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Remote diastereoselective control via organoiron methodology: stereoselective preparation of 4,6-, 5,7- and 6,8-dien-2-ol (tricarbonyl)iron complexes

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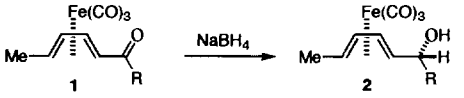
Abstract

The diastereoselective preparation of 2,3-, 2,4- and 2,5-diol iron complexes was accomplished in the following fashion: (2,4,6-octatriene)$Fe(CO)_3$ undergoes diastereoselective osmylation to provide (4,6-octadien-2,3-diol)$Fe(CO)_3$; (4-hydroxy-5,7-nonadien-2-one)$Fe(CO)_3$ may be reduced in a diastereoselective fashion to give mixtures predominating in either the *syn*- or *anti*-(5,7-nonadien-2,4-diol)$Fe(CO)_3$; and diastereospecific addition of $MeTi(O^iPr)_3$ to the lactol of (5-hydroxy-6,8-decadienal)$Fe(CO)_3$ gives (6,8-decadien-2,5-diol)$Fe(CO)_3$. In each of the cases noted above, the hydroxyl group adjacent to the (diene)$Fe(CO)_3$ group may be removed via ionic hydrogenation. The ionization of this hydroxyl is rationalized on the basis of the intermediacy of a transoid (pentadienyl)$Fe(CO)_3$ cation species.

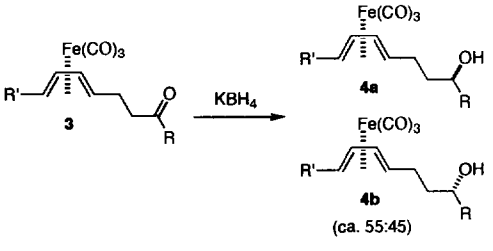
Keywords: Iron; Diene complexes; Diastereoselective synthesis

1. Introduction

Attachment of a (tricarbonyl)iron adjunct to an acyclic diene has been shown to protect the diene against reduction, oxidation, and cycloaddition reactions [1]. In addition, the steric bulk of the $Fe(CO)_3$ group serves to effect diastereoselective bond formation at unsaturated centers adjacent to the (diene) [1]. For example, the reduction of (dienone)$Fe(CO)_3$ complexes (**1**) proceeds in a highly diastereoselective fashion to provide the ψ-*endo* (dienol)$Fe(CO)_3$ products (**2**, Eq. (1)) (the ψ-*exo* and ψ-*endo* nomenclature was first used by Lillya [2]). This type of selectivity has been utilized for the preparation of members of the leukotriene family of natural products [3]. For unsaturated centers more remote to the coordinated diene, reactions which proceed with any diastereoselectivity are virtually unknown. Thus, for example, the reduction of the (dienone)$Fe(CO)_3$ complex (**3**) gives a nearly equimolar ratio of the two diastereomeric dienol complexes (**4a** and **4b** respectively, Eq. (2)) [4]. We herein report on a strategy for diastereoselective preparation of dienol complexes in which the alcohol center is 2, 3, or 4 carbons removed from the tricarbonyl(diene)iron group. Such molecular arrays may be found in carbomycin B [5], curacin A [6], and macrolactin A [7] respectively (Fig. 1). This methodology relies on stereoselective generation of a chiral center adjacent to the (diene)$Fe(CO)_3$, relaying of this stereochemical information to a new stereocenter more remote to this functionality, followed by the subsequent removal of the former stereocenter [8].



(1)



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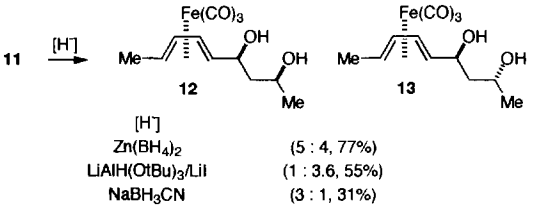
2. Results and discussion

All compounds described are racemic mixtures of enantiomers. Only one enantiomer has been diagrammed for clarity. Resolution of (sorbaldehyde)$Fe(CO)_3$ has been accomplished [1].

Peterson methenylation of (sorbaldehyde)$Fe(CO)_3$ (**5**) by the literature procedure [9] gave the known [10] (3-6-η^4-1,3,5-heptatriene)$Fe(CO)_3$ (**6**). Wittig ethenylation of **5** gave (4-7-η^4-2,4,6-octatriene)$Fe(CO)_3$ (**7**) as an inseparable mixture of Z,E,E- and E,E,E-isomers (ca. 4:1 respectively, Scheme 1).

