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Reactivity of (3-Methylpentadienyl)iron(1+) Cation: Late-stage Introduction of a (3-Methyl-2Z,4-pentadien-1-yl) Side Chain

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Abstract: The 3-methyl-2*Z*,4-pentadien-1-yl sidechain is found in various sesquiterpenes and diterpenes. A route for the late stage introduction of this functionality was developed which relies on nucleophilic attack on the (3-methylpentadienyl)iron(1+) cation, followed by oxidative decomplexation. This methodology was applied to the synthesis of the proposed structure of heteroscyphic acid A methyl ester. Realization of this synthesis led to a correction of the proposed structure.

Keywords: Organoiron complexes; Alkylation; Diene ligands; Terpenoids

Introduction

The 3-methyl-2Z,4-pentadienyl sidechain is a functionality appearing in a number of naturally occurring sesquiterpenes and diterpenes. For example, (+)-striatene [1] (**1**, Figure 1), and the labdane diterpenes (+)-solidagol [2] **2** and (-)-*ent*-3 β-acetoxylabda-8(17),12*Z*,14-trien-2α-ol [3] **3** were isolated from the liverwort *Ptychanthus striatus*, from Canadian golden rod (*Solidago canadensis*) and from the ornamental plant *Plectranthus fruticosus* respectively. Similarly, the clerodane diterpene (+)-caseargrewiin E **4** [4], isolated from a Thai shrubby tree, exhibited cytotoxic activity against KB, BC1 and NCI-H187 cancer cell lines in the range 0.15-0.91 μg/mL range. In spite of these and other examples [5], only a single synthesis of a terpene containing this functionality has been reported [6]. Audran and co-workers reported the synthesis of **1** which involved enolate alkylation with 5*Z*-bromo-3-methylpent-3-en-1-yne, followed by hydrozirconation (Scheme 1). It should be noted that attempts at reduction of the **5** using H_2 and a poisoned catalyst were unsuccessful.

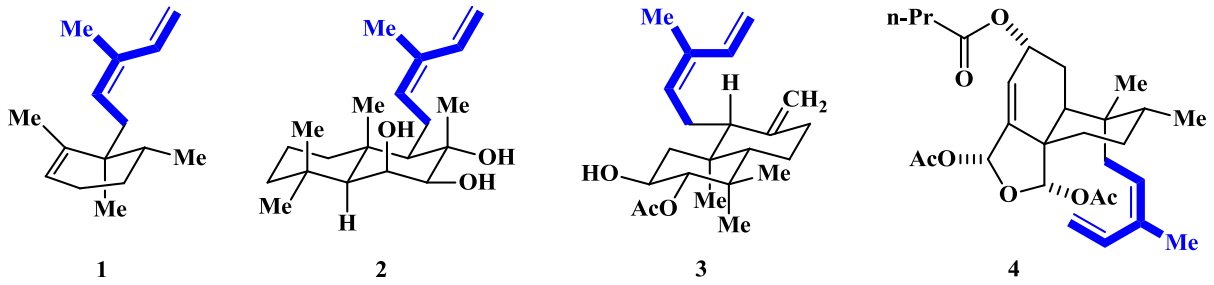

Figure 1. Sesquiterpenes and diterpenes possessing a 3-methyl-2Z,4-pentadienyl sidechain.

As part of our interest in the application of organoiron complexes to organic synthesis [7], we have examined the reactivity the (3-methylpentadienyl)$Fe(CO)_2PPh_3^+$ cation (**6**, Scheme 2) with nucleophiles as a means for late-stage introduction of the 3-methyl-2Z,4-pentadienyl sidechain [8].

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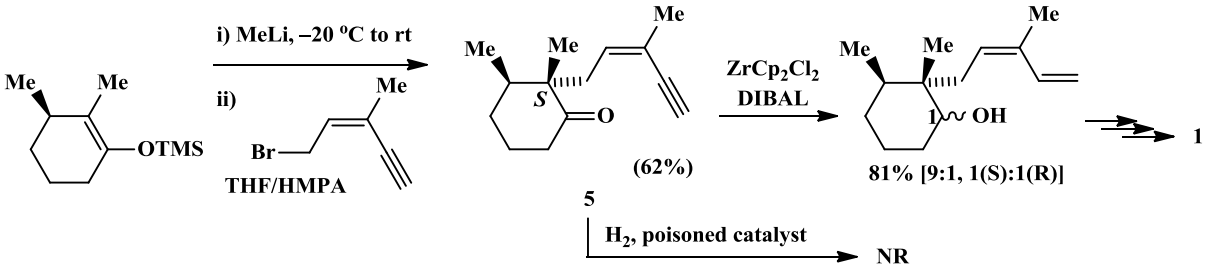


Scheme 1. Synthesis of the (3-methyl-2Z,4-pentadien-1-yl) side chain of (+)-striatene (ref. 5).

