) in glacial acetic acid (10 ml) was added sodium triacetoxyborohydride (0.070 g, 0.31 mmol). The mixture was stirred at rt for 15 min and then extracted with ether. The ether layer was washed with water (3×), followed by saturated aqueous $NaHCO_3$ (2×), dried ($MgSO_4$) and concentrated. Purification by column chromatography (hexane:ethyl acetate (7:3)) gave a mixture (1:1.5) of diastereomeric diols **7** and **8** as a yellowish oil (0.070 g, 69%). It was not possible to separate this mixture by column chromatography. When the reaction was carried out at −25°C in a mixture of acetic acid:acetonitrile (2:1, 5 ml) as solvent, the diastereomeric diols **7** and **8**were formed as a 1:10 mixture, respectively. The *anti*-diol **8** was isolated as a yellow crystalline solid by vapor diffusion recrystallization[15] (ethyl acetate:pentane) (0.240 g, 75%). **8**: mp 123–125°C; IR ($CDCl_3$) 3595, 2042, 1973, 1645 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.24 (dd, *J*=4.8, 8.4 Hz, 1H), 5.05 (dd, *J*=4.8, 8.4 Hz, 1H), 4.79 (dd, *J*=3.3, 5.1 Hz, 1H), 4.33 (br m, 1H), 4.11 (m, 2H), 3.99 (br m, 1H), 3.84–3.55 (br m, 4H), 2.19–2.06 (br m, 1H), 1.96–1.65 (br m, 4H), 1.40 (d, *J*=6.0 Hz, 3H), 1.34 (m, 1H), 1.26 (m, 1H), 1.03 (t, *J*=8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 101.5, 86.5, 82.7, 72.1, 66.8, 66.5, 64.0, 58.3, 42.7, 40.7, 25.5, 19.1. Anal. calcd for $C_{16}H_{22}O_7Fe$: C, 50.28; H, 5.80. Found C, 50.35; H, 5.92.

3.9. Preparation of (+)-8

The preparation of (+)-**8** from (+)-**6** (0.350 g, 0.921 mmol) was carried out in the same fashion as for the preparation of *rac*-**8** (0.210 g, 60%); $[\alpha]_D$ +46.2 (c=1.00, $CHCl_3$); mp 59–61°C. All spectral data were identical with those of *rac*-**8**.

3.10. Reduction of *rac*-6 with $NaBH_3CN$

To a sample of *rac*-**6** (0.280 g, 0.737 mmol) in glacial acetic acid (5 ml) at 23°C was added $NaBH_3CN$ (20 mg, 0.322 mmol). The reaction mixture was stirred for 1 h, and then quenched with water and extracted with ether (2×10 ml). The combined ethereal extracts were washed with saturated aqueous $NaHCO_3$, followed by water, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (hexanes:ethyl acetate (7:3)) to give a mixture of *syn*-**7** and *anti*-**8** (10:1) as a yellow oil (0.100 g, 36%). **7**: IR ($CDCl_3$) 3437, 2862, 2042, 1973 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.26 (dd, *J*=5.2, 8.2 Hz, 1H), 5.05 (dd, *J*=5.1, 8.8 Hz, 1H), 4.78 (m, 1H), 4.19 (OH), 4.11 (m, 3H), 3.77 (m, 3H), 3.63 (OH), 2.19–2.04 (broad m, 1H), 1.78 (m, 1H), 1.69 (m, 3H), 1.40 (d, *J*=6.0 Hz, 3H), 1.35

(d, *J*=5.4 Hz, 1H), 1.22 (m, 1H), 0.96 (t, *J*=7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 101.3, 86.3, 82.4, 74.7, 69.3, 66.9, 64.8, 58.2, 44.2, 41.8, 25.6, 19.1; EI-HRMS *m/z* 326.0822 (calcd for $C_{16}H_{22}O_7Fe$ $(M-2CO)^+$ *m/z* 326.0817).

3.11. Attempted decomplexation of *rac*-8 with NMO

To a solution of *rac*-**8** (0.500 g, 1.31 mmol) in C_6H_6 (8 ml) at 23°C was added N-methylmorpholine-N-oxide (0.23 g, 1.96 mmol). The reaction mixture was stirred for 3 h, concentrated and the residue was purified by column chromatography (hexanes:ethyl acetate (7:3)) to give a mixture of *rac*-**6** and *rac*-**11**(1:2.5) as a yellow oil (0.260 g, 52%). **11**: ^{1}H NMR (partial, $CDCl_3$) δ 5.77 (ddd, *J*=0.9, 5.1, 8.1 Hz, 1H), 5.22 (dd, *J*=5.1, 8.1 Hz, 1H), 4.75 (t, *J*=5.1 Hz, 1H), 4.26 (br m, 1H), 1.54 (m, 1H), 1.45 (d, *J*=6.0 Hz, 3H), 1.21 (dd, *J*=0.9, 8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 205.0, 100.5, 88.8, 80.9, 66.8, 64.3, 59.4, 53.6, 48.8, 41.2, 25.6, 19.1.

