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Development of Organoiron Methodology for Preparation of the Polyene Natural Product Macrolactin A

This article is dedicated to Prof. Myron Rosenblum, a pioneer in organoiron chemistry

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Abstract

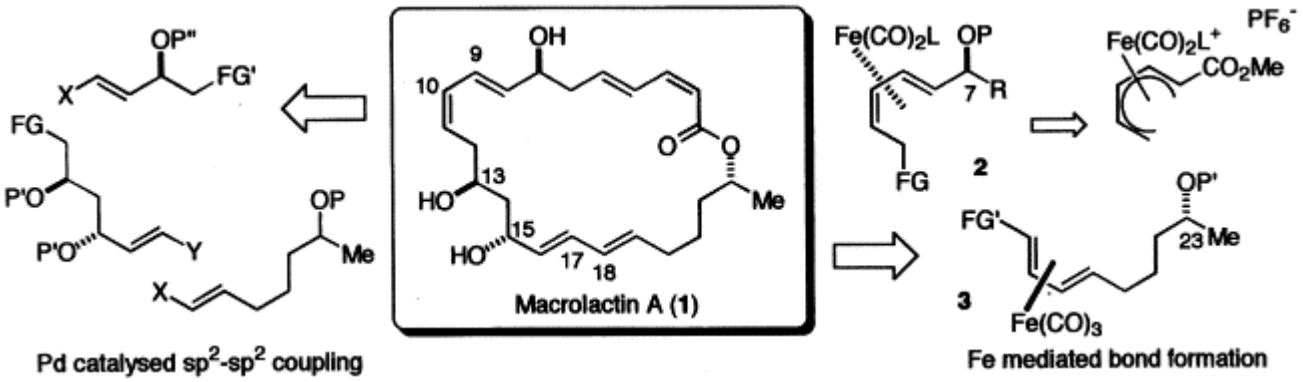
Methodology for the synthesis of the C7–C13 segment (**19**) and C14–C24 segment (**41**) of macrolactin A have been developed. Dicarbonyl(methyl 7-nitro-2*E*,4*Z*-heptadienoate)triphenylphosphineiron (**19**) is prepared by nucleophilic addition to a (1-methoxycarbonylpentadienyl)iron cation. The C23 stereocenter of **41** is established by introduction of a C20 stereocenter, chirality transfer from C20 to C23 followed by (diene)iron mediated selective ionic reduction of the C20 hydroxyl. The C15 stereocenter may be established by nitrile oxide–olefin cyclocondensation.

Keywords

Organoiron, macrolactin A, cyclocondensation

Macrolactin A (**1**) is a 24-membered polyene macrolide isolated from a taxonomically undefined deep sea bacterium.[1a] This compound exhibits antiviral activity against Herpes Simplex I and II and against HIV. The macrocyclic lactone structure of **1**, assigned on the basis of NMR spectroscopy,[1a] consists of three sets of conjugated dienes (C2–C5, C8–C11 and C16–19). The absolute stereochemistry of the four chiral centers (C7, C13, C15 and C23) were later assigned on the basis of chemical degradation and synthesis of the fragments.[1b]

Since the culturing of this bacterium has been 'unreliable', further biological research must rely on total synthesis. Two elegant syntheses of macrolactin A[2a,b] and one of its 13,15-di-*O*-methyl derivative[2c] have been reported. Each of these syntheses utilizes Pd-catalyzed cross-coupling for installation of the C17–C18 and the C9–C10 bonds (Scheme 1). While the former coupling proceeds in excellent yields (82%), the latter coupling proceeds in only modest yield and was described in one case as 'capricious'. In these syntheses, generation of the C7, C13, and C15 stereocenters was addressed in a variety of ways (chiral pool,[2c] asymmetric Sharpless epoxidation,[2c] asymmetric allylboration,[2a] or asymmetric aldol[2b]). Additional work concerning preparation of various segments of macrolactin A have been reported.[3]



Scheme 1. Y/X=I or SnR_3 or $B(OH)_2$; FG/FG'='functional group'.

An alternative organometallic route to macrolactin A relies on the application of *stoichiometric* acyclic (diene)iron complexes to organic synthesis.4., 5. One of the advantages of stoichiometric organometallic reagents is the ability to repeatedly utilize the same metal center to control a number of different bond forming reactions. Attachment of a carbonyl–iron adjunct to an acyclic diene has been shown to protect the diene against reduction, oxidation, and cycloaddition reactions.[6] In addition, the steric bulk of the $Fe(CO)_3$ group serves to effect diastereoselective bond formation at unsaturated centers *adjacent* to the coordinated diene. Finally, the electron-donor ability of the carbonyl–iron group allows for the generation of cationic centers adjacent to the coordinated diene (i.e. pentadienyl cations). Generation of the pentadienyl cation from an (*E*,*E*-dienol)iron

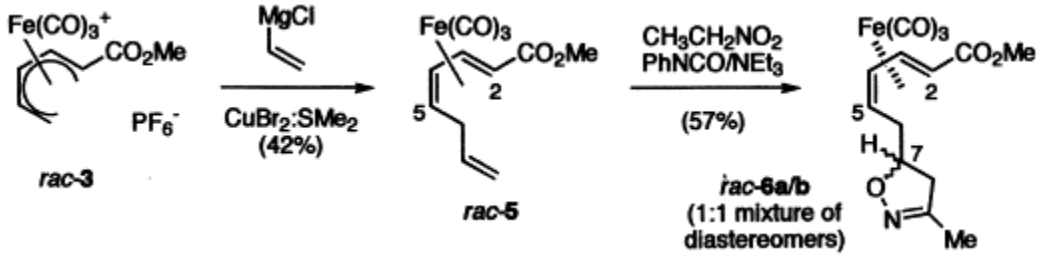
complex in the presence of a weak nucleophile results in the formation of *E*,*E*-diene complexes, while reaction of isolable cisoid (pentadienyl)iron cations with stronger nucleophiles can lead to the formation of *E*,*Z*-diene complexes.[7]

Our proposed synthetic strategy involves disconnection at the C13,C15 anti-diol group into two fragments **2** and **3** (Scheme 1). Recently, two groups independently reported the (diene)iron mediated, stereoselective preparation of this type of functionality via aldol condensations.5., 8. We focused our attention on utilizing nitrile oxide–olefin cycloaddition methodology[9] for joining fragments **2** and **3** (FG/FG'=CH_2NO_2/CH□CH_2). Moreover, the 8*E*,10*Z*-diene segment **2** might be generated via nucleophilic addition to a cisoid (pentadienyl)iron cation.

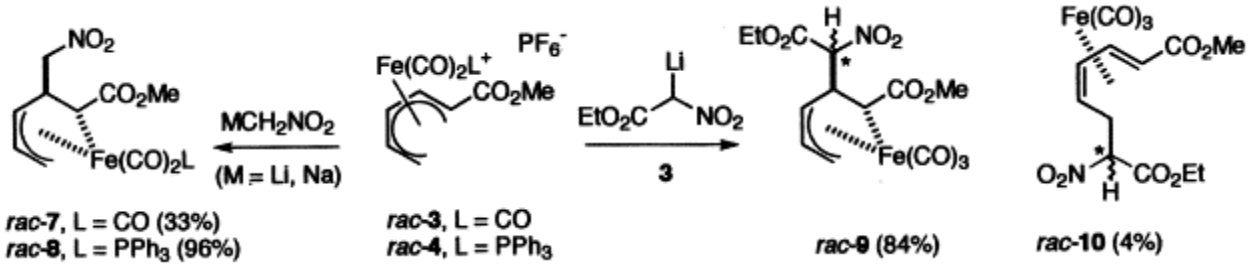
1. Results and Discussion

1.1. Preparation of the C7–C13 segment of macrolactin A

The (1-methoxycarbonylpentadienyl)Fe(CO)$_2$L$^+$ cations (**3**, L=CO)[10] and (**4**, L=PPh_3)[11] were prepared by literature methods. We and others have shown that organocuprates react with acyclic (pentadienyl)iron(1+) cations with excellent regioselectivity.10., 12. The reaction of vinyl magnesium chloride with *rac*-**3** in the presence of CuBr·Me_2S gave (methyl 2*E*,4*Z*,7-octatrienoate)Fe(CO)$_3$ (*rac*-**5**) (Scheme 2). The reaction of *rac*-**5** with acetonitrile oxide (derived from nitroethane under Mukaiyama conditions[13]) gave an equimolar mixture of isoxazolines *rac*-**6a**/**b**. The 2*E*,4*Z*-stereochemistries of triene **5** and isoxazolines **6a**/**b** were assigned on the basis of their NMR spectral data. In particular, the signals for H2, H3, H4, and H5 appear at ca. δ (2.1 (d), 6.06 (dd), 5.35 (dd), and 2.7–2.8 (m) ppm, respectively. Additionally the signals for C3 and C4 of **5** appear at δ 92.9 and 85.4 ppm, respectively. The diastereomeric isoxazolines **6a** and **6b** differ in the relative stereochemistry at C7 with respect to the diene–iron coordination. In contrast to the diastereoselective addition of nitrile oxides to (1,3,5-triene)Fe(CO)$_3$ complexes, the formation of **6a**/**b** in a 1:1 ratio indicates that the steric bulk of the Fe(CO)$_3$ group is too far distant from the pendent olefin and/or there is not a preferred reactive conformers about the C5–C6 and C6–C7 bonds.