Heteroscyphic acids A, B and C, isolated from cultured cells of *Heteroscyphus planus*, were assigned the proposed structures **7a**, **7b**, and **7c** (Figure 2) containing a 3-methyl-2*Z*,4-pentadienyl sidechain on the basis of their spectroscopic data [9]. We have previously [8a] utilized the (3-methylpentadienyl)Fe^+ cation **6** to prepare the methyl ester of the 8-desmethyl-analog (**8**) of **7a**. Comparison of the NMR spectral data for **8** with that reported for heteroscyphic acid A led to the conclusion that the structures of the heteroscyphic acids were more consistent with a 3-methyl-2*E*, 4-pentadienyl sidechain. We herein report the full experimental details for these studies.

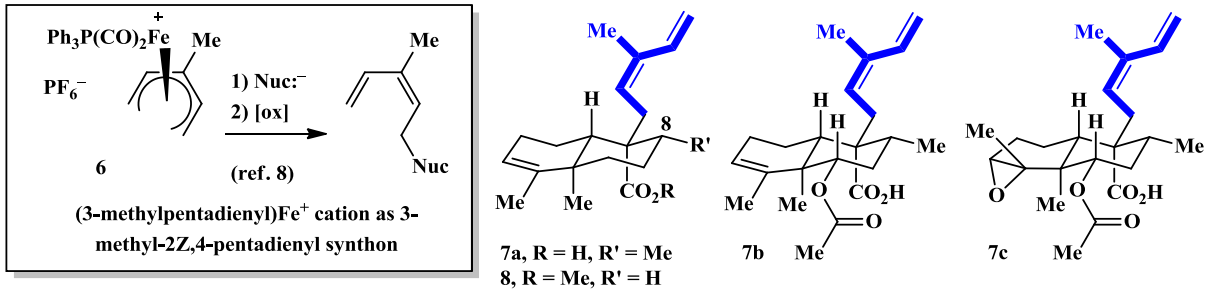
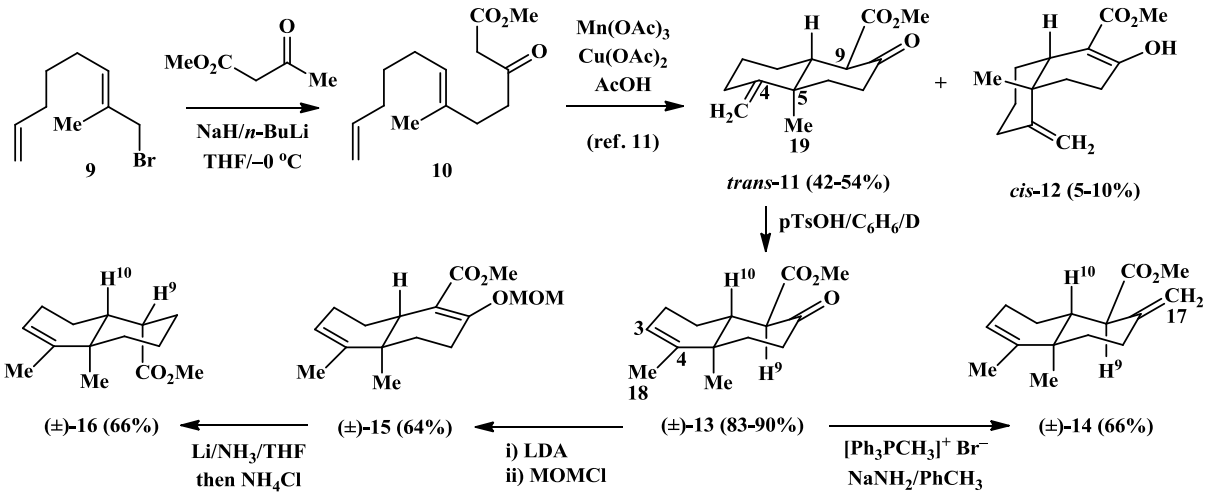


Figure 2. (3-Methylpentadienyl)Fe^+ cation as a synthon for 3-methyl-2Z,4-pentadien-1-yl and the "proposed" structures for heteroscyphic acids A, B and C.



Scheme 2. Synthesis of octahydronaphthalene synthons (heteroscyphic atom numbering).

Results and Discussion

Alkylation of the dianion of methylacetoacetate with the known [10] bromide **9** gave the acyclic β-ketoester **10** (Scheme 2). Oxidative cyclization of **10**, according to the literature procedure [11] gave a chromatographically separable mixture of *trans*-decalone (±)-**11** along with minor amounts of the *cis*-isomer (±)-**12**. Separation of these two isomers was facilitated by the fact that **12** exists almost entirely in its enol tautomer. Compounds **11** and **12** were characterized by comparison to the literature data for the corresponding ethyl esters [11]. Acid catalyzed