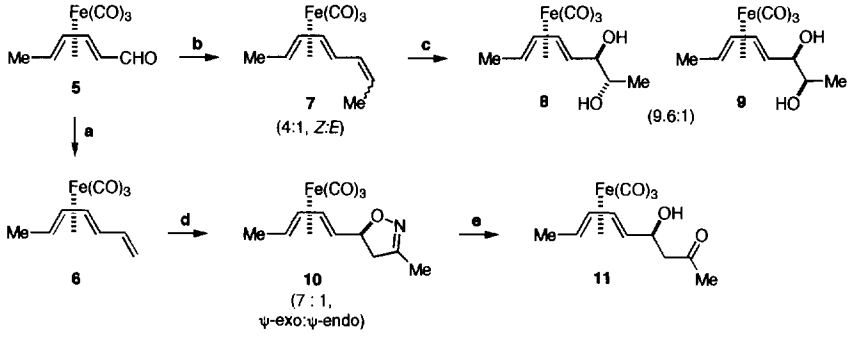
Osmylation of the diastereomeric triene mixture **7** gave a separable mixture of diastereomeric 2,3-diol complexes **8** and **9** (9.6:1, 53%), **5** (4%) and unreacted **7** (20%) (Scheme 1). On the basis of literature precedent [11], both diol complexes **8** and **9** are assigned the ψ-*exo* stereochemistry at C3. In addition, the major and minor diastereomeric 2,3-diols are assigned the *erythro* and *threo* relative stereochemistries by comparison of the relative chemical shifts of the C2-methyl groups (δ 16.8 and 19.6 ppm respectively) with that of the corresponding methyl groups of *erythro* and *threo* 2,3-butanediol (δ 16.9 and 19.3 ppm respectively) [12]. Thus the predominant product, **8**, arises via osmylation of the major 6-Z-triene while the lesser diastereomer, **9**, arises from the minor 6-E-triene complex. The minor amount of (sorbaldehyde)$Fe(CO)_3$ (**5**) obtained is presumably due to subsequent oxidative cleavage of the 2,3-diols.

The 1,3-dipolar cycloaddition of **6** with the nitrile-oxide derived from nitroethane has been previously reported to give a mixture of diastereomeric isoxazolines (ca. 7:1) from which **10** can be isolated by column chromatography [9]. We herein report the spectral details for **10**. Reductive hydrolysis of isoxazoline **10** gave the β-hydroxyketone **11**. The relative stereochemistry of **11** (ψ-*exo*) was tentatively assigned on the basis of the stereochemical assignment for the precursor **10**. Reduction of **11** with $Zn(BH_4)_2$ [13] gave a mixture of *syn*- and *anti*-2,4-diol complexes **12** and **13** (5:4, 77%, Eq. (3)). A pure sample of diol **12** was obtained by fractional crystallization of this mixture. The relative stereochemistry of **12** at C2 (*syn*) and C4 (ψ-*exo*) was established by X-ray diffraction analysis [14], thus also corroborating the ψ-*exo* assignments of **10** and **11**. Since **13** also arises from reduction of **11**, and in order to have a unique structure, **13** is assigned the C2 (*anti*) and C4 (ψ-*exo*) relative configurations. Reduction of **11** with $LiAlH(O^tBu)_3$ in the presence of LiI (ether/−78 °C) [15] gave a mixture of **12** and **13** (1:3.6, 55%, Eq. (3)), while reduction of **11** with $NaBH_3CN$ (0.3 equiv.) in acetic acid [16] gave a mixture of **12** and **13** (3:1, 31% based on consumed starting material).



(3)

Reaction of dienal complex **5** with the Grignard reagent generated from 2-(2-bromoethyl)-1,3-dioxane gave a mixture of hydroxyacetals **14** and **15** in nearly



Scheme 1. Reagents: (a) Me_3SiCH_2Cl/Mg, SiO_2 (93%); (b) $MeCH_2PPh_3^+I^-$/ⁿBuLi (40%); (c) OsO_4 (53%); (d) $CH_3CH_2NO_2/PhNCO/NEt_3$ (63%); (e) H_2Ra-Ni/$B(OH)_3$ (79%).