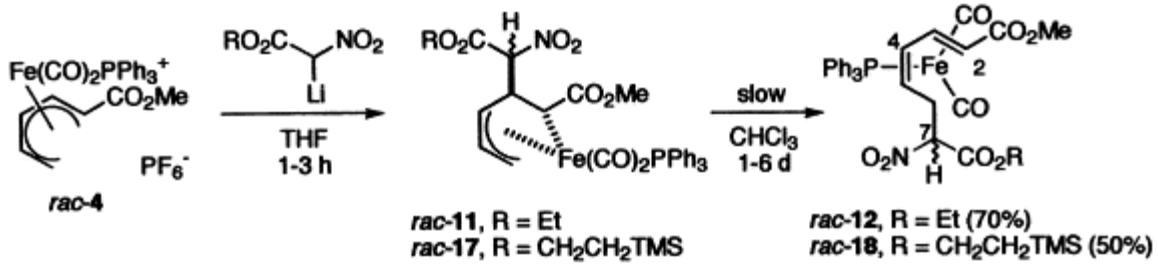
Scheme 2. As the above approach was not diastereoselective, we sought to interchange the reactive functionality in fragments **2** and **3** by preparing a (7-nitro-2*E*,4*Z*-dienoate)iron complex. The reaction of cations *rac*-**3** or *rac*-**4** with the anion of nitromethane gave the pentenediyl complexes *rac*-**7** or *rac*-**8**, respectively (Scheme 3). In a similar fashion, the reaction of cation *rac*-**3** with the anion of ethyl nitroacetate gave predominantly (pentenediyl)Fe(CO)$_3$ complex *rac*-**9** (84%) accompanied by very minor amounts of (diene)Fe(CO)$_3$ complex *rac*-**10** (4%) as a separable mixture. Both **9** and **10** were isolated as mixtures of diastereomers at the (∗) carbon with respect to the ligand–iron coordination.



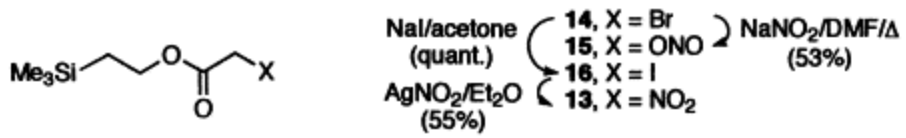
Scheme 3. The structures of **7**–**9** were assigned by comparison of their NMR spectral data with that of other known (pentenediyl)iron complexes.[11] In particular, the signals at ca. δ 7–9 ppm in their ^{13}C NMR spectra are characteristic of a carbon which is σ-bound to iron while the signals at ca. δ 0.2–0.0 ppm in their ^{1}H NMR spectra are characteristic of a proton on this type of carbon. The structural assignment for **10** was made by comparison of its NMR spectral data with that of known[11] (*E*,*Z*-diene)Fe(CO)$_3$ complexes.

Nucleophilic attack of a variety of soft carbon nucleophiles, including nitromethane anion, on (*cyclohexadienyl*)Fe(CO)$_3^+$ cations occurs at the cyclohexadienyl terminus to afford substituted (cyclohexadiene)iron products.[14] In contrast, the attack of 'soft' carbon nucleophiles, such as malonate anions, on *acyclic* (pentadienyl)iron(1+) cations bearing an electron withdrawing substituent proceeds at the C2 internal carbon to afford predominantly (pentenediyl)iron products.11., 15. This latter regioselectivity has been rationalized[11] as being the result of charge control (i.e. greater δ+ charge at C2/C4) of cations **3** and **4**. Since the p*K*a of nitromethane (17.2, DMSO as reference) is similar to that of dimethylmalonate (15.7), it might not be surprising that the regioselectivity for attack by nitromethane anion would be similar to that of malonate anion.

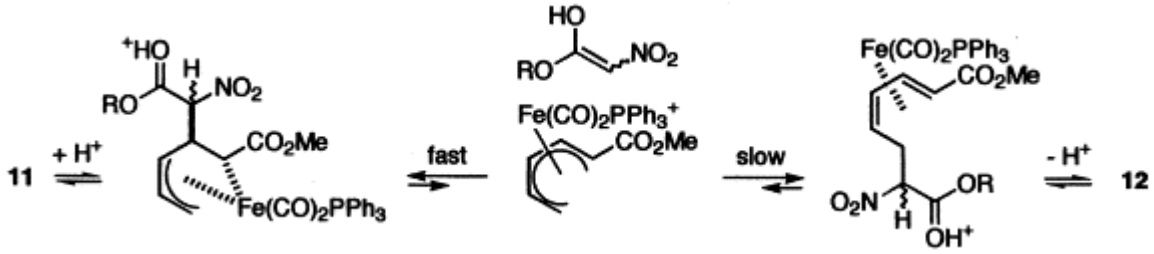
The reaction of cation *rac*-**4** with the anion of ethyl nitroacetate, followed by *aqueous* workup, gave the (pentenediyl)Fe(CO)$_2$PPh$_3$ complex *rac*-**11** as an equimolar mixture of diastereomers (Scheme 4). In contrast to (pentenediyl)iron complex **9**, which is constitutionally stable in solution, *(pentenediyl)iron complex rac-**11** rearranges to (E,Z-diene)iron complex rac-**12** upon standing in CDCl$_3$ for 1–2 days!* Thus, it may be inferred that attack of nitroacetate anion at C2 of **4** is the result of kinetic control.



Scheme 4. Since several attempts to remove the C8 ethoxycarbonyl group from diene complex **12** were unsuccessful, the preparation of 2-(trimethylsilyl)ethyl nitroacetate (**13**) was undertaken (Scheme 5). Reaction of 2-(trimethylsilyl)ethyl 2-bromoacetate (**14**)[16] with NaNO$_2$ (DMF/Δ) led to formation of the undesired nitrite **15** via *O*-alkylation. Reaction of **14** with NaI/acetone gave the iodoacetate **16**, which without further purification was treated with AgNO$_2$ in ether[17] to give **13** via *N*-alkylation (55% based on consumed **16**) along with minor amounts of the nitrite **15**. The reaction of cation *rac*-**4** with the anion of **13**, followed by aqueous workup, gave the (pentenediyl)Fe(CO)$_2$PPh$_3$ complex *rac*-**17** as an equimolar mixture of diastereomers (Scheme 4). Pentenediyl complex *rac*-**17** rearranges to *rac*-**18** standing in CHCl$_3$ solution for 6 days (50% yield from **4**).

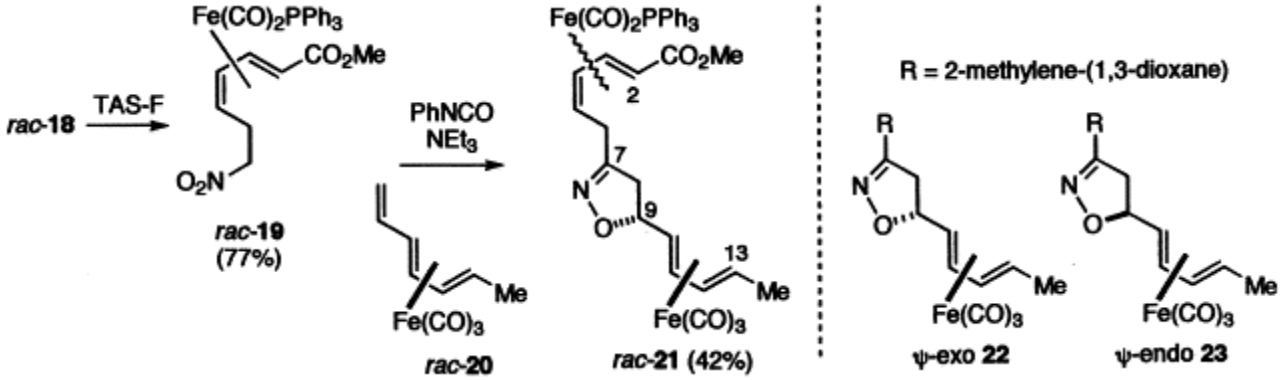


Scheme 5. The interconversion of **11** to **12** occurs slower in C_6D_6 solution (as compared to $CDCl_3$) such that ca. 30% of **11** remained after 7 days. In addition, treatment of an ethyl acetate solution of **11** with saturated aqueous NH_4Cl effected *rapid* rearrangement (<15 min) to **12**. We propose that interconversion of the kinetically controlled product **11** into the thermodynamically more stable diene complex **12** (and likewise **17**→**18**) occurs via protonation at the carbonyl oxygen followed by dissociation into the pentadienyl cation **4** and the ketene hemiacetal (Scheme 6). Recombination at C5 and deprotonation gives **12**. Notably, we[18] and others[19] have previously reported that nucleophilic attack on acyclic (pentadienyl)iron cations is reversible in certain cases.



Scheme 6. The structural assignments for **11**, **12**, **17** and **18** were made on the basis of their NMR spectral data. In particular, the signals at ca. δ 0.18 ppm in the ^{1}H NMR spectra of both **11** and **17** are characteristic of a proton on a carbon which is σ-bound to iron. For both diene complexes **12** and **18** the two diastereomeric signals for H7 appear as two sets of doublet of doublets at δ 4.69 and 4.57 ppm, indicating attachment of the nitroacetate group adjacent to a methylene carbon. Additionally, the signals for C3 and C4 appear at δ 90.4 and 86.9 ppm respectively, which is characteristic of a (2*E*,4*Z*-dienoate)iron complex (cf. **5**). Notably, while the signals for H3 of **12**, **18** and **10** are relatively similar (δ 5.91, 5.92 and 6.08 ppm respectively) the signals for H4 of **12** and **18** (δ 4.35 and 4.33, respectively) are shifted upfield compared to the corresponding signal of **10** (δ 5.31). This upfield shift may be attributed to the anisotropic effects of the triphenylphosphine ligand situated in the basal position of complexes **12** and **18** (cf. structure in Scheme 4).