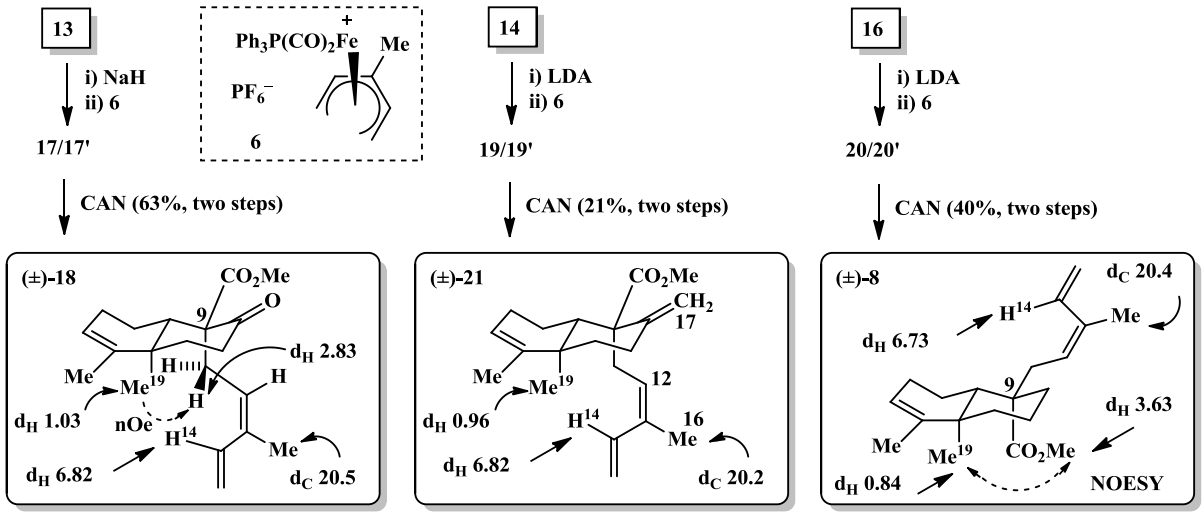
isomerization of the exocyclic olefin of **11** gave the endocyclic isomer (±)-**13**. The structural assignment of **13** was based on its NMR spectral data. In particular signals at δ 140.1 and 122.2 ppm in the ^{13}C NMR spectrum and at δ 5.29 (1H, m) and 1.65 ppm (3H, d, *J* = 1.5 Hz) in the ^{1}H NMR spectrum are characteristic of the C-3 and C-4 olefinic carbons and their associated proton and methyl group respectively.

Attempted olefination of **13** with the ylide generated from the reaction of butyl lithium with methyltriphenylphosphonium bromide in THF gave recovered starting material; presumably due to deprotonation of the acidic β-ketoester in polar solvents. Alternatively, addition of the salt-free ylide generated from trimethylphosphonium bromide with sodium amide in toluene [12] to **13** gave (±)-**14** in moderate yield. The structural assignment of **14** was based on its NMR spectral data. In particular, signals at δ 146.2 and 107.9 ppm in the ^{13}C NMR spectrum and at δ 4.80 (1H, br s) and 4.49 ppm (1H, br s) in the ^{1}H NMR spectrum are characteristic of the exocyclic olefinic carbons and the attached protons.

β-Ketoester **13** was converted into its methoxymethyl vinyl ether (±)-**15** by treatment with LDA followed by reaction with MOMCl. *O*-alkylation (as compared to *C*-alkylation) was evident by the presence of two olefinic peaks in the ^{13}C NMR spectrum of **15** at δ 151.1 and 116.3 ppm. Treatment of **15** with Li/NH_3 gave (±)-**16** via reduction of the enoate of **15**, followed by elimination of $CH_3OCH_2O^-$ anion and reduction of the resultant enoate [13]. The ester substituent in **16** was assigned to occupy an axial orientation on the basis of its ^{1}H NMR spectral data. In particular, the signal for H-9 (δ 2.57-2.49 ppm) of **16** did not evidence any large couplings, and thus pointed to an equatorial orientation for H-9.

With octahydronaphthalene synthons **13**, **14**, and **16** successfully prepared, attention was turned to installation of the 3-methyl-2*Z*,4-pentadien-1-yl sidechain. Toward this end, the sodium salt of **13**, generated by reaction with sodium hydride, was reacted with (3-methylpentadienyl)iron(1+) cation **6** to afford a mixture of diastereomeric complexes **17**/**17'** (Scheme 3). While the mixture of **17**/**17'** gave a satisfactory combustion analysis, interpretation of the NMR spectra was complicated due to signal overlap of the diastereomers as well as ^{31}P coupling. Nonetheless, oxidative decomplexation of this mixture gave a single product (±)-**18**. In a similar fashion, the lithium salt of **14** or **16** (generated by reaction with LDA) with **6**, gave a mixture of isomeric complexes **19**/**19'** or **20**/**20'** respectively; decomplexation of each mixture gave a single product (±)-**21** or (±)-**8**.