3.12. Tricarbonyl[η^4-2-(3′,5′-diacetoxy-6,8-decadienyl)-1,3-dioxane]iron *rac*-12

To a cooled solution of *rac*-**8** (1.28 g, 3.31 mmol) in dichloromethane (30 ml) at 0°C was added pyridine (1.36 g, 16.5 mmol) and acetic anhydride (1.35 g, 13.2 mmol). The reaction mixture was allowed to warm to rt and stirred overnight. The mixture was extracted with ether (3×25 ml) and the combined organic layers were washed twice with water, saturated aqueous $NaHCO_3$, dried ($MgSO_4$) and concentrated. Purification by column chromatography (hexanes:ethyl acetate (7:3)) gave *rac*-**12** as a yellow solid (1.48 g, 97%): mp 75–78°C; ^{1}H NMR ($CDCl_3$) δ 5.43 (ddd, *J*=1.1, 5.1, 8.3 Hz, 1H), 5.09 (m, 1H), 5.00 (dd, *J*=5.0, 8.8 Hz, 1H), 4.48 (m, 2H), 4.08 (br m, 2H), 3.72 (dt, *J*=2.4, 12.1 Hz, 2H), 2.02 (s, 3H), 1.95 (s, 3H), 2.0–1.75 (broad m, 5H), 1.40 (d, *J*=6.0 Hz, 3H), 1.36–1.20 (m, 2H), 0.76 (dt, *J*=0.9, 9.3 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 170.8, 170.5, 99.6, 86.8, 83.3, 72.3, 66.9, 66.8, 66.2, 59.3, 58.7, 40.7, 40.4, 25.6, 21.2, 20.8, 19.1. Anal. calcd for $C_{20}H_{26}O_9Fe$: C, 51.52; H, 5.62. Found C, 51.72; H, 5.70.

3.13. Preparation of (+)-12

The preparation of (+)-**12** from (+)-**8** (0.200 g, 0.520 mmol) was carried out in the same fashion as for the preparation of *rac*-**12** (0.199 g, 82%); $[\alpha]_D$ +1.90 (c=1.37, $CHCl_3$). All spectral data were identical with those of *rac*-**12**.

3.14. (3′,5′-Diacetoxy-6,8-decadienyl)-1,3-dioxane *rac*-13

To a solution of *rac*-**12** (1.43 g, 3.05 mmol) in a mixture of acetonitrile (16 ml) and water (4 ml) at 0°C was added ceric ammonium nitrate (8.22 g, 15.0 mmol). After stirring for 1 h, the reaction mixture was quenched with water (8 ml) and extracted with ether (3×20 ml). The combined organic layers were washed with water (3×), followed by brine, then dried ($MgSO_4$) and concentrated. Purification by column chromatography (hexanes:ethyl acetate (3:2)) gave *rac*-**13** as a colorless oil (0.709 g, 72%): IR ($CDCl_3$) 2974, 2858, 1734, 1248 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.20 (dd, *J*=10.3, 15.1 Hz, 1H), 5.96 (ddd, *J*=1.5, 10.5, 15.0 Hz, 1H), 5.73 (dq, *J*=14.9, 6.6 Hz, 1H), 5.44 (dd, *J*=7.3, 15.2 Hz, 1H), 5.31 (m, 1H), 5.15 (m, 1H), 4.56 (t, *J*=4.8 Hz, 1H), 4.09 (m, 2H), 3.70 (dt, *J*=2.4, 11.7 Hz, 2H), 2.05 (m, 1H), 2.02 (s, 3H), 2.00 (s, 3H), 1.92–1.75 (broad m, 4H), 1.74 (br d, *J*=6.0 Hz, 3H), 1.31 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 170.4, 170.3, 133.1, 131.3, 130.4, 127.8, 99.7, 70.4, 66.8, 66.5, 40.5, 39.3, 25.6, 21.2, 21.1, 18.1; EI-HRMS *m/z* 266.1515 (calcd for $C_{15}H_{22}O_4$ (M−AcOH) *m/z* 266.1518).

3.15. Preparation of (+)-13

The preparation of (+)-**13** from (+)-**12** (0.199 g, 0.426 mmol) was carried out in the same fashion as for the preparation of *rac*-**12** (45.1 mg, 32%); $[\alpha]_D$ +15.3 (c=0.71, $CHCl_3$). All spectral data were identical with those of *rac*-**13**. Analysis of (+)-**13** by ^{1}H NMR spectroscopy in the presence of a chiral shift reagent (Eu[hfc]$_3$, $CDCl_3$) indicated it to be 58% ee.

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