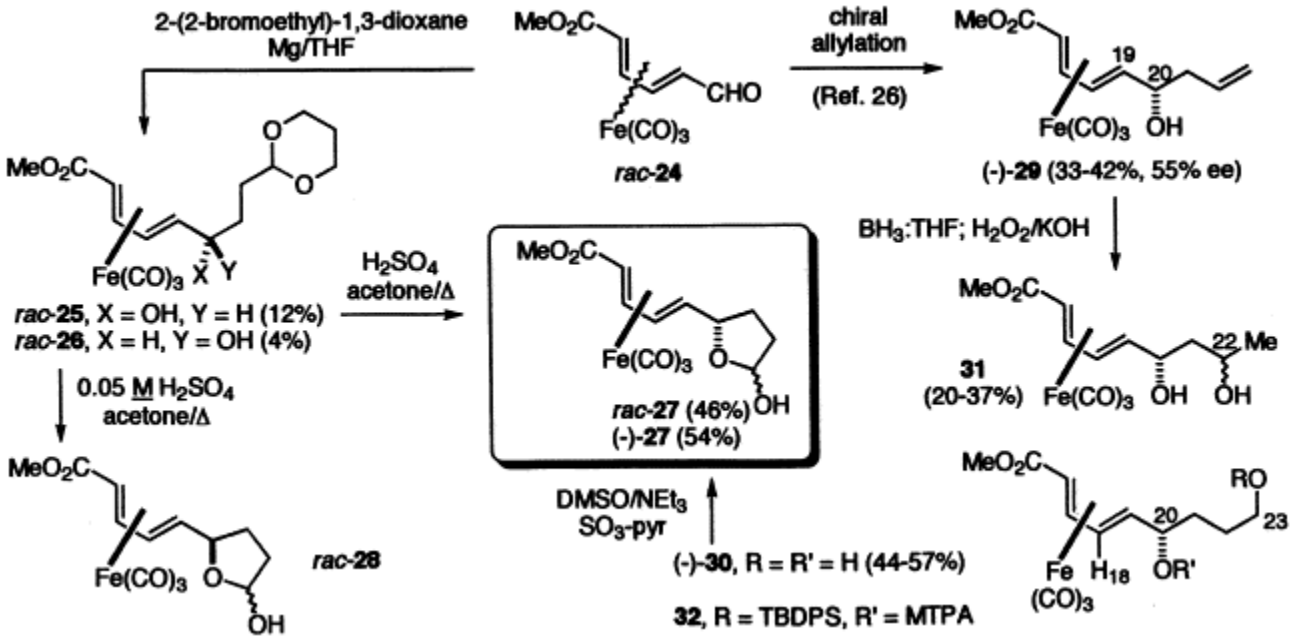
Removal of the 2-(trimethylsilyl)ethyl ester and decarboxylation of *rac*-**18** to afford *rac*-**19** could be achieved with TBAF (34–40%), however use of tris(dimethylamino)sulfur (trimethylsilyl)difluoride (TAS-F)[20] gave considerably better yields (77%, Scheme 7). Reaction of triene–iron complex *rac*-**20**[21a] with the nitrile oxide generated in situ from *rac*-**19** under Mukaiyama conditions gave the bimetallic tetraene isoxazoline **21**. While four sets of racemic diastereomers are possible, examination of the NMR spectra of **21** indicated the presence of *only two diastereomers*. The ψ-exo relative stereochemistry at C-9 of *rac*-**21** was assigned by comparison of the ^{13}C NMR chemical shifts for C-9, C-10, and C-11 with those of the known[21b] ψ-*exo* and ψ-*endo* dienylisoxazoline complexes **22** and **23**. In particular, the diastereomeric signals for **21** (ca. δ 60, 44 and 84 ppm) more closely match those of **22** (δ 59.4, 45.0 and 83.6 ppm) than those of **23** (δ 63.1, 48.0, and 85.5 ppm).



Scheme 7. In contrast to the non-diastereoselective nitrile oxide cyclocondensation to 'skipped' triene complex **5** (Scheme 2), addition of the nitrile oxide derived from **19** to the conjugated triene complex **20** occurs in a diastereoselective fashion. These results are consistent with approach of the nitrile oxide to a conjugated (triene)$Fe(CO)_3$ complex, in its *s-trans* conformer, on the face opposite to the metal.21., 22. The $Fe(CO)_2PPh_3$ group present in **19** does not influence the stereochemical outcome of this condensation.

1.2. Preparation of the C14–C24 segment of macrolactin A[23]

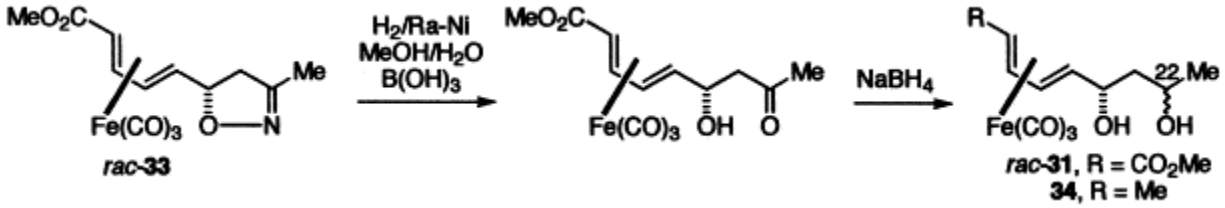
The strategy for preparation of the C14–C24 segment, based on our model studies,[4a] relied on diastereoselective introduction of an asymmetric center adjacent to the (diene)$Fe(CO)_3$ functionality at C20, relaying this asymmetry to the C23 center, and eventual removal of the initial stereocenter at C20. To this end, reaction of dienal complex *rac*-**24** with the Grignard reagent generated from 2-(2-bromoethyl)-1,3-dioxane gave a mixture of *rac*-**25** and *rac*-**26** in disappointing yield (Scheme 8). Reaction of *rac*-**24** with the alkyl lithium reagent derived from 2-(2-iodoethyl)-1,3-dioxane gave similar yields. The diastereoisomers are partially separable by column chromatography. The relative stereochemistries at C20 (macrolactin numbering) of **25** and **26** were tentatively assigned as ψ-*exo* and ψ-*endo*, respectively, on the basis of their relative chromatographic mobility (**25** more polar than **26**). It has been empirically found that ψ-*exo* diastereomeric alcohols are in general less mobile than their ψ-*endo* counterparts.[24] Hydrolysis of *rac*-**25** or *rac*-**26** gave lactols *rac*-**27** (46%) or *rac*-**28** (14%), respectively; each lactol is a mixture of diastereomers at the hemiacetal carbon.



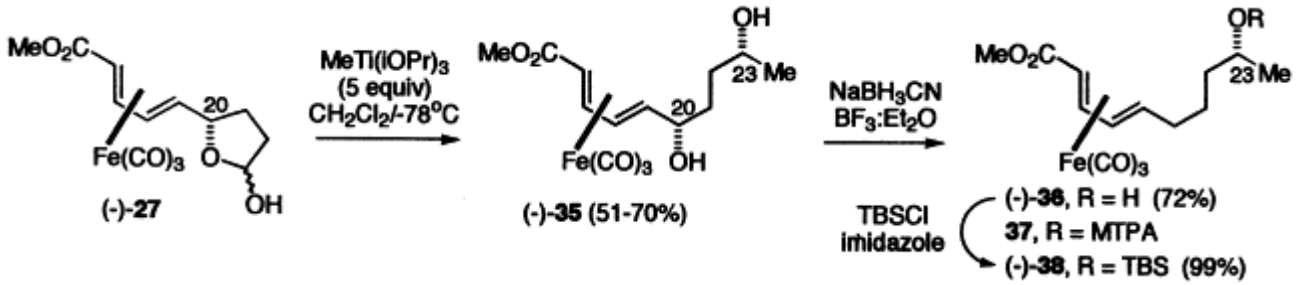
Scheme 8. Due to the low yields of this two step route to the lactols, an alternative three step route was explored. The reaction of *rac*-**24** with the allyl borane derived from (−)-$(IPC)_2BOMe$,[25] followed by oxidative workup gave (−)-**29** (33–42% yield, 54–56% ee). Full details of this allylation, as well as chiral allylation of other (dienal)$Fe(CO)_3$ complexes will be reported separately.[26] The hydroboration–oxidation of **29** has been previously reported[27] to afford only the 1,4-diol **30** (91%). In our hands, treatment of (−)-**29** by the literature procedure gave a separable mixture of (−)-**30** (44–57%) *and* 1,3-diol diastereomers **31** (20–37%) (Scheme 8). The ^1H NMR spectral data for (−)-**30** was identical with the literature data, while the identity **31** was established by independent synthesis (vide infra). Analysis of the ^1H NMR spectra (C_6D_6) of the 20-(*S*)- and 20-(*R*)-MTPA ester-23-TBDPS ethers **32** (derived from **30**) indicated separation of the H18 signals (δ 5.16 and 5.24 ppm, respectively). The Mosher's esters **32** were determined to be ca. 55–57% de by integration of these signals. The absolute stereochemistry at C20 (*S*) was assigned based on the relative chemical shifts of the signals for H19 of

each ((*S*)-**32** δ 0.78 ppm vs. (*R*)-**32** δ 0.66 ppm).[28] Oxidation of 1,4-diol (−)-**30** gave the lactol (−)-**27** as a mixture of epimers. The spectral data for (−)-**27** was identical with that of *rac*-**27**.

Reductive hydrolysis of the known[22] isoxazoline *rac*-**33**, followed by $NaBH_4$ reduction of the resultant hydroxyketone gave *rac*-**31** as a mixture of C22 epimers (Scheme 9). The ψ-*exo* relative stereochemistry of the diastereomeric mixture **31** was assigned by comparison of the ^{13}C NMR chemical shifts of the diol methine carbons with those of the known[21a] isomers of (5,7-nonadien-2,4-diol)$Fe(CO)_3$, *anti*-**34** and *syn*-**34**, for which the structure of *syn*-**34** was determined by X-ray diffraction analysis. In particular, the signals for the diastereomers **31** (δ 74.1, 71.3, 69.1 and 66.1 ppm) are similar to those of *anti*-**34** (δ 72.4 and 65.8 ppm) and *syn*-**34** (δ 75.5 and 69.1 ppm). The ^1H NMR spectral data for *rac*-**31** obtained in this fashion was identical to that for **31** obtained as a by-product of the hydroboration–oxidation of **29**. The formation of significant amounts of product resulting from Markovnikov addition in the hydroboration of 4-hydroxy-1-alkenes has been previously noted.[29]