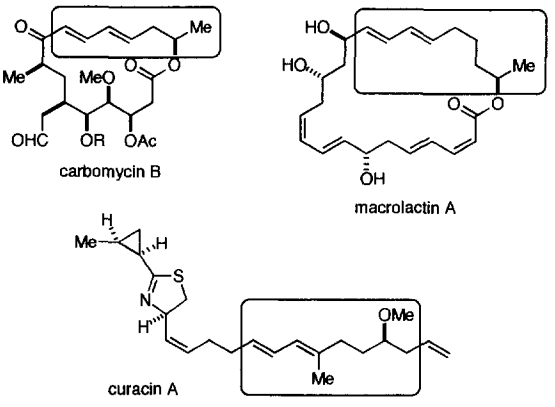
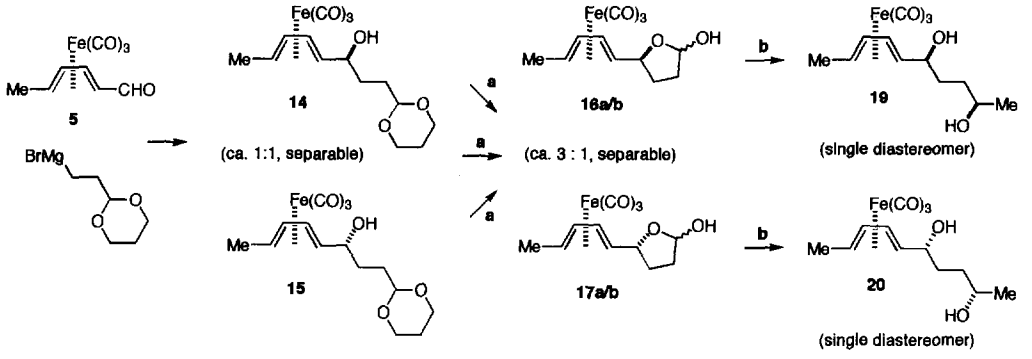


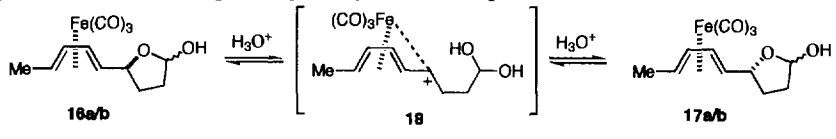
Fig. 1. Dienol-containing natural products.



Scheme 2. Reagents: (a) H_2SO_4/acetone/reflux (62–77%), $MeTi(O^iPr)_3/CH_2Cl_2$ (86%).

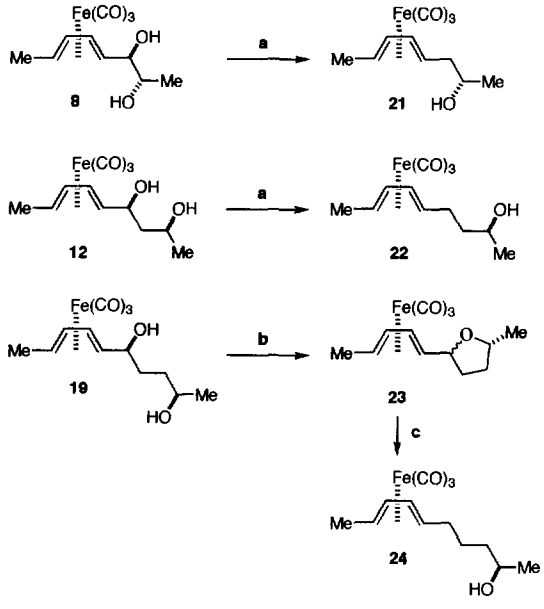
equimolar amounts (Scheme 2). The diastereoisomers **14** and **15** are separable by careful column chromatography; however, it proved more convenient and practical to separate the two diastereomeric series after the next step. The relative stereochemistry of **14** and **15** at C4 was tentatively assigned as ψ-*exo* and ψ-*endo* respectively on the basis of their relative chromatographic mobility (**14** more polar than **15**) and on the relative chemical shift of their 4-H protons (**14**, δ 3.43; **15**, δ 3.53 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 [17].

Hydrolysis of either pure hydroxyacetal **14**, pure **15**, or a mixture of **14/15** gave a mixture of diastereomeric lactols **16a/b** and **17a/b** (**16**:**17** ca. 3:1, Scheme 3). This mixture could be readily separated by column chromatography into a mixture of **16a/16b** and a mixture of **17a/17b**. Additionally, treatment of **16a/16b** or **17a/17b** under the hydrolysis conditions generates the same mixture of four diastereoisomers. The equilibration of **16** and **17** may be rationalized by ionization of the C4 lactol C–O bond under acidic conditions to generate the transoid pentadienyl cation **18** (Eq. (4)). Rotation about the C4–C5 bond and attack of oxygen on the face opposite to iron effects epimerization [18]. Thus the lack of diastereoselectivity for Grignard addition to **5** is of no consequence, since the stereocenter adjacent to the diene is epimerized under the reaction conditions.



(4)

Treatment of lactol **16** with $MeTi(^iPrO)_3$ [19] gave the diol complex **19** as a single diastereomer (Scheme 2). It had been anticipated, on the basis of literature precedent [19], that **19** would possess the *syn*-1,4-diol configuration. This was unambiguously established by X-ray diffraction analysis [8], thus also corroborating the ψ-*exo* assignments of **14** and **16**. Similarly, treatment of **17** with $MeTi(^iPrO)_3$ gave a single diol complex **20** (Scheme 2). Diol **20** was assigned the ψ-*endo*–*syn* relative stereochemistry by analogy to the formation of the *syn*-diol **19** from lactol **16**. It has been proposed [19] that the *syn*-selectivity observed in the preparation of diols from the corresponding lactol is due to chelation-control via a seven-membered chelate (Fig. 2). The sterically bulky (diene)$Fe(CO)_3$ fragment would preferentially occupy an equatorial position in the chair conformer of the 'cycloheptene-like' structure (it should be noted that the chair conformer of cycloheptene is predicted to be lower in energy than the boat [20]). External nucleophilic attack on the sterically more accessible face of the chelated aldehyde leads to the *syn*-diol diastereomer.