The structural assignments for **18**, **21** and **8** were based on their NMR spectral data. For products **18** and **21**, the pentadienyl sidechain was assigned the β-orientation, while for **8** the sidechain was assigned the α-orientation. In particular, for **18** the singlet for Me-19 appears at δ 1.03 ppm while for **8** this singlet appears at δ 0.84 ppm. The upfield chemical shift for this signal of **8** is consistent with an axial ester group at C-9 [14]. In addition, there is an nOE interaction observed between Me-19 and one of the H-12 protons of **18**, while a NOESY interaction was observed between the Me-19 and the methyl ester of **8**. For **21** the upfield chemical shifts of the H-17 olefinic methylene protons (δ 4.78 and 5.00 ppm) may be attributed to the anisotropic effect of the neighboring ester substituent in an α-orientation. Notably, these orientations are consistent with the known [15] stereoselectivity for alkylation on the α-face of other bicyclo[4.4.0]decane β-ketoesters while alkylation of the exocyclic enolate derived from a bicyclo[4.4.0]decane 2-carboxylate generally proceeds on the β-face [16]. In addition, the 3-methyl-2,4-pentadienyl side chain for **18**, **21** and **8** were all assigned the *Z*-configuration. In particular, the signals for H-14 appear at ca. δ 6.8-6.7 ppm while signals for the C-14, C-15 and the dienyl methyl C-16 appear at ca. δ 135, 114 and 20 ppm respectively. These chemical shifts are characteristic of a 3-methyl-2Z,4-pentadienyl group [2-5]. This was found to be in sharp contrast to the chemical shifts reported [9] for H14 (δ 6.37 ppm) C14, C15 and the dienyl methyl C16 (δ 141.7, 111.1 and 12.1 ppm) of the sidechain of heteroscyphic acid methyl ester. In fact, these chemical shifts are more consistent with those reported [17] for diterpenes which possess a 3-methyl-2*E*,4-pentadienyl sidechain.



Scheme 3. Dienylation of octahydronaphthalenes **13**, **14** and **16** followed by decomplexation (heteroscyphic acid atom numbering).

Conclusion

The ability to rapidly introduce a 3-methyl-2*Z*, 4-pentadienyl sidechain was demonstrated by the synthesis of **8**, a nor-diterpene related to the *proposed* structure of heteroscyphic acid A, as well as **18** and **21**. While this synthetic exercise revealed that the sidechains of the heteroscyphic acids more likely possess the *E*-stereochemistry, this methodology might be applied to the synthesis of compounds such as **1**-**4**.

Acknowledgements

This work was supported by the National Science Foundation (CHE-0415771). Mass spectrometry was provided by the Washington University Mass Specrometry Resource, an NIH Research Resource.

Experimental Section

^{1}H and proton-decoupled ^{13}C NMR spectra were recorded at 300 MHz and 75 MHz respectively. Proton and carbon assignments refer to heteroscyphic acid skeleton numbering. High-resolution mass spectra were obtained from the Washington University Resource for Biomedical and Bioorganic mass spectrometry. Tetrahydrofuran was distilled from sodium benzophenone ketyl prior to use. Anhydrous CH_2Cl_2 and anhydrous DMF were purchased from Aldrich Chemical Company. Compounds **6**[8b] and **9**[10] were prepared by literature procedures.

Methyl 6-methyl-3-oxo-6,11-dodecadienoate (10). To a flame-dried round-bottom flask, NaH (60% dispersion in mineral oil, 2.53 g, 63.3 mmol) was suspended in dry THF (165 mL) under N_2. The suspension was cooled in an ice bath and methyl acetoacetate (6.81 g, 58.7 mmol) was added slowly (CAUTION: hydrogen gas is evolved during the addition). The mixture was stirred for 10 min, and then a solution of *n*-butyl lithium in THF (2.5 M, 25.3 mL, 63.3 mmol) was added. During this addition, the solution became a bright orange in color. After stirring at 0 °C for 10 min, a solution of 1-bromo-2-methyl-2,7-octadiene (5.96 g, 29.4 mmol) in THF (15 mL) was added. The ice bath was removed and the solution stirred at room temperature for 30 min. A solution of 3 M HCl (50 mL) was added followed by ether (50 mL). The mixture was separated and the aqueous layer was extracted several time with ether. The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2, hexanes-ethyl-acetate = 8:1 → 5:1 gradient) to afford **10** (5.21 g, 75%) as a pale yellow oil**;**
IR (neat) 3076, 2927, 1750, 1717, 1637, 911 cm^{-1}.
^{1}H NMR ($CDCl_3$): δ = 5.80 (1H, dtd, *J* = 16.9, 6.8, 3.3 Hz, H-11), 5.13 (1H, br t, *J* = 7.7 Hz, H-7), 4.97 (2H, m, =CH_2), 3.74 (3H, s, OMe), 3.46 (2H, s, H-2), 2.64 (2H, br t, *J* = 7.5 Hz), 2.27 (2H, br t, *J* = 7.8 Hz), 2.04-1.78 (4H, m), 1.59 (3H, s, Me-6), 1.41 (2H, pent, *J* = 7.3 Hz).
^{13}C NMR ($CDCl_3$): δ = 202.5 (C-3), 167.7 (C-1), 138.9 (C-10), 133.3 (C-6), 125.4 (C-7), 114.6 (C-11), 52.6 (OMe), 49.2, 42.0, 33.6, 33.4, 29.2, 27.6, 16.4 (Me-6).
Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30. Found: C, 70.65; H, 9.17.