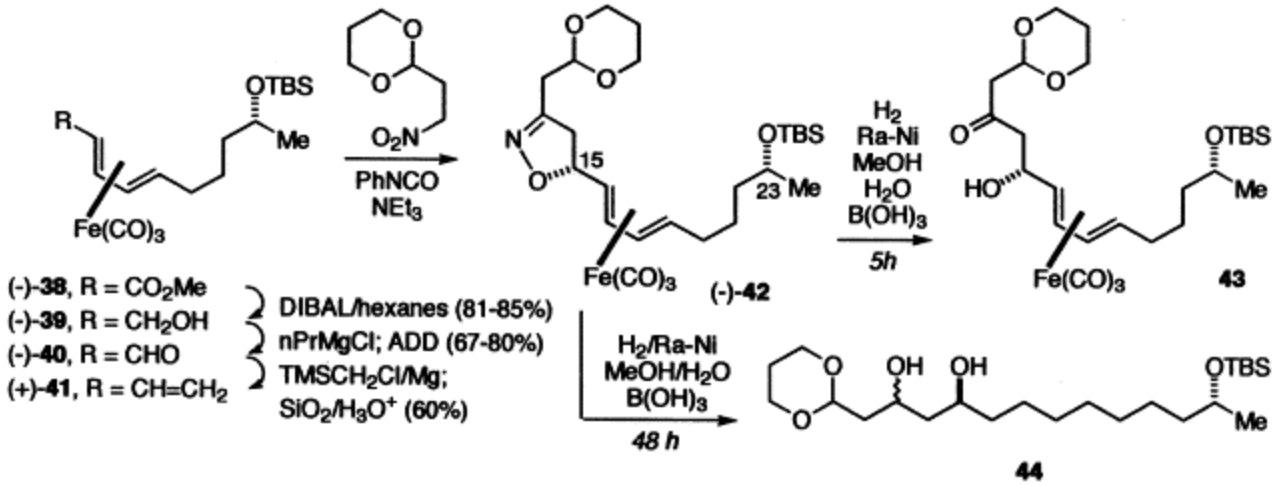


Scheme 9. Tsuchihashi et al.[30] have reported the methodology for the formation of *syn*-1,4-diols from lactols. They propose that this diastereoselectivity is the result of addition of a methyl–titanium nucleophile to a seven-membered titanium chelate of the hydroxy-aldehyde. In the event, reaction of dienyl lactol (−)-**27** with $MeTi(iPrO)_3$ gave a *single* diastereomeric diol, (−)-**35** (Scheme 10). After introduction of the C23 stereocenter by this methodology, removal of the superfluous C20 hydroxyl was required. Since dienyl dinitrobenzoate iron complexes undergo S_N1 solvolysis with retention of configuration due to the generation of a transoid (pentadienyl)iron cation,[31] it was anticipated that selective ionic reduction of the ψ-exo alcohol could be utilized.4., 5., 21. Reaction of (−)-**35** with $NaBH_3CN$ in the presence of $BF_3{\cdot}Et_2O$ gave the alcohol (−)-**36**. The absolute stereochemistry of (−)-**36** (i.e. 23R) was assigned on the basis of the relative chemical shifts of the C24 methyl groups of the corresponding (*R*)- and (*S*)-MTPA esters **37** (δ 1.35 and 1.27 ppm, respectively).[28] Integration of the MTPA methoxy signals (δ 3.54 and 3.57 ppm, respectively) indicated that the 23-Mosher's esters **37** were ca. 50–54% de. Protection of (−)-**36** as its TBS ether gave (−)-**38**.



Scheme 10. The *E*,*E*-stereochemistries of dienoate complexes **25**–**28**, **30**–**32**, and **35**–**38** were assigned on the basis of their NMR spectral data. In particular the signals for H17 and H18 (macrolactin numbering) appear at ca. δ 5.8–5.7 and 5.5–5.2 ppm while the signals for C17 and C18 appear at ca. δ 87–85 and 85–83 ppm, respectively. These signals are distinctly different compared to the those of (*E*,*Z*-dienoate)$Fe(CO)_3$ complexes (cf. **5**).

Reduction of ester (−)-**38** (DIBAL/hexanes) followed by oxidation of the resultant primary alcohol (−)-**39** (*n*PrMgCl; 1,1′-(azodicarbonyl)dipiperidine) gave aldehyde (−)-**40** (Scheme 11). The enantiomeric excess of (−)-**40** was assayed by treatment with (1*S*,2*S*)-*N*,*N*′-dimethyl-1,2-diphenyl-ethylenediamine/molecular sieves[32] to generate the diastereomeric imidazolidines. Integration of the diastereomeric methyl groups of the crude product (δ 2.54 and 2.19 ppm vs. δ 2.35 and 2.25 ppm) indicated the imidazolidines to be 55% de. Peterson olefination of (−)-**40** gave the complexed triene (+)-**41**. Reaction of (+)-**41** with 2-(2′-nitroethyl)-1,3-dioxane in the presence of phenylisocyanate and triethylamine led to the isolation of (−)-**42**. The relative stereochemistry of isoxazoline (−)-**42** was assigned as ψ-exo by comparison of its ^{13}C NMR spectral data for C15, C16, and C17 (macrolactin numbering, δ 59.6, 45.0 and 83.5 ppm) to that of **22** and **23** (vide supra). This sequence of nine steps, (−)-**29**→(−)-**42**, allows for introduction of the C15 and C23 stereocenters, *which are nine carbons separated*, in a diastereoselective fashion. Reductive hydrolysis of (−)-**42** (H_2, Ra-Ni, MeOH/H_2O, $B(OH)_3$) for 5 h gave the β-hydroxy ketone **43**, while reductive hydrolysis over 48 h resulted in loss of the $Fe(CO)_3$ adjunct, and reduction of the conjugated diene and ketone functionalities to give **44**. For **43** and **44**, the stereochemistries at C15 and C23 are assigned as indicated based on the assignments for **42**.



Scheme 11. The *E*,*E*-diene stereochemistries of complexes **39**, **41**, **42**, and **43** were assigned on the basis of their NMR spectral data. In particular the signals for H17 and H18 (macrolactin numbering) appeared at ca. δ 5.3–5.1 and 5.05 ppm while the signals for C17 and C18 appear at ca. δ 85.5 and 83 ppm, respectively. These signals are characteristic of (*E*,*Z*-dienol)$Fe(CO)_3$ complexes.[33]

1.3. Summary

Methodology for the construction of the C7–C13 and C14–C24 segments (**19** and **41**, respectively) of macrolactin A have been developed. For the former segment, the stereochemistry of the 8*E*,10*Z*-diene segment is established by a thermodynamically controlled addition of 2-(trimethylsilyl)ethyl nitroacetate to (1-methoxy-carbonylpentadienyl)$Fe(CO)_2PPh_3^+$ cation. For the latter segment, the C23 hydroxyl group is established by first generation of a C20 hydroxyl, followed by chirality relay of this asymmetry to the C23 center, and finally selective removal of the C20 hydroxyl. Furthermore, we have demonstrated that introduction of the C15 stereocenter relative to the C16–C19 (diene)$Fe(CO)_3$ group is possible by nitrile oxide–olefin cyclocondensation. Preparation of these segments in optically active form and eventual joining will be reported in due course.

2. Experimental

2.1. General data

Spectrograde solvents were used without purification with the exception of tetrahydrofuran and ether which were distilled from sodium benzophenone ketyl, and dichloromethane which was distilled from P_2O_5. Anhydrous hexanes and DMSO were purchased as Aldrich sure-seal solvents and were used without further purification. Hexanes for chromatography was distilled through a 60 cm Vigreux column prior to use. Column chromatography was performed on silica gel 60 (60–200 mesh, Aldrich) and 'flash' chromatography was performed on silica gel 60 (230–400 mesh, Aldrich).

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 and ^{13}C NMR spectra were recorded on a GE Omega GN-300 instrument at 300 and 75 MHz, respectively. Diastereoisomeric carbon resonances are reported in brackets [ ]. Elemental analyses were obtained from Midwest Microlabs, Ltd., Indianapolis, IN, and high resolution mass spectra were obtained either from the Nebraska Center for Mass Spectrometry or the Washington University Resource for Biomedical and Bioorganic Mass Spectrometry.

(Pentadienyl)iron cations **3**[10] and **4**[11] and (diene)iron complexes **24**,[10] (−)-**29**,[26] and **33**[22] were prepared by literature procedures.

Tricarbonyl(methyl-2*E*,4*Z*,7-octatrienoate)iron (5). A solution of vinyl magnesium chloride (0.84 mL, 1.0 M in THF, 0.84 mmol) was diluted with dry ether (2 mL) and THF (8 mL). The solution was cooled to −78°C, and solid CuBr·Me_2S (57 mg, 0.28 mmol) was added. The mixture was stirred for 15 min, and then solid **3** (100 mg, 0.244 mmol) was added. The reaction mixture was stirred for 1.5 h at −78°C and then warmed to 0°C and quenched with saturated aqueous NH_4Cl and extracted with ether. The combined organic extracts were dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (SiO_2, hexanes–ethyl acetate (10:1)) to afford **5** as a yellow oil (30 mg, 42%): ^{1}H NMR ($CDCl_3$) δ 6.06 (dd, *J*=5.3, 8.5 Hz, 1H), 5.74 (dddd, *J*=6.1, 7.2, 10.2, 16.8 Hz, 1H), 5.33 (dd, *J*=5.3, 7.6 Hz, 1H), 5.04–4.97 (m, 2H), 3.69 (s, 3H), 2.76 (dt, *J*=8.1, 7.8 Hz, 1H), 2.27 (dt, *J*=15.3, 6.5 Hz, 1H), 2.17 (d, *J*=8.5 Hz, 1H), 1.90 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 173.1, 138.0, 115.4, 92.9, 85.4, 59.1, 46.0, 45.9, 33.2. This compound was used in the next reaction without further characterization.