Scheme 3. Reagents: (a) $NaBH_3CN$/AcOH (53–76%); (b) pTsOH/C_6H_6 (87%); (c) $NaBH_3CN/Et_2O{:}BF_3$/THF (42%).

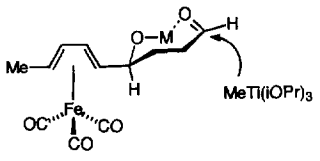


Fig. 2. Seven-membered chelation control.

Clinton and Lillya [21] have shown that dienyl dinitrobenzoate iron complexes undergo solvolysis with retention of configuration. This S_N1 ionization *exo* to iron occurs to generate a *transoid* (pentadienyl)iron cation. This type of reactivity has been exploited for diastereospecific C–C bond formation via ionization of dienyl acetate iron complexes in the presence of weak carbon nucleophiles such as allylsilanes or trialkylaluminums [22]. It was thus anticipated that ionic reduction of the ψ-*exo* alcohols **8**, **12**, and **19** in the presence of a weak hydride source could be utilized for the removal of this stereocenter. The reactions of **8** and of **12** with $NaBH_3CN$ in glacial acetic acid each gave a single alcohol product (**21** and **22** respectively, Scheme 3). In comparison, the attempted ionic reduction of **19** gave a mixture of products of which the tetrahydrofuran **23** was the predominant species. This product presumably arises via ionization of the ψ-*exo* hydroxyl group followed by intramolecular nucleophilic attack of the remote hydroxyl substitutent to form a five-membered heterocycle [23]. The formation of **23** was maximized by the reaction of **19** with p-toluenesulfonic acid in benzene. Reduction of **23** required stronger ionization conditions than for **8** and **12**. Thus reaction of tetrahydrofuran **23** with $Et_2O \cdot BF_3$ in the presence of $NaBH_3CN$ gave a single alcohol **24** in modest yield.

In summary, the diastereoselective preparation of dienol complexes in which the alcohol center is 2, 3, or 4 carbons removed from the tricarbonyl(diene)iron group has been achieved. Application of this methodology to the preparation of polyene natural products will be reported in due course.

3. Experimental section

All m.p. measurements were carried out on a Mel-Temp apparatus and are uncorrected. IR spectra were obtained on a Matteson 4020 FT-IR spectrometer. All ^1H and ^{13}C NMR spectra were recorded on a GE Omega 300-GN instrument operating at 300 or 75 MHz respectively. Elemental analyses were obtained from Midwest Microlabs, Ltd., Indianapolis. High resolution mass spectra were performed at the Nebraska Center for Mass Spectrometry, Lincoln, NE. Dry tetrahydrofuran (THF) and dry ether were distilled from potassium and sodium benzophenone ketyl respectively and dry CH_2Cl_2 was distilled from P_2O_5 prior to use. All other solvents were spectral grade and were used without further purification.

3.1. Tricarbonyl(1,3E,5E-heptatriene)iron (6)

To a solution of chloromethyltrimethylsilane (2.50 g, 19.9 mmol) in dry ether (35 ml) was added magnesium turnings (1.01 g, 41.6 mmol). The mixture was stirred at room temperature for 1 h, then cooled to −78 °C. Tricarbonyl(sorbaldehyde)iron (**5**) (2.50 g, 10.6 mmol) was added and the solution was stirred at −78 °C for 1 h. The solvent was evaporated under reduced pressure, and the residue was taken up in CH_2Cl_2 (14 ml). To this solution was added 2% aqueous H_2SO_4 (6 ml) and silica gel (60–200 mesh, 15 g) and the mixture was stirred overnight at room temperature. The mixture was extracted with ether, the combined extracts were washed with H_2O, followed by brine, dried ($MgSO_4$) and concentrated. The residue was purified by bulb-to-bulb distillation under high vacuum to give the known triene complex **6** as a reddish oil (2.3 g, 93%).

6. ^1H NMR ($CDCl_3$): δ 5.73 (dt, J = 12, 15 Hz, 1H), 5.18 (m, 2H), 5.02 (dd, J = 6.6, 6 Hz, 1H), 4.90 (dd, J = 1.2, 10.2 Hz, 1H), 1.72 (dd, J = 9.0, 9.3 Hz, 1H), 1.41 (d, J = 5.7 Hz, 3H), 1.34 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 139.1, 114.4, 85.4, 81.6, 61.0, 57.2, 19.7. The ^1H NMR spectral data for this compound is identical with the literature values [9].