Decahydro-4a-methyl-5-methylene-2-oxo-1-naphthalenecarboxylic acid methyl ester (11). To a degassed solution of **10** (3.31 g, 13.9 mmol) dissolved in glacial acetic acid (35 mL) was added solid $Mn(OAc)_3$ (1.75 g, 6.53 mmol), followed by solid $Cu(OAc)_2$ (0.590 g, 3.24 mmol). The reaction mixture was stirred under N_2 for 7 h at room temperature and then filtered through a bed of celite. The filter bed was washed several times with ether,

the combined ethereal extracts were washed with saturated $NaHCO_3$, followed by water, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2, hexanes-ethyl acetate = 8:1 → 5:1 gradient) to afford (±)-**11**
(1.45 g, 44%) as a colorless oil, followed by a variable but minor amount of the *cis*-isomer (**10**).
11: IR (neat) 3086, 1715, 1635 cm^{-1}.
^{1}H NMR ($CDCl_3$): δ = 4.74 (1H, br s, $=CH_2$), 4.65 (1H, br s, $=CH_2$), 3.75 (3H, s, OMe), 3.27 (1H, d, *J* = 12.9 Hz, H-9), 2.55-2.47 (2H, m), 2.40-2.32 (1H, m), 2.05-1.76 (6H, m), 1.45-1.37 (2H, m), 1.22 (3H, s, Me-19).
^{13}C NMR ($CDCl_3$): δ = 205.6 (C-8), 170.3 (CO_2R), 155.0 (C-4), 106.3 ($=CH_2$), 60.3 (C-9), 52.3 (OMe), 47.7, 38.1, 38.0, 36.1, 32.7, 27.6, 27.4, 17.5 (Me-19).
FAB-HRMS *m/z* 237.1485 (calcd for $C_{14}H_{21}O_3$ [M+H$^+$] *m/z* 237.1491).

1,2,3,4,4a,7,8,8a-Octahydro-4a,5-dimethyl-2-oxo-1-naphthalenecarboxylic acid methyl ester (13). To a solution of **11** (200 mg, 0.847 mmol) in benzene (10 mL) was added *p*-toluenesulfonic acid monohydrate (30 mg, 0.16 mmol). The mixture was heated at reflux for 2 d under N_2. The mixture was cooled to room temperature and then a few drops of triethylamine were added to neutralize the acid. The mixture was filtered through a pad of celite, the filter bed washed with ether, and the combined organic layers were concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2, hexanes-ethyl acetate = 8:1) to afford (±)-**13**
(708 mg, 84%) as a colorless oil;
IR (neat) 1746, 1712 cm^{-1}.
^{1}H NMR ($CDCl_3$): δ = 5.29 (1H, br s, H-3), 3.74 (3H, s, OMe), 3.29 (1H, d, *J* = 13.5 Hz, H-9), 2.50-2.42 (2H, m), 2.19 (1H, td, *J* = 13.2, 2.7 Hz, H-10), 2.10-1.97 (3H, m), 1.65 (3H, d, *J* = 1.5 Hz, Me-18), 1.60-1.30 (3H, m), 1.16 (3H, s, Me-19).
^{13}C NMR ($CDCl_3$): δ = 206.0 (C-8), 170.5 (CO_2R), 140.1 (C-4), 122.2 (C-3), 60.0 (C-9), 52.2 (OMe), 45.2, 37.9, 36.4, 35.3, 25.7, 23.8, 18.8 (Me-18), 17.7 (Me-19).
FAB-HRMS *m/z* 237.1485 (calcd for $C_{14}H_{21}O_3$ [M+H$^+$] *m/z* 237.1491).

1,2,3,4,4a,7,8,8a-Octahydro-4a,5-dimethyl-2-methylene-1-naphthalenecarboxylic acid methyl ester (14). To a suspension of $NaNH_2$ (637 mg, 16.3 mmol) in dry toluene (41 mL) under N_2, was added methyltriphenylphosphonium bromide (4.48 g, 12.5 mmol), and the mixture was heated at reflux for 3 h. During this time formation of the ylide was detected by change of the solution to a bright orange color. The warm solution was transferred by a cannula to a solution of **13** (593 mg, 2.51 mmol) in toluene (6 mL) under N_2. The reaction mixture was stirred at room temperature for 6 h and then filtered through a pad of celite. The filtrate was concentrated under reduced pressure and the residue was dissolved in hexanes to induce the precipitation of triphenylphosphine oxide and then filtered again. The filtrate was washed with water, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (SiO_2, hexanes-ethyl acetate = 8:1) to afford (±)-**14**
(382 mg, 66%) as a colorless oil.
IR (neat) 2937, 1740, 1645, 891 cm^{-1}.
^{1}H NMR ($CDCl_3$): δ = 5.27-5.22 (1H, narrow m, H-3), 4.80 (1H, br s, $=CH_2$), 4.49 (1H, br s, $=CH_2$), 3.75 (3H, s, OMe), 3.09 (1H, d, *J* = 12.5 Hz, H-9), 2.36-2.29 (2H, m), 2.10-1.96 (2H, m), 1.82 (1H, td, *J* = 12.3, 3.1 Hz, H-10), 1.62 (3H, br s, Me-18), 1.55-1.20 (4H, m), 1.06 (3H, s, Me-19).
^{13}C NMR ($CDCl_3$): δ = 174.1 (CO_2R), 146.2 (C-8), 141.7 (C-4), 121.1 (C-3), 107.9 ($=CH_2$), 52.0 (OMe), 51.6, 45.7, 37.0, 36.7, 31.4, 25.9, 23.2, 18.8, 18.2.
FAB-HRMS *m/z* 234.1615 (calcd for $C_{15}H_{22}O_3$ [M$^+$] *m/z* 234.1620).