Diastereomeric isoxazolines (6). To a solution of **5** (60 mg, 0.20 mmol) and phenyl isocyanate (0.98 g, 8.3 mmol) in benzene (5 mL) was added a solution of nitroethane (0.31 g, 4.1 mmol) and triethylamine (3 drops) in benzene (2 mL). The mixture was stirred at room temperature for 48 h. The reaction mixture was passed through a short bed of SiO_2 and the filter bed washed (hexane–ethyl acetate (1:1)). The filtrate was concentrated and purified by column chromatography (SiO_2, hexane–ethyl acetate (10:1→10:3 gradient)) to give a mixture of diastereomers **6** as a yellow oil (40 mg, 57%): R_f 0.27 (hexanes–ethyl acetate (10:1)); ^{1}H NMR ($CDCl_3$) δ 6.06 (dd, *J*=5.2, 8.5 Hz, 1H), 5.40 and 5.38 (2×dd, *J*=5.4, 7.5 Hz, 1H), 4.53 (ddt, *J*=4.4, 10.1, 7.2 Hz, 0.5H), 4.40 (ddt, *J*=5.4, 10.3, 7.4 Hz, 0.5 H), 3.67 and 3.66 (2×s, 3H), 3.00 and 2.96 (2×ddd, *J*=1.0, 4.1, 17.1 Hz, total 1H), 2.79 (dddd, *J*=1.2, 4.0, 7.9, 10.7 Hz, 0.5H), 2.68 (dddd, *J*=1.2, 4.3, 7.8, 9.9 Hz, 0.5H), 2.48 and 2.46 (2×ddd, *J*=1.0, 10.4, 17.1 Hz, total 1H), 2.08 and 2.05 (2×d, *J*=8.8 Hz, total 1H), 1.97 (s, 3H), 1.29 (ddd, *J*=7.3, 10.1, 14.5 Hz, 1H), 1.16 (ddd, *J*=5.4, 10.7, 14.1 Hz, 1H).

(Tricarbonyl)(1-methoxycarbonyl-2-nitromethylene-3-pentene-1,5-diyl)iron (7). To absolute ethanol (20 mL) under N_2, was added, in small portions, sodium metal (0.30 g, 13 mmol). Following the disappearance of sodium metal, nitromethane (1.60 g, 26 mmol) was added to the reaction mixture. The reaction mixture was concentrated to give a white solid. Freshly prepared sodium nitromethanate (0.40 g, 4.8 mmol) was dissolved in nitromethane (20 mL) and the cation **3** (1.00 g, 2.44 mmol) was added and the mixture was stirred for 45 min at

5°C. Water (30 mL) was added to the mixture, the layers were separated, and the aqueous layer was extracted with ethyl acetate (3×50 mL). The combined organic layers were washed with brine (50 mL), dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (SiO_2, hexanes–ethyl acetate (4:1)) to afford **7** as a yellow oil (260 mg, 33%): IR (neat, cm^{-1}) 3055, 2073, 2012, 1552, 1265; ^1H NMR ($CDCl_3$) δ 4.69 (td, *J*=7.3, 11.7 Hz, 1H), 4.48 (t, *J*=6.4 Hz, 1H), 3.88 (m, 4H), 3.69 (s, 3H), 2.45 (dd, *J*=2.4, 12.5 Hz, 1H), 0.07 (d, *J*=7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 209.6, 209.4, 202.9, 179.2, 98.6, 80.2, 59.9, 54.8, 51.7, 37.4, 9.0; HRMS (EI) *m/z* 268.9996 (calcd for $C_9H_{11}NO_5Fe$ (M−2CO) *m/z* 268.9987).

Dicarbonyl(1-methoxycarbonyl-2-nitromethylene-3-pentene-1,5-diyl)triphenylphosphineiron (8). To a solution of *n*-butyl lithium (0.2 mL, 1.6 M in hexanes) in THF (10 mL) at 0°C was added nitromethane (0.3 mL). To this solution was added a solution of **4** (250 mg, 0.406 mmol) in nitromethane (2 mL). The mixture was stirred at 0°C for 2 h and then poured into water (10 mL). The mixture was extracted with ethyl acetate (3×20 mL) and the combined organic extracts were washed with brine, followed by water, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (SiO_2, hexanes–ethyl acetate (3:1)) to afford **8** as a yellow solid (180 mg, 96%): mp 152–153°C; ^1H NMR ($CDCl_3$) δ 7.50–7.20 (m, 15H), 4.20 (t, *J*=6.6 Hz, 1H), 4.04–3.88 (m, 2H), 3.81–3.72 (m and s, 5H), 2.68 (m, 1H), 2.24 (ddd, *J*=2.7, 6.3, 11.7 Hz, 1H), 0.00 (dd, *J*=3.6, 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 217.2 (J_{PC}=21.8 Hz), 216.8 (J_{PC}=15.8 Hz), 180.7, 132.6 (J_{PC}=9.6 Hz), 132.1, 130.4, 128.6 (J_{PC}=9.7 Hz), 97.9, 80.3, 57.7, 57.4, 51.3, 38.4, 7.1 (J_{PC}=15.7 Hz); Anal. Calcd for $C_{28}H_{26}NO_6PFe2H_2O$: C, 56.49; H, 5.08. Found: C, 56.38; H, 4.62.

2.2. Reaction of 3 with ethyl nitroacetate anion

To a solution of ethyl nitroacetate anion (0.28 mmol, freshly prepared from ethyl nitroacetate and *n*-butyl lithium) in THF (10 mL) cooled to 0°C was added solid cation **3** (0.10 g, 0.24 mmol). The reaction mixture was stirred for 30 min, warmed to room temperature and stirred overnight. Water (10 mL) was added, the layers were separated, and the aqueous layer was extracted several times with ethyl acetate and the combined organic layers were washed with brine, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (SiO_2, hexanes–ethyl acetate (10:1)) to afford **10** as a yellow oil (38 mg, 4%), followed by **9** as a yellow oil (0.80 g, 84%).

10: IR (neat, cm^{-1}) 2073, 2011, 1552, 1265; ^1H NMR ($CDCl_3$) δ 6.08 (2× dd, each *J*=5.4, 8.8 Hz, 1H), 5.31 (dd, *J*=5.4, 6.8 Hz, 1H), 5.09 (dd, *J*=3.4, 10.3 Hz, 1H), 4.90 (dd, *J*=6.1, 8.2 Hz, 1H), 4.27 (q, *J*=7.1 Hz, 2H), 3.70 (s, 3H), 2.49 (m, 2H), 2.13 (dd, *J*=5.6, 8.3 Hz, 1H), 1.30 (t, *J*=7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 172.5, 163.3, 93.8, 89.3 [89.1], 85.3 [85.1], 63.4 [63.3], 51.8 [51.3], 50.5, 46.3 [46.2], 30.9 [30.5], 13.9.

9: IR (neat, cm^{-1}) 3059, 2075, 2011, 1749, 1699, 1562, 1267; ^1H NMR ($CDCl_3$) δ 4.68 (m, 1H), 4.46 (m, 2H), 4.30 (qd, *J*=7.1, 7.1 Hz, 1H), 4.12 (m, 2H), 3.67 (s, 3H), 2.49 (d, *J*=12.5 Hz, 1H), 1.30 (t, *J*=7.1 Hz, 1H), 1.19 (t, *J*=7.1 Hz, 3H), 0.22 (d, *J*=8.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 209.0, 209.4, 178.8, 162.2, 98.7 [98.3], 91.9, 63.1, 58.4, 55.1 [54.5], 51.6, 39.9 [39.5], 13.9 [13.6], 9.0 [8.9]; HRMS (EI) *m/z* 267.0318 (calcd for $C_{11}H_{15}O_4Fe$ (M−3CO–NO_2) *m/z* 267.0324).

2.3. Reaction of 4 with ethyl nitroacetate anion

The reaction ethyl nitroacetate anion (0.232 mmol, freshly prepared from ethyl nitroacetate and *n*-butyl lithium) with **4** (100 mg, 0.155 mmol) was carried out in THF for 1 h, followed by workup with water. The mixture is extracted several times with Et_2O, and the combined organic extracts were dried ($MgSO_4$) and concentrated. The ^1H NMR spectrum of the crude product indicated this to be (pentenediyl)iron complex **11**: ^1H NMR ($CDCl_3$) δ 7.5–7.2 (m, 15H), 4.36–4.28 (m, 2H), 4.24–4.09 (m, 3H), 3.92 (m, 1H), 3.74 (s, 3H), 2.68 (m, 1H), 2.29 (m, 1H), 1.35–1.15 (m, 3H), 0.18 (m, 1H). Workup of the above reaction mixture with saturated aqueous NH_4Cl solution (instead of water) led to the exclusive formation of (diene)iron complex **12**. Allowing a solution of **11** in

$CDCl_3$ to stand for 24–48 h, resulted in isomerization to **12**. The isomerization of **11** to **12** proceeded considerably slower in C_6D_6 solution, such that ca. 30% of **11** remained after 7 days.

2.4. Preparation of dicarbonyl(methyl ethyl 7-nitro-2*E*,4*Z*-octadienedioate)triphenylphosphineiron (12)

To a solution of ethyl nitroacetate anion (0.58 mmol, freshly prepared from ethyl nitroacetate and *n*-butyl lithium) in THF (10 mL) at 0°C was added a solution of cation **4** (250 mg, 0.387 mmol) in THF (10 mL). The mixture was stirred at 0°C for 3 h. Saturated aqueous NH_4Cl (20 mL) was added and the mixture was extracted with ethyl acetate (2×25 mL). The combined organic extracts were washed with water, followed by brine, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (SiO_2, hexanes–ethyl acetate (10:1→3:1 gradient)) to afford **12** as a yellow solid (170 mg, 70%): mp 54–59°C; IR ($CHCl_3$) 1994, 1934, 1703 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.50–7.35 (m, 15H), 5.95–5.87 (m, 1H), 4.69 (dd, *J*=4.5, 9.6 Hz, 0.5H), 4.57 (dd, *J*=4.5, 9.9 Hz, 0.5H), 4.37–4.28 (m, 1.5H), 4.20–4.10 (m, 2.5H), 3.68 (s, 3H), 2.65 (br m) and 2.30 (br m) total 1H, 1.90 (br s, 1H), 1.40 (m, 1H), 1.22 (t, *J*=7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 174.5, 163.6, 133.7 (br), 133.0 (J_{PC}=9.7 Hz), 130.3, 128.4 (J_{PC}=9.7 Hz), 90.4 (br), 90.1, 89.4, 86.9 (br), 62.8, 51.3, 40.0 (br), 30.6 (br), 13.7; Anal. Calcd for $C_{31}H_{30}NO_8PFe$: C, 58.97; H, 4.79. Found: C, 58.91; H, 4.92.