3.2. Tricarbonyl(2,4E,6E-octatriene)iron (7)

To a solution of ethyltriphenylphosphonium iodide (0.40 g, 9 mmol) in dry THF (35 ml) at −78 °C was added dropwise a solution of n-butyl lithium (4.7 ml, 1.6 M in hexanes, 7.5 mmol). The mixture was stirred for 30 min, after which a precooled solution of tricarbonyl(sorbaldehyde)iron (**5**) (1.77 g, 7.50 mmol) in dry THF (15 ml) was added dropwise. The reaction mixture was stirred for 45 min at −78 °C and then warmed to room temperature over a period of 30 min. Saturated aqueous NH_4Cl (4 ml) was added and the mixture extracted with ether. The ethereal extracts were washed with H_2O, followed by brine, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (hexane–ethyl acetate (10:1)) to give an inseparable mixture of **Z-7** and **E-7** (ca. 4:1) as a yellow oil (0.75 g, 40%) followed by recovered **5** as a yellow oil (0.79 g, 45%).

7. IR ($CDCl_3$): 3616, 2040, 1970 cm^{-1}.

Z-7. ^1H NMR ($CDCl_3$): δ 5.50–5.36 (m, 2H), 5.14 (dd, J = 5.4, 8.7 Hz, 1H), 5.03 (dd, J = 5.1, 7.8 Hz, 1H), 1.97 (t, J = 8.4 Hz, 1H), 1.69 (d, J = 5.1 Hz, 3H), 1.43 (s, 3H), 1.45–1.40 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 212.4, 131.6, 125.4, 85.3, 82.0, 56.8, 56.6, 19.2, 13.3.

E-7. ^1H NMR ($CDCl_3$, partial): δ 5.7–5.6 (m, 1H), 5.09 (dd, J = 5.4, 9.3 Hz, 1H), 4.98 (m, 1H), 1.63 (dd,

J = 1.5, 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$, partial): δ 132.6, 126.9, 84.6, 80.9, 62.4, 18.1. This mixture was used without further characterization.

3.3. Tricarbonyl(4S*,6-octadien-2,3S*-diol)iron (8) and (9)

To a solution of **7** (375 mg, 1.51 mmol) in acetone (3 ml) was added $Et_4N^+AcO^-$ (95 mg). The mixture was stirred for 30 min at room temperature, cooled to 0 °C, and OsO_4 (252 mg, 1.80 mmol) was added followed by ^{t}BuOOH (3 mmol). The mixture was stirred at 0 °C for 3 h, and then cautiously quenched with saturated aqueous $NaHSO_3$ and slowly warmed to room temperature. The mixture was stirred for 18 h, diluted with ethyl acetate, and filtered through filter-aid. The filtrate was washed with brine, followed by 10% aqueous HCl, followed by saturated aqueous $NaHCO_3$, dried ($MgSO_4$) and concentrated. The residue was separated by column chromatography (hexane–ethyl acetate (8:3 to 7:3 gradient)) to give first recovered **7** (75 mg, 20%), followed by **5** (15 mg, 4%), **8** as a yellow solid (204 mg, 48%), and finally **9** as a yellow oil (20 mg, 5%). An analytically pure sample of diol **8** was prepared by diffusion of pentane into a concentrated solution of **8** in ethyl acetate.

8. M.p. 77–80 °C. IR (KBr): 3323, 2039, 1960 cm^{-1}. ^{1}H NMR (acetone-d_6/D_2O): δ 5.43 (dd, J = 5.1, 8.7 Hz, 1H), 5.25 (br t, J = 6.3 Hz, 1H), 3.64 (m, 1H), 3.48 (dd, J = 3.5, 6.2 Hz, 1H), 1.39 (s, 3H), 1.37 (m, 1H), 1.18 (dd, J = 6.3, 8.7 Hz, 1H), 1.13 (d, J = 6.0 Hz, 3H). ^{13}C NMR (acetone-d_6/D_2O): δ 86.6, 83.1, 76.7, 71.2, 63.0, 58.5, 19.1, 16.8. Anal. Found: C, 44.40; H, 5.39. $C_{11}H_{14}O_5Fe \cdot H_2O$ Calc.: C, 44.03; H, 5.37%.

9. ^{1}H NMR ($CDCl_3$): δ 5.30 (dd, J = 5.0, 8.5 Hz, 1H), 5.09 (dd, J = 4.8, 8.7 Hz, 1H), 3.77 (m, 1H), 3.22 (dd, J = 2.4, 7.2 Hz, 1H), 2.30 (OH), 1.99 (OH), 1.42 (d, J = 6.3 Hz, 3H), 1.25 (m, 1H and d, J = 6.3 Hz, 3H), 1.10 (t, J = 8.0 Hz, 1H). ^{13}C NMR (acetone-d_6/D_2O): δ 86.2, 83.0, 76.4, 71.1, 64.3, 58.2, 19.6, 19.0.