3,4,4a,7,8,8a-Hexahydro-2-(methoxymethoxy)-4a,5-dimethyl-1-naphthalenecarboxylic acid methyl ester (15). To a suspension of NaH (40 mg, 1.0 mmol) in HMPA (3 mL) at 0 ^{o}C under N_2 was added a solution of **13** (200 mg, 0.847 mmol) in HMPA (3 mL). The reaction mixture was warmed to room temperature over a 2 h period. To this solution was added chloromethyl methyl ether (82 mg, 1.0 mmol) and the reaction mixture was stirred for an additional 3 h. The resulting mixture was poured into a separatory funnel containing ice-water, saturated $NaHCO_3$ (10 mL) and ether (15 mL). The layers were separated, and the aqueous layer was extracted several times with ether. The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2, hexanes-ethyl acetate = 10:1) to afford (±)-**15**
(150 mg, 64%) as a colorless solid; mp 65-68 ^{o}C;
IR (neat) 2949, 2830, 1725, 1680 cm^{-1}.
^{1}H NMR ($CDCl_3$): δ = 5.23 (1H, br s, H-3), 4.91 (1H, d, *J* = 6.9 Hz, $OC\underline{H_2}OMe$), 4.85 (1H, d, *J* = 6.9 Hz, $OC\underline{H_2}OMe$), 3.73 (3H, s, $CO_2\underline{Me}$), 3.42 (3H, s, $OCH_2O\underline{Me}$), 2.57-2.49 (1H, m), 2.39-2.30 (2H, m), 2.10-2.02 (2H, m), 1.97-1.88 (1H, m), 1.64 (3H, br s, Me-18), 1.56-1.40 (3H, m), 0.98 (3H, s, Me-19).
^{13}C NMR ($CDCl_3$): δ = 169.5 (CO_2R), 151.1 (C-8), 141.4 (C-4), 121.2 (C-3), 116.3 (C-9), 93.2 ($O\underline{C}H_2OMe$), 56.5 ($OCH_2O\underline{Me}$), 51.6 ($CO_2\underline{Me}$), 41.7, 35.9, 31.8, 25.7, 22.8, 21.4, 18.9, 18.2.
Anal. Calcd for $C_{16}H_{24}O_4$: C, 68.55; H, 8.63. Found: C, 68.69; H, 8.46.

1,2,3,4,4a,7,8,8a-Octahydro-4a,5-dimethyl-1-naphthalenecarboxylic acid methyl ester (16). To a dispersion of lithium metal (80 mg, 12 mmol) in liquid NH_3 at -78 ^{o}C under N_2 was added a solution of **15** (460 mg, 1.64 mmol) in ether (8 mL). The reaction mixture was stirred at -78 ^{o}C for 15 min, and then quenched by addition of solid NH_4Cl (2.46 g) in one portion. The mixture was stirred for

an additional 30 min at -78 °C and then slowly warmed to room temperature. Additional ether (30 mL) was added, and the mixture was filtered through a pad of filter-aid. The inorganic salts were washed several times with ether and the combined ethereal layers were concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2, hexanes-ethyl acetate = 10:1) to afford (±)-**16**
(240 mg, 66%) as a colorless oil.
IR (neat) 1728 cm^{-1}.
^{1}H NMR ($CDCl_3$): δ = 5.23 (1H, m, H-3), 3.66 (3H, s, OMe), 2.53 (1H, br t, *J* = 4.8 Hz, H-9), 2.21-2.12 (1H, m), 2.06-1.85 (4H, m), 1.80-1.72 (2H, m), 1.66-1.61 (1H, m), 1.57 (3H, d, *J* = 1.8 Hz, Me-18), 1.44-1.30 (2H, m), 1.13 (1H, dt, *J* = 13.2, 4.1 Hz), 0.86 (3H, s, Me-19);
^{13}C NMR ($CDCl_3$): δ = 176.2 (CO_2R), 143.0 (C-4), 121.2 (C-3), 51.3 (OMe), 46.1, 43.3, 38.3, 36.8, 28.6, 27.0, 25.5, 19.3, 18.2, 17.5.
EI-HRMS *m/z* 222.1619 (calcd for $C_{14}H_{23}O_2$ [M+H$^+$] *m/z* 222.1620).