2-(Trimethylsilyl)ethyl nitroacetate (13). To a solution of sodium iodide (4.37 g, 29.1 mmol) in acetone (30 mL) was added dropwise 2-(trimethylsilyl)ethyl 2-bromoacetate[16] (3.48 g, 14.6 mmol). The reaction mixture was stirred for 16 h, and then washed with water, followed by brine. The mixture was extracted with ethyl acetate and the combined organic extracts were dried ($MgSO_4$) and concentrated to give crude 2-(trimethyl-silyl)ethyl 2-iodoacetate as a brown liquid (4.17 g). ^1H NMR ($CDCl_3$) δ 4.23 (m, 2H), 3.68 (s, 2H), 1.02 (m, 2H), 0.05 (s, 9H). The crude iodoacetate was added to a suspension of $AgNO_3$ (3.36 g, 21.8 mmol) in dry ether (85 mL) at 0°C. The reaction mixture was stirred for 32 h with protection from light. The reaction mixture was filtered, and the filter bed washed with CH_2Cl_2. The combined filtrates were concentrated and the residue was purified by column chromatography (SiO_2, hexanes–ethyl acetate (5:1)) to give recovered iodoacetate (2.57 g), followed by nitroacetate **13** as a pale oil (631 mg), and finally nitrite **15**.

13: ^1H NMR ($CDCl_3$) δ 5.14 (s, 2H), 4.35 (m, 2H), 1.06 (m, 2H), 0.05 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 161.9, 76.4, 65.8, 17.2, −1.7; Anal. Calcd for $C_7H_{15}NO_4Si$: C, 40.96; H, 7.36. Found: C, 41.75; H, 7.41.

15: ^1H NMR ($CDCl_3$) δ 4.27 (m, 2H), 4.11 (s, 2H), 1.02 (m, 2H), 0.02 (s, 9H).

2.5. Reaction of 4 with 2-(trimethylsilyl)ethyl nitroacetate anion

To a solution of 2-(trimethylsilyl)ethyl nitroacetate anion (0.58 mmol, freshly prepared from 2-(trimethylsilyl)ethyl nitroacetate and *n*-butyl lithium at 0°C) in THF (40 mL) was added solid cation **4** (1.00 g, 1.55 mmol) in one portion. The mixture was stirred at room temperature for 2 h. The reaction mixture was diluted with water and extracted several times with Et_2O, and the combined organic extracts were dried ($MgSO_4$) and concentrated. The ^1H NMR spectrum of the crude product indicated it to be (pentenediyl)iron complex **17** (1.1 g): ^1H NMR ($CDCl_3$) δ 7.46–7.26 (m, 15H), 4.38 (m, 2H), 4.18 (m, 3H), 3.92 (br m, 1H), 3.74 (s, 3H), 2.66 (m, 1H), 2.28 (m, 1H), 1.06 (m, 2H), 0.18 (m, 1H), 0.05 and 0.00 (2×s, 9H). The product was divided into three roughly equal samples and each was dissolved in $CHCl_3$ (1 L each). The flasks were protected from the light and allowed to stand for 6 days. The solvent was evaporated and the combined residues were purified by column chromatography ('flash' SiO_2, hexanes–ethyl acetate (15:1) to afford **18** as a yellow oil (544 mg, 50%). ^1H NMR ($CDCl_3$) δ 7.48–7.36 (m, 15H), 5.95 (dd, *J*=4.7, 7.9 Hz, 0.5H), 5.90 (dd, *J*=4.7, 7.7 Hz, 0.5H), 4.69 (dd, *J*=4.9, 10.5 Hz, 0.5H), 4.57 (dd, *J*=4.4, 10.6 Hz, 0.5H), 4.39–4.26 (m, 1H), 4.22–4.16 (m, 2H), 3.69 (s, 3H), 2.65 (br m) and 2.32 (br m) total 1H, 1.92 (br s, 1H), 1.39 (br m, 2H), 0.90 (dd, *J*=8.2, 10.8 Hz, 2H), 0.20 and 0.14 (2×s, 9H). This product was used in the next reaction without further characterization.

Dicarbonyl(methyl 7-nitro-2*E*,4*Z*-heptadienoate)(triphenylphosphine)iron [*rac*-(19)]. To a solution of **18** (540 mg, 0.768 mmol) in DMF (5 mL) was added tris(dimethylamino)sulfur (trimethylsilyl)difluoride (TAS-F) (215 mg, 0.783 mmol) and the reaction mixture was stirred for 18 h. The mixture was diluted with water and extracted with ethyl acetate. The combined extracts were dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (SiO_2, hexanes–ethyl acetate (10:1)) to afford **19** as a yellow oil (330 mg, 77%): ^{1}H NMR ($CDCl_3$) δ 7.49–7.36 (m, 15H), 5.93 (ddd, *J*=1.2, 5.1, 7.9 Hz, 1H), 4.37 (br m, 1H), 4.03 (m, 2H), 3.68 (s, 3H), 2.20 (m, 2H), 1.88 (br d, *J*=7.7 Hz, 1H), 1.42 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 212.1, 211.8, 175.4, 134.4 (J_{PC}=41 Hz), 133.8 (J_{PC}=11 Hz), 131.1, 129.2 (J_{PC}=10 Hz), 91.0, 87.6 (br), 77.8, 55.1, 52.1, 40.9 (br), 28.1; HRMS (FAB) *m*/*z* 566.0998 (calcd for $C_{28}H_{26}NO_6PFeLi$ (M+Li$^+$) *m*/*z* 566.0998).

Isoxazoline *rac*-(21). To a solution of nitrodienoate iron complex *rac*-**19** (150 mg, 0.270 mmol) and triene iron complex *rac*-**20** (64 mg, 0.270 mmol) in benzene (5 mL) was added phenyl isocyanate (45 µL, 0.405 mmol) and triethylamine (38 µL, 0.270 mmol). The mixture was stirred for 24 h. Water (10 mL) was added and mixture extracted with ether. The organic layer was washed with water, brine, dried ($MgSO_4$) and concentrated. The white crystalline byproduct formed was washed with hexanes to extract the product. Purification by (SiO_2, hexane–ethyl acetate (10:1)) gave a mixture of diastereomers **21** as a yellow oil (88 mg, 42%): ^{1}H NMR ($CDCl_3$) δ 7.51–7.31 (m, 15H), 5.93 (m, 1H), 5.15 (dd, *J*=4.0, 8.3 Hz, 1H), 5.08 (m, 1H), 4.37 (br m, 1H), 4.1–4.0 (m, 1H), 3.68 (s, 3H), 2.62 (m, 1H), 2.4–2.2 (m, 3H), 1.96–1.81 (m, 2H), 1.43 and 1.42 (2×d, *J*=6.0 Hz, 3H), 0.93–0.78 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 212.1, 175.4, 159.8, 134.6 (J_{PC}=41 Hz), 133.8 (J_{PC}=10 Hz), 131.0, 129.2 (J_{PC}=9 Hz), 91.3, 88.2, 84.2 [84.1], 83.6, 60.0, 59.9, 59.6, 55.5 (br), 52.0, 44.1, 41.3 (br), 28.2, 19.8; HRMS (FAB) *m*/*z* 782.0879 (calcd for $C_{38}H_{34}NO_8PFe_2Li$ (M+Li$^+$) *m*/*z* 782.0880).

2.6. Grignard addition to *rac*-(24)

To a suspension of flame dried magnesium turnings (1.68 g, 0.07 mol) in THF (50 mL) was added, dropwise, a solution of 2-(2-bromoethyl)-1,3-dioxane (10.34 g, 0.053 mol) in THF (50 mL). After completion of the addition, the mixture was heated at reflux for 90 min, and then cooled in an ice-water bath. A solution of *rac*-**24** (10 g, 0.035 mol) in THF (100 mL) was added dropwise. The reaction mixture was warmed to room temperature and stirred for 16 h. Ice and saturated aqueous NH_4Cl (30 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with ether (2×40 mL) and the combined organic layers were washed successively with saturated aqueous NH_4Cl (2×40 mL), water (2×40 mL), and brine (40 mL), dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (SiO_2, hexanes–ethyl acetate (4:1)) to afford **26** as a yellow solid (0.52 g, 4%), followed by a mixture of **26** and **25** (1.95 g, 14%) and finally **25** as a yellow solid (1.71 g, 12%).

***rac*-25**: IR ($CHCl_3$, cm^{-1}) 3449, 2058, 1989, 1711; ^{1}H NMR ($CDCl_3$) δ 5.83 (ddd, *J*=0.7, 5.0, 8.1 Hz, 1H), 5.51 (dd, *J*=4.9, 8.7 Hz, 1H), 4.60 (t, *J*=4.2 Hz, 1H), 4.11 (m, 2H), 3.77 (dt, *J*=2.4, 11.8 Hz, 2H), 3.65 (s, 3H), 3.59 (m, 1H), 3.26 (d, *J*=4.6 Hz, OH), 2.04 (m, 1H), 1.9–1.6 (m, 5H), 1.30 (m, 1H), 1.02 (d, *J*=8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 172.5, 101.6, 85.4, 83.9, 72.4, 67.0, 66.9, 51.6, 45.9, 32.7, 30.8, 25.5, 14.1; HRMS (EI) *m*/*z* 340.0592 (calcd for $C_{14}H_{20}O_6Fe$ (M−2CO)$^+$ 340.0612).

***rac*-26**: IR ($CHCl_3$, cm^{-1}) 3462, 2058, 1987, 1711; ^{1}H NMR ($CDCl_3$) δ 5.80 (dd, *J*=5.1, 8.2 Hz, 1H), 5.43 (dd, *J*=4.9, 8.8 Hz, 1H), 4.60 (t, *J*=3.9 Hz, 1H), 4.09 (m, 2H), 3.76 (m, 3H), 3.65 (s, 3H), 3.20 (d, *J*=3.2 Hz, OH), 2.04 (m, 1H), 1.84–1.63 (m, 5H), 1.34 (m, 1H), 0.92 (d, *J*=8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 172.7, 101.6, 84.0, 82.8, 72.4, 66.9, 51.6, 45.4, 34.3, 31.8, 25.4, 15.2; HRMS (EI) *m*/*z* 340.0606 (calcd for $C_{14}H_{20}O_6Fe$ (M−2CO)$^+$ 340.0612).