3.4. Isoxazoline (10)

To a solution of **6** (1.34 g, 5.70 mmol) in benzene (12 ml) was added nitroethane (1.08 g, 11.0 mmol) and phenyl isocyanate (1.31 g, 11.0 mmol). To this mixture was added triethylamine (1.11 g, 11.0 mmol) and the mixture was stirred at room temperature for 24 h. The reaction mixture was diluted with water (20 ml) and extracted with ether (3 × 20 ml). The combined organic extracts were washed with H_2O, followed by brine, dried ($MgSO_4$) and concentrated. The product was extracted from the residue by dissolving in hexanes, in which the white crystalline by-product is not soluble. The combined hexane extracts were purified by column chromatography (hexane–ethyl acetate (10:1)) to give **10** as a yellow oil (1.04 g, 63%).

10. ^{1}H NMR ($CDCl_3$): δ 5.21 (dd, J = 5.1, 8.1 Hz, 1H), 5.09 (dd, J = 4.8, 8.4 Hz, 1H), 4.24 (q, J = 9.6 Hz, 1H), 1.96 (s, 3H), 2.74 (dd, J = 9.0, 16.8 Hz, 1H), 3.09 (dd, J = 9.9, 17.1 Hz, 1H), 1.42 (d, J = 5.7 Hz, 3H), 1.34 (m, 1H), 0.98 (t, J = 8.4 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 155.3, 87.4, 83.5, 82.9, 59.2, 45.7, 19.1, 13.1. This compound was used without further characterization.

3.5. Tricarbonyl(4-hydroxy-5E,7E-nonadien-2-one)iron (11)

To a solution of **10** (1.00 g, 3.44 mmol) in MeOH–H_2O (15:1, 20 ml) in a three-necked flask was added Raney-nickel (1 ml slurry in H_2O) and $B(OH)_3$ (1.0 g). The flask was fitted with a balloon, the flask purged twice with H_2, and the balloon inflated with H_2 gas. The reaction mixture was stirred for 24 h at room temperature, and then the mixture was filtered through filter-aid and extracted with ether. The combined ethereal extracts were concentrated and the residue was purified by chromatography (SiO_2, hexane–ethyl acetate (7:3)) to afford **11** as a yellow solid (0.80 g, 79%).

11. M.p. 65–67 °C. IR (CH_2Cl_2): 2042, 1971, 1709, 1265 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 5.26 (dd, J = 5.1, 7.8 Hz, 1H), 5.08 (dd, J = 5.1, 8.6 Hz, 1H), 3.73 (m, 1H), 3.47 (br s, OH), 2.80 (dd, J = 2.5, 17.8 Hz, 1H), 2.69 (dd, J = 8.2, 17.8 Hz, 1H), 2.21 (s, 3H), 1.41 (d, J = 6.0 Hz, 3H), 1.25 (m, 1H), 0.90 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 212.0, 209.6, 86.7, 82.6, 70.3, 61.9, 58.7, 50.4, 30.6, 19.1. Anal. Found: C, 49.17; H, 4.74. $C_{12}H_{14}O_5Fe$ Calc.: C, 49.01; H, 4.80%.

3.6. Reduction of tricarbonyl(4-hydroxy-5E,7E-nonadien-2-one)iron

To a solution of $Zn(BH_4)_2$ (1.6 g, 20 mmol) in ether (20 ml) was added a solution of **11** (0.50 g, 1.7 mmol) in dry benzene (5 ml) and ether (20 ml). The mixture was stirred at room temperature for 24 h, and then treated with water (4 ml). The ether layer was separated and the aqueous layer was diluted with water and further extracted with ether. The combined ether layers were washed with water, followed by brine, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (SiO_2, hexane–ethyl acetate (5:1)) to give a mixture of ***syn*-12** and ***anti*-13** as a yellow oil (5:4 ratio, 0.39 g, 77%). Diffusion controlled recrystallization of the mixture (ethyl acetate-pentane) gave ***syn*-12** as yellow crystals. Reduction of **11** with $LiAlH(O^tBu)_3$/LiI in dry ether (−78 °C) gave a mixture of **12** and **13** (1:3.6, 55%), while reduction of **11** with $NaBH_3CN$ (0.3 equiv.) in glacial acetic acid (23 °C,

45 min) gave a mixture of **12** and **13** (3:1, 31% based on consumed **11**).