1,2,3,4,4a,7,8,8a-Octahydro-4a,5-dimethyl-1-(3-methyl-2*Z*,4-pentadien-1-yl)-2-oxo-1-naphthalenecarboxylic acid methyl ester (18). To a solution of NaH (25 mg, 0.64 mmol) in dry THF (10 mL) at 0 °C under N_2, was added a solution of **13** (150 mg, 0.635 mmol) in THF (10 mL). The mixture was stirred for 30 min, and then solid cation **6** (381 mg, 0.635 mmol) was added in one portion. The reaction mixture was stirred at 0 °C for 1 h and then 30 min at room temperature. The reaction mixture was poured into saturated NaCl solution (15 mL), and extracted several times with ethyl acetate. The combined extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2, hexanes-ethyl acetate = 8:1) to afford a mixture of diastereomeric diene-iron complexes **17**/**17'**
(325 mg, 75%) as a yellow solid. mp (decomposes) 89-100 °C.
The ^{1}H and ^{13}C NMR spectra for this product were too complex for complete interpretation due to the presence of diastereomers.
^{1}H NMR (partial, $CDCl_3$): δ = 7.56-7.30 (m, 15H, PPh_3), 5.32-5.26 (m, 1H), 4.24-4.07 (br m, 1H), 3.63 and 3.61 (2 x s, 3H).
Anal. calcd. for $C_{40}H_{43}O_5PFe$: C, 69.57; H, 6.27. Found: C, 69.42; H, 6.40.

To a solution of the **17/17'** (110 mg, 0.159 mmol) in methanol (10 mL) was added solid ceric ammonium nitrate [CAN] (220 mg, 0.401 mmol) in two portions. Monitoring of the reaction by TLC indicated that complete disappearance of **17/17'** in 30 min. Water (15 mL) was added and the reaction mixture was extracted several times with ether. The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2, hexanes-ethyl acetate = 10:1) to afford (±)-**18**
(50 mg, 99%) as a colorless oil;
IR (neat) 2950, 1713, 1435, 1217 cm^{-1}.
^{1}H NMR ($CDCl_3$): δ = 6.82 (1H, dd, *J* = 17.3, 10.7 Hz, H-14), 5.30-5.18 (3H total, br m & d, *J* = 16.6 Hz, H-3, H12 and H-15$_Z$), 5.12 (1H, d, *J* = 10.9 Hz, H-15$_E$), 3.66 (3H, s, OMe), 2.83 (1H, dd, *J* = 14.7, 6.5 Hz, H-11), 2.62 (1H, dd, *J* = 14.4, 9.1 Hz, H-11'), 2.47 (1H, ddd, *J* = 15.5, 4.7, 2.3 Hz, H-7$_{eq}$), 2.10-1.96 (1H, m), 1.90-1.78 (2H, m), 1.72 (3H, s, Me-16), 1.65-1.63 (1H, m), 1.54 (3H, s, Me-18), 1.43 (1H, td, *J* = 16.5, 4.9 Hz), 1.08-1.04 (2H, m), 1.03 (3H, s, Me-19).
^{13}C NMR ($CDCl_3$): δ = 208.0 (C-8), 173.9 (CO_2Me), 141.2 (C-4), 135.1 (C-14), 133.3, 125.1, 122.4 (C-3), 114.6 (C-15), 61.8 (C-9), 52.3 (OMe), 50.0, 38.1, 37.7, 36.4, 31.0, 27.2, 21.1, 20.5 (Me-16), 18.6, 17.5.
FAB-HRMS *m/z* 323.2182 (calcd for $C_{20}H_{28}O_3Li$ (M+Li$^+$) *m/z* 323.2199).

1,2,3,4,4a,7,8,8a-Octahydro-4a,5-dimethyl-1-(3-methyl-2*Z*,4-pentadien-1-yl)-2-methylene-1-naphthalenecarboxylic acid methyl ester (21). To a solution of **14** (100 mg, 0.427 mmol) in dry THF (10 mL) at 0 °C under N_2, was added a solution of lithium diisopropylamine in THF (1.8 M, 0.3 mL, 0.5 mmol). The mixture was stirred for 1 h at 0 °C, and then solid cation **6** (0.31 g, 0.54 mmol) was added in one portion. The reaction mixture was stirred for 3 h and then worked up in a fashion similar to that for **17**/**17'**. Purification of the residue by column chromatography (SiO_2, hexanes-ethyl acetate = 20:1) gave a diastereomeric mixture of diene-iron complexes **19/19'**
(70 mg, 30%) as a yellow oil.
The ^{1}H and ^{13}C NMR spectra for this product were too complex for complete interpretation due to the presence of diastereomers.
^{1}H NMR (partial, $CDCl_3$): δ = 7.56-7.32 (m, 15H, PPh_3), 5.26-5.05 (m, 3H), 4.21-4.10 (br m, 1H), 3.64 and 3.61 (2 x s, 3H).
^{13}C NMR (partial, $CDCl_3$, diastereomeric signals reported as pairs: δ = 176.6 and 175.8 ($\underline{C}O_2Me$), 149.7, 146.9, 142.9 and 142.6 (C3), 136.3 (d, J_{PH} = 37.5 Hz), 133.3 (d, J_{PH} = 10.2 Hz), 129.8, 128.3 (d, J_{PH} = 8.7 Hz), 121.7 and 121.2, 112.0 and 111.1, 103.1 and 102.3, 94.1 and 93.45.
Anal. calcd. for $C_{41}H_{45}O_4PFe \cdot H_2O$: C, 69.70; H, 6.70. Found: C, 69.77; H, 6.95.