2.7. Preparation of lactol *rac*-27 via hydrolysis of 25

To a solution of *rac*-**25** (0.18 g, 0.45 mmol) in degassed acetone (30 mL) was added 0.05 M H_2SO_4 (4 mL). The mixture was heated at reflux for 6 h. The mixture was cooled, solid $NaHCO_3$ was added and the mixture

concentrated. The residue was extracted with ether and the combined organic extracts were washed with H_2O followed by brine, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (SiO_2, hexanes–ethyl acetate (4:1)) to give *rac*-**27** as a yellow solid (0.07 g, 46%): IR (KBr, cm^{-1}) 3374, 2066, 2014, 1973, 1715; ^1H NMR (300 MHz, $CDCl_3$) δ 5.85 (dd, *J*=5.1, 8.1 Hz, 1H), 5.58 (m, 0.5H), 5.48 (t, *J*=4.1 Hz, 0.5H), 5.43 (m, 1H), 4.03 (q, *J*=7.8 Hz, 0.5H), 3.84 (q, *J*=8.3 Hz, 0.5H), 3.67 (s, 3H), 2.56 (br s, OH), 2.3–1.7 (m, 4H), 1.33 (t, *J*=8.3 Hz, 0.5H), 1.17 (d, *J*=8.1 Hz, 1H), 1.10 (d, *J*=8.7 Hz, 0.5H); ^{13}C NMR ($CDCl_3$) δ(172.4 [172.3], 99.4 [99.2], 86.1 [86.0], 85.0 [84.8], 82.8 [80.0], 65.5 [63.0], 51.7, 46.6 [46.5], 34.5 [33.6], 32.1 [31.3]; HRMS (EI) *m/z* 338.0079 (calcd for $C_{13}H_{14}O_7Fe$ (M^+) 338.0093); Anal. Calcd for $C_{13}H_{14}O_7Fe$: C, 46.18; H, 4.17. Found: C, 46.42; H, 4.17.

2.8. Preparation of lactol *rac*-28 via hydrolysis of 26

The hydrolysis of *rac*-**26** was carried out in the same fashion as the hydrolysis of *rac*-**25** (14%): IR (KBr, cm^{-1}) 3374, 2066, 2014, 1973, 1715; ^1H NMR (300 MHz, $CDCl_3$) δ 5.80 (dd, *J*=5.1, 8.2 Hz, 1H), 5.53 and 5.49 (2×t, *J*=2.7 Hz, 1H), 5.38 and 5.30 (2×dd, *J*=5.1, 8.7 Hz, 1H), 4.21 (q, *J*=6.8 Hz, 0.5H), 3.80 (q, *J*=8.1 Hz, 0.5H), 3.66 (s, 3H), 2.59 (m, OH), 2.4–1.8 (m, 4H), 1.46 (t, *J*=8.7 Hz, 0.5H), 1.29 (dd, *J*=8.6 Hz, 0.5H), 1.03 and 0.96 (2×d, *J*=8.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ(172.6, 98.5 [98.4], 84.8 [84.1], 83.6 [83.3], 82.7 [78.8], 68.6 [66.6], 51.7, 46.0 [45.6], 34.6 [33.3], 32.5 [31.8]; HRMS (EI) *m/z* 282.0198 (calcd for $C_{11}H_{14}O_5Fe$ $(M-2CO)^+$ 282.0185); Anal. Calcd for $C_{13}H_{14}O_7Fe$: C, 46.18; H, 4.17. Found: C, 46.50; H, 4.20.

2.9. Hydroboration–oxidation of 29[26]

To a solution of (−)-**29** (2.43 g, 7.55 mmol) in dry THF (25 mL), cooled to 0°C was added a solution of BH_3·THF complex (9.1 mL, 1.0 M, 9.1 mmol) in THF. The mixture was stirred at 0°C for 1 h and then treated with a solution of 30% H_2O_2 (8.5 mL) and 1.0 M aqueous KOH. After stirring for 1 min, the mixture was poured into a separatory funnel containing brine (50 mL) and ether (50 mL). The layers were separated and the organic layer was washed with water, followed by brine, dried ($MgSO_4$) and concentrated. The resultant orange oil was purified by column chromatography (SiO_2, hexanes–ethyl acetate (1:1) to give **31** (0.95 g, 37%). The spectral data for **31** was identical with that obtained of a sample prepared by an independent route (vide infra). Further elution with ethyl acetate gave (−)-**30** as a yellow solid (1.30 g, 51%).

(−)-**30**: mp 72–75°C [lit.[26] mp 86–87°C (*rac*-**30**)]; $[\alpha]_D$=−109° (*c* 0.60, MeOH); ^1H NMR ($CDCl_3$) δ 5.84 (dd, *J*=5.1, 8.1 Hz, 1H), 5.50 (dd, *J*=5.1, 8.6 Hz, 1H), 3.72 (m, 2H), 3.66 (s, 3H), 3.60 (m, 1H), 2.60 (br s, OH), 1.95–1.62 (m, 5H), 1.33 (t, *J*=7.8 Hz, 1H), 1.05 (d, *J*=8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ(172.6, 85.6, 84.0, 72.9, 66.7, 62.6, 51.7, 46.0, 36.1, 28.4; HRMS (FAB) *m/z* 341.0321 (calcd for $C_{13}H_{17}O_7Fe$ (M+H) 341.0324). The ^1H NMR spectrum of (−)-**30** in C_6D_6 was identical with the literature[26] data for *rac*-**30**.

Tricarbonyl(methyl 9-*tert*-butyldiphenylsilyloxy-6-hydroxy-2,4-nonadienoate)iron. To a solution of (−)-**30** (100 mg, 0.294 mmol) in CH_2Cl_2 (3 mL) was added *t*-butyldiphenylsilylchloride (81 mg, 0.294 mmol) and imidazole (20 mg). The reaction mixture was stirred for 3 h at which time TLC monitoring (SiO_2, hexanes–ethyl acetate (1:1)) indicated completion. The mixture was concentrated and the residue was purified by column chromatography (SiO_2, hexanes–ethyl acetate (4:1)) to give a yellow oil (130 mg, 76%): ^1H NMR ($CDCl_3$) δ 7.69–7.66 (m, 4H), 7.46–7.35 (m, 6H), 5.84 (ddd, *J*=1.0, 5.1, 8.1 Hz, 1H), 5.53 (dd, *J*=5.2, 8.4 Hz, 1H), 3.75–3.59 (m, 3H), 3.67 (s, 3H), 3.18 (br s, OH), 1.88 (m, 1H), 1.74–1.60 (m, 3H), 1.34 (dd, *J*=7.2, 7.8 Hz, 1H), 1.05 (s and m, 10H); ^{13}C NMR ($CDCl_3$) δ(172.6, 135.5, 133.1, 129.8, 127.7, 85.3, 83.8, 72.8, 67.2, 64.3, 51.7, 45.9, 36.6, 28.6, 26.7, 19.1. This compound was used in the next reaction without further characterization.

(*S*)-MTPA ester of tricarbonyl(methyl 9-*tert*-butyldiphenylsilyloxy-6-hydroxy-2,4-nonadienoate)iron [(*S*)-(32)]. To a solution of the above secondary alcohol (55 mg, 0.095 mmol) in CH_2Cl_2 (3 mL) was added (*S*)-α-methoxy(trifluoromethyl)phenyl acetic acid (67 mg, 0.285 mmol), DMAP (7 mg) and DCC (60 mg, 0.285 mmol).

The reaction mixture was stirred for 2 h, and then quenched by the addition of H_2O (5 drops). The mixture was extracted several times with ether, and the combined extracts washed with 3% aqueous HCl, followed by water and finally brine, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (SiO_2, hexanes–ethyl acetate (4:1)) to give (S)-**32** as a yellow oil (50 mg, 89%). Analysis by ^{1}H NMR spectroscopy (C_6D_6) indicated that the product was 57% de. The ^{1}H NMR spectral data for the major diastereomer is as follows: (C_6D_6) δ 7.78–7.73 (m, 3H), 7.64 (br d, *J*=6.9 Hz, 2H), 7.28–7.21 (m, 6H), 7.12–7.06 (m, 4H), 5.38 (dd, *J*=5.4, 8.4 Hz, 1H), 5.16 (dd, *J*=5.1, 8.4 Hz, 1H), 4.90 (dt, *J*=3.0, 9.6 Hz, 1H), 3.69–3.46 (m, 2H), 3.43 (s, 3H), 3.30 (s, 3H), 1.92 (m, 1H), 1.7–1.4 (m, 3H), 1.17 (s, 9H), 0.92 (d, *J*=8.4 Hz, 1H), 0.78 (t, *J*=8.7 Hz, 1H).

(*R*)-MTPA ester of tricarbonyl(methyl 9-*tert*-butyldiphenylsilyloxy-6-hydroxy-2,4-nonadienoate)iron [(*R*)-(32)]. The preparation of the (*R*)-MTPA ester **32** was carried out in the same fashion as the preparation of the (S)-MPTA ester **32** (97%). Integration of analysis by ^{1}H NMR spectroscopy (C_6D_6) indicated that the product was 55% de. The ^{1}H NMR spectral data for the major diastereomer is as follows: ^{1}H NMR (C_6D_6) δ 7.78–7.73 (m, 3H), 7.64 (br d, *J*=6.9 Hz, 2H), 7.28–7.21 (m, 6H), 7.12–7.06 (m, 4H), 5.42 (ddd, *J*=0.9, 5.1, 8.4 Hz, 1H), 5.24 (ddd, *J*=0.9, 5.1, 8.4 Hz, 1H), 4.85 (dt, *J*=3.3, 9.3 Hz, 1H), 3.62–3.48 (m, 2H), 3.41 (s, 3H), 3.28 (s, 3H), 1.92 (m, 1H), 1.7–1.4 (m, 3H), 1.17 (s, 9H), 0.84 (d, *J*=8.4 Hz, 1H), 0.66 (t, *J*=8.7 Hz, 1H).