***syn*-12**. M.p. 135–138 °C. IR; ^{1}H NMR ($CDCl_3$): δ 5.22 (dd, J = 4.2, 8.1 Hz, 1H), 5.07 (dd, J = 4.9, 8.7 Hz, 1H), 4.03 (m, 1H), 3.60 (dt, J = 2.4, 9.2 Hz, 1H), 3.50 (OH), 2.80 (OH), 1.78–1.60 (m, 3H), 1.41 (d, J = 6.0 Hz, 3H), 1.23 (d, J = 6.6 Hz, 3H), 0.94 (dt, J = 0.6, 8.4 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 86.6, 82.1, 75.5, 69.1, 64.2, 58.6, 45.7, 24.3, 19.1. Anal. Found: C, 48.72; H, 5.50. $C_{12}H_{16}O_5Fe$ Calc.: C, 48.67; H, 5.45%.

***anti*-13**. IR ($CDCl_3$): 3429, 2044, 1973, 1641 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 5.23 (dd, J = 4.8, 8.4 Hz, 1H), 5.07 (dd, J = 4.8, 8.4 Hz, 1H), 4.21 (sextet, J = 5.7 Hz, 1H), 3.71 (m, 1H), 3.36 (OH), 2.54 (OH), 1.75 (t, J = 5.3 Hz, 2H), 1.41 (d, J = 6.3 Hz, 3H), 1.25 (d, J = 6.3 Hz, 3H), 1.20 (t, J = 6.0 Hz, 1H), 1.02 (t, J = 8.6 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 86.6, 82.4, 72.4, 65.8, 63.5, 58.5, 44.5, 23.3, 19.1. This compound was only characterized as a mixture with **12**.

3.7. Preparation of alcohols 14 / 15

To Mg turnings (1.22 g, 50.2 mmol) in dry THF (140 ml) was slowly added dropwise a solution of 2-(2-bromoethyl)-1,3-dioxane (9.52 g, 48.8 mmol) in dry THF (15 ml). Grignard formation was initiated by addition of one crystal of I_2. Once addition of the bromoethyldioxane was complete, the solution was heated at a gentle reflux for 1.5 h. The Grignard solution was cooled with an ice bath, and a solution of tricarbonyl(sorbaldehyde)iron (7.70 g, 33.0 mmol) in dry THF (15 ml) was added dropwise, and the mixture stirred for 18 h at room temperature. The mixture was poured into ice/saturated aqueous NH_4Cl, and the resultant heterogenous mixture filtered through filter-aid. The phases were separated, and the aqueous layer further extracted with ether. The combined ethereal layers were washed with H_2O, followed by brine, dried (Na_2SO_4) and concentrated. The residue (9.1 g, 79%) was purified by flash chromatography (hexanes followed by hexane–ethyl acetate gradient) to give **15** as a yellow–orange solid (4.4 g) followed by **14** as a yellow–orange oil (4.5 g).

15. R_f 0.27 (hexanes–ethyl acetate (7:3)). ^{1}H NMR ($CDCl_3$): δ 5.16 (dd, J = 4.8, 8.3 Hz, 1H), 5.03 (dd, J = 4.9, 8.8 Hz, 1H), 4.57 (t, J = 4.4 Hz, 1H), 4.10 (dd, J = 4.5, 11.2 Hz, 2H), 3.76 (dt, J = 2.4, 12.2 Hz, 2H), 3.53 (m, 4H), 2.46 (d, J = 3.2 Hz, 1H), 2.06 (m, 2H), 1.8–1.6 (m, 4H), 1.40 (d, J = 6.4 Hz, 3H), 1.11 (dq, J = 8.3, 6.4 Hz, 1H), 1.02 (t, J = 8.0, 1H). ^{13}C NMR ($CDCl_3$): δ 101.8, 85.1, 80.7, 73.3, 68.4, 66.9, 57.6, 34.1, 31.7, 25.5, 19.1. IR (KBr): 3468, 2047, 1962, 1134 cm^{-1}. Anal. Found: C, 51.33; H, 5.83. $C_{17}H_{20}O_5Fe$ Calc.: C, 51.60; H, 5.72%.

14. R_f 0.15 (hexanes–ethyl acetate (7:3)). ^{1}H NMR ($CDCl_3$): δ 5.23 (dd, J = 4.9, 8.3 Hz, 1H), 5.04 (dd, J = 5.0, 8.8 Hz, 1H), 4.58 (t, J = 4.6 Hz, 1H), 4.08 (dd, J = 4.1, 11.2 Hz, 2H), 3.75 (dd, J = 2.4, 11.9 Hz, 2H), 3.43 (m, 4H), 3.01 (d, J = 4.6 Hz, 1H), 2.05 (m, 2H), 1.9–1.5 (m, 4H), 1.40 (d, J = 6.4 Hz, 3H), 1.20 (m, 1H), 0.95 (t, J = 8.3 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 212.0, 101.9, 86.3, 82.4, 73.4, 66.9, 64.7, 58.1, 32.5, 31.0, 25.5, 19.1. IR (KBr): 3421, 2041, 1969, 1146 cm^{-1}. Anal. Found: C, 51.10; H, 5.81. $C_{17}H_{20}O_5Fe$ Calc.: C, 51.60; H, 5.72%.