Decomplexation of the mixture of **19/19'** (70 mg, 0.16 mmol) in methanol (10 mL) with CAN (112 mg, 0.204 mmol) was carried out in a fashion similar to the decomplexation of **17**/**17'**. Purification of the residue by column chromatography (SiO_2, hexanes-ethyl acetate = 10:1) gave (±)-**21**
(22 mg, 70%) as a colorless oil;
IR (neat) 2963, 1718, 1436, 1265 cm^{-1}.
^{1}H NMR ($CDCl_3$): δ = 6.82 (1H, dd, *J* = 17.4, 10.9 Hz, H-14), 5.34 (1H, t, *J* = 6.5 Hz, H-12), 5.28-5.20 (2H, m, H-3 and H-15$_Z$), 5.13 (1H, d, *J* = 10.6 Hz, H-15$_E$), 5.00 (1H, s, H-17$_E$), 4.78 (1H, s, H-17$_Z$),

3.65 (3H, s, OMe), 2.86-2.63 (3H, m), 2.34-2.25 (1H, m), 2.02-1.78 (8H, m), 1.57 (3H, br s, Me-18), 1.30-1.20 (2H, m), 0.95 (3H, s, Me-19).
^{13}C NMR ($CDCl_3$): δ = 176.4 (CO_2R), 148.8 (C-8), 142.7 (C-4), 133.9, 133.7, 125.6, 121.7 (C-3), 114.5 (C-15), 110.6 (C-17), 53.7, 50.6, 38.9, 38.4, 32.4, 31.6, 29.9, 27.5, 20.8, 20.2 (Me-16), 18.4, 17.8.
FAB-HRMS *m/z* 314.2240 (calcd for $C_{21}H_{30}O_2$ [M+H$^+$] *m/z* 314.2246).

1,2,3,4,4a,7,8,8a-Octahydro-4a,5-dimethyl-1-(3-methyl-2*Z*,4-pentadienyl)-1-naphthalenecarboxylic acid methyl ester (8). To a solution of **16** (100 mg, 0.451 mmol) in dry THF (4 mL) at -78 ^{o}C under N_2, was added a solution of lithium diisopropylamine in THF (0.5 mmol, freshly prepared from diisopropylamine and *n*-butyl lithium). The mixture was stirred for 30 min, and then solid cation **6** (207 mg, 0.451 mmol) was added in one portion. The reaction mixture was warmed at room temperature and stirred for an additional 3 h. The reaction mixture was quenched with 1M HCl (10 mL), and extracted several times with ether. The combined extracts were washed with water, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2, hexanes-ethyl acetate = 10:1) to afford a diastereomeric mixture of diene-iron complexes **20/20'**
(304 mg, 100%) as a yellow solid, which was used in the next step without further characterization.
Decomplexation of **20/20'** (200 mg, 0.296 mmol) with CAN (405 mg, 0.741 mmol) was carried out in a fashion similar to that for the decomplexation **17/17'** except that in DMF (15 mL) was used a solvent instead of methanol. Purification of the residue by column chromatography (SiO_2, hexanes-ethyl acetate = 10:1) followed by a second purification by column chromatography (SiO_2 impregnated with ~10 % $AgNO_3$, hexanes) gave (±)-**8** (35 mg, 40%) as a colorless oil;
IR (neat) 3054, 2987, 1720, 1422, 1265 cm^{-1}.
^{1}H NMR ($CDCl_3$): δ = 6.73 (1H, dd, *J* = 17.3, 10.8 Hz, H-14), 5.34-5.08 (4H total, m, H-3, H-12, H15$_E$ and H-15$_Z$), 3.63 (3H, s, OMe), 2.77 (1H, dd, *J* = 14.1, 8.3 Hz), 2.22-2.16 (2H, m), 2.06-1.87 (3H, m), 1.83 (3H, s, Me-16), 1.80-1.70 (2H, m), 1.58 (3H, br s, Me-18), 1.50-1.40 (2H, m), 1.26-0.86 (3H, m), 0.83 (3H, s, Me-19**)**.
^{13}C NMR ($CDCl_3$): δ = 177.3 (CO_2R), 143.2 (C-4), 135.2 (C-14), 133.6, 125.3, 121.5 (C-3), 114.3 (C-15), 55.9, 51.3 (OMe), 48.3, 38.8, 37.9, 37.0, 34.3, 27.5, 20.6, 20.4 (Me-16), 19.4, 18.5, 17.7.
FAB-HRMS *m/z* 303.2320 (calcd for $C_{20}H_{31}O_2$ [M+H$^+$] *m/z* 303.2324).

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