3.8. Hydrolysis of 15

A solution of **15** (1.2 g, 3.4 mmol) and 0.05 M H_2SO_4 (30 ml) in degassed acetone (200 ml) was heated at reflux for 15 h. The mixture was cooled, neutralized with saturated aqueous $NaHCO_3$, concentrated, and extracted with CH_2Cl_2. The combined organic extracts were washed with H_2O, followed by brine, dried (Na_2SO_4) and concentrated. The residue was purified by chromatography (hexanes followed by hexanes–ether gradient) to give **17a/b** as a yellow solid (0.20 g) followed by **16a/b** as an orange oil (0.45 g) [**16**:**17** (2.3:1, 65%)].

16a/16b. ^{1}H NMR ($CDCl_3$): δ 5.50 and 5.41 (two br m, 1H), 5.14 (dd, J = 5.1, 8.5 Hz, 1H), 5.02 (dd, J = 4.4, 8.3 Hz, 1H), 4.26 and 4.22 (two br s, 1H), 3.87 and 3.68 (two m, 1H), 2.2–1.6 (m, 4H), 1.39 (d, J = 4.9 Hz, 3H), 1.35–1.20 (m, 1H), 0.95 and 0.78 (two t, J = 9.0 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 212.0, 99.1, 98.9, 87.0, 86.9, 83.5, 82.9, 82.8, 80.9, 62.8, 60.5, 58.5, 58.4, 34.2, 33.4, 31.0, 30.9, 19.1. Anal. Found: C, 49.20; H, 4.82. $C_{12}H_{14}O_5Fe$ Calc.: C, 49.01; H, 4.80%.

17a/17b. ^{1}H NMR ($CDCl_3$): δ 5.53 and 5.47 (two br m, 1H), 5.13 (dd, J = 5.1, 8.6 Hz, 1H), 5.02 (dd, J = 4.9, 8.6 Hz, 1H), 4.16 and 3.76 (two br m, 1H), 2.94 and 2.80 (two br s, 1H), 2.3–1.5 (m, 4H), 1.40 (d, J = 6.4 Hz, 3H), 1.1–0.9 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 212.0, 98.5, 98.4, 85.7, 85.4, 83.2, 81.0, 80.3, 79.3, 66.3, 64.5, 57.7, 57.2, 34.4, 33.2, 32.6, 31.9, 19.1. Anal. Found: C, 49.12; H, 4.80. $C_{12}H_{14}O_5Fe$ Calc.: C, 49.01; H, 4.80%.

Treatment of **14** (0.50 g, 1.4 mmol) in a similar fashion gave a mixture of **16/17** (3:1, 62%), while treatment of a mixture of **14/15** (1:1, 9.10 g, 25.5 mmol) under the hydrolysis conditions gave a mixture of **16/17** (2.9:1, 77%).

3.9. Tricarbonyl(6S*,8-decadien-2R*,5S*-diol)iron (19)

To a solution of triisopropoxytitanium chloride (1.2 g, 4.6 mmol) in dry Et_2O (15 ml), cooled in a CH_3CN/liquid N_2 bath, was added dropwise via syringe a solution of MeLi (3.3 ml, 1.4 M in Et_2O, 4.6 mmol). The solution was warmed to 0 °C and stirred for 1 h. The solvent was evaporated under high vacuum,

and the resultant residue taken up in dry CH_2Cl_2 (10 ml) and cooled to −78 °C. A solution of **16** (0.10 g, 0.34 mol) in dry CH_2Cl_2 (3 ml) was added via syringe

δ 85.5, 84.0, 69.3, 57.5, 57.4, 43.5, 22.8, 19.1. HRMS m/z 182.0398 [calc. for $C_8H_{14}OFe$ (M − 3CO), m/z 182.0304]

trated. The residue was purified by flash chromatography (hexanes followed by hexane–ethyl acetate gradient) to give **24** as a yellow oil (36.8 mg, 42%).

24. ^{1}H NMR ($CDCl_3$): δ 4.99 (d, $J = 8.1$ Hz, 2H), 3.80 (m, 1H), 1.6–1.4 (m, 5H), 1.38 (d, $J = 6.1$ Hz, 3H), 1.19 (d, $J = 6.1$ Hz, 3H), 1.10 (quintet, $J = 6.3$ Hz, 1H), 1.01 (q, $J = 7.6$ Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 212.0, 85.1, 83.7, 67.9, 63.3, 57.2, 38.8, 34.2, 28.3, 23.6, 19.1. HRMS m/z 294.0537 [calc. for $C_{13}H_{18}O_4Fe$, m/z 294.0557].

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