Tricarbonyl(methyl 6,8-dihydroxy-2,4-nonadienoate)iron [*rac*-(31)]. To a solution of *rac*-**33**[22] (130 mg; 0.388 mmol) in MeOH–H_2O (15:1, 5 mL) in a three-necked flask was added Raney-nickel (ca. 0.5 mL slurry in H_2O) and $B(OH)_3$ (60 mg). 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 5 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 (SiO_2, hexanes–ethyl acetate (17:3→3:1 gradient)) to give (methyl 6-hydroxy-8-oxo-2,4-nonadienoate)$Fe(CO)_3$ as a yellow oil (40 mg, 30%): ^{13}C NMR ($CDCl_3$) δ 208.9, 172.3, 85.4, 84.2, 69.0, 64.4, 51.6, 50.7, 46.3, 30.5. This product was used without further characterization. To a solution of the hydroxyketone (40 mg, 0.12 mmol) in EtOH (5 mL), at 0°C, was added solid $NaBH_4$ (3 mg). The solution was stirred for 10 min, at which time TLC monitoring (hexanes–ethyl acetate (2:3)) indicated disappearance of the ketone. The reaction mixture was diluted with water and extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (SiO_2, hexanes–ethyl acetate (1:1) to give *rac*-**31** (15 g, 37%). ^{1}H NMR ($CDCl_3$) δ 5.84 (m, 1H), 5.50 (dd, *J*=5.1, 8.6 Hz, 1H), 4.25 (m, 0.3H), 4.05 (m, 0.7H), 3.84 (m, 0.3H), 3.75 (m, 0.7H), 3.66 (s, 3H), 2.60 (br s, OH), 1.8–1.6 (m, 3H), 1.27 and 1.25 (m and 2×d, *J*=7.2 Hz, 4H), 1.07 (d, *J*=8.5 Hz, 0.3 H), 1.05 (d, *J*=8.4 Hz, 0.7H); ^{13}C NMR ($CDCl_3$) δ 172.5, 85.1 [85.5], 84.1 [84.2], 74.1 [71.3], 69.1 [66.1], 65.8 [66.8], 51.7, 46.2 [46.1], 44.7, 24.5 [23.5].

2.10. Preparation of lactol (−)-27 via oxidation of (−)-30

To a solution of (−)-**30** (130 mg, 0.382 mmol), DMSO (0.08 mL) and triethylamine (0.16 mL) in CH_2Cl_2 (8 mL) at 0°C was added SO_3pyridine (182 mg, 1.15 mmol). The reaction mixture as stirred at 0°C for 2 h, and for an additional 3.5 h at room temperature. The reaction mixture was quenched with cold water (3 mL) and extracted with ethyl acetate. The combined organic layers were washed successively with saturated aqueous NH_4Cl, saturated aqueous $NaHCO_3$, and finally brine, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (SiO_2, hexanes–ethyl acetate (4:1→13:7 gradient)) to give (−)-**27** as a yellow oil (70 mg, 54%): $[\alpha]_D$=−263° (*c* 0.60, MeOH). The ^{1}H NMR spectrum of (−)-**27** was identical to that of *rac*-**27**.

Tricarbonyl(methyl 6,9-dihydroxy-2,4-decadienoate)iron (−)-35. A solution of chlorotriisopropoxy–titanium in hexanes (6.9 mL, 1.0 M, 6.9 mmol) was diluted with dry Et_2O (20 mL) and cooled in a CH_3CN/liquid N_2 bath. To this solution was added dropwise via syringe a solution of MeLi (4.96 mL, 1.4 M, 4.6 mmol) in Et_2O. The solution was warmed to 0°C and stirred for 1 h. The resulting suspension was allowed to settle and the liquid layer was transferred, by cannula under N_2 pressure, to a filtration apparatus containing a celite filter bed. The solution

was filtered, and the solvent was evaporated under high vacuum. The residue was taken up in dry CH_2Cl_2 (20 mL) and cooled to −78°C. A solution of (−)-**27** (470 mg, 1.39 mmol) in dry CH_2Cl_2 (6 mL) was slowly added via syringe. The mixture was warmed to room temperature and stirred for 18 h. The mixture was cooled to 0°C and quenched with CH_3OH until gas evolution ceased. The mixture was poured into ice water (100 mL) and additional CH_2Cl_2 was added. The layers were separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic phases were washed with H_2O, followed by brine, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (SiO_2, hexanes–ethyl acetate (3:2) followed by ethyl acetate) to give (−)-**35** as a pale yellow solid (250 mg, 51%): mp 108–111°C; $[\alpha]_D$=−110° (*c* 0.16, MeOH); ^{1}H NMR ($CDCl_3$) δ 5.83 (dd, *J*=5.1, 8.1 Hz, 1H), 5.50 (dd, *J*=5.1, 8.7 Hz, 1H), 3.88 (m, 1H), 3.66 (s, 3H), 3.57 (m, 1H), 1.92–1.82 (m, 1H), 1.76–1.50 (m, 5H), 1.33 (t, *J*=7.8 Hz, 1H), 1.23 (d, *J*=6.3 Hz, 3H), 1.04 (d, *J*=8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 172.6, 85.5, 83.9, 73.4, 68.2, 67.2, 51.7, 46.0, 35.5, 35.3, 23.7; HRMS (FAB) *m*/*z* 355.0468 (calcd for $C_{14}H_{19}O_7Fe$ $(M+H)^+$ 355.0480); Anal. Calcd for $C_{14}H_{18}O_7Fe$: C, 48.04; H, 5.25. Found: C, 47.48; H, 5.12.

Tricarbonyl(methyl 9-hydroxy-2,4-decadienoate)iron [(−)-36]. To a solution of (−)-**35** (250 mg, 0.706 mmol) in dry THF (25 mL) cooled to −78°C was added $NaBH_3CN$ (0.45 g, 7.0 mmol). The mixture was stirred at this temperature for 1 h, and then $Et_2O{\cdot}BF_3$ (7 mL) was added dropwise. The mixture was allowed to warm overnight. Water (10 mL) was added dropwise, and the mixture was partially concentrated, extracted with ether, and the combined organic phases washed with saturated aqueous $NaHCO_3$, water, and finally brine, dried ($MgSO_4$) and concentrated. The residue was purified by chromatography (SiO_2, hexane–ethyl acetate (4:1)) to give (−)-**36** as a yellow oil, (170 mg, 71%): $[\alpha]_D$=−120° (*c* 0.16, MeOH); ^{1}H NMR ($CDCl_3$) δ 5.78 (dd, *J*=5.1, 8.1 Hz, 1H), 5.22 (dd, *J*=5.1, 8.7 Hz, 1H), 3.80 (m, 1H), 3.65 (s, 3H), 1.76–1.30 (m, 8H), 1.20 (d, *J*=6.3 Hz, 3H), 0.97 (d, *J*=8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 172.6, 87.2, 83.0, 67.7, 65.3, 51.6, 45.6, 38.6, 34.1, 28.2, 23.6. The spectral data for (−)-**35** was identical with that provided by Dr Grée.

(*S*)-MTPA ester of tricarbonyl(methyl 9-hydroxy-2,4-decadienoate)iron [(*S*)-(37)]. The preparation of the (*S*)-MTPA ester of (−)-**36** was carried out in the same fashion as the preparation of the (*S*)-MPTA ester **32** (98%). Analysis by ^{1}H NMR spectroscopy ($CDCl_3$) indicated that the product was ca. 50% de. The ^{1}H NMR spectral data for the major diastereomer is as follows: ^{1}H NMR ($CDCl_3$) δ 7.59–7.51 (m, 2H), 7.44–7.38 (m, 3H), 5.77 (dd, *J*=5.1, 8.1 Hz, 1H), 5.15 (m) and 5.11 (dd, *J*=5.1, 8.7 Hz) total 2H, 3.66 (s, 3H), 3.57 (s, 3H), 1.8–1.4 (m, 5H), 1.35 (d, *J*=6.0 Hz, 3H), 1.3–1.13 (m, 2H), 0.93 (d, *J*=8.7 Hz, 1H).

(*R*)-MTPA ester of tricarbonyl(methyl 9-hydroxy-2,4-decadienoate)iron [(*R*)-(37)]. The preparation of the (*R*)-MTPA ester of (−)-**36** was carried out in the same fashion as the preparation of the (*S*)-MPTA ester of **32** (91%). Analysis by ^{1}H NMR spectroscopy ($CDCl_3$) indicated that the product was ca. 54% de. The ^{1}H NMR spectral data for the major diastereomer is as follows: ^{1}H NMR ($CDCl_3$) δ 7.59–7.51 (m, 2H), 7.44–7.38 (m, 3H), 5.78 (dd, *J*=4.8, 7.5 Hz, 1H), 5.15 (m, 2H), 3.66 (s, 3H), 3.54 (s, 3H), 1.8–1.4 (m, 5H), 1.3–1.13 (m) and 1.27 (d, *J*=6.0 Hz) total 5H, 0.96 (d, *J*=8.1 Hz, 1H).

Tricarbonyl[methyl 9-(*t*-butyldimethylsilyl)oxy-2,4-decadienoate]iron [(−)-38]. To a solution of (−)-**36** (270 mg, 0.799 mmol) in CH_2Cl_2 (8 mL) was added imidazole (110 mg, 1.60 mmol), *t*-butyldimethylsilyl chloride (170 mg, 1.12 mmol) and a few crystals of DMAP. The reaction mixture was stirred for 18 h, at which time TLC (hexane–ethyl acetate (7:3)) indicated the disappearance of the alcohol. The solvent was evaporated and the residue was purified by column chromatography (SiO_2, hexanes–ethyl acetate (9:1)) to give (−)-**38** as a yellow oil (357 mg, 99%): $[\alpha]_D$=−92° (*c* 0.08, MeOH); ^{1}H NMR ($CDCl_3$) δ 5.78 (ddd, *J*=1.0, 5.1, 8.0 Hz, 1H), 5.21 (dd, *J*=5.1, 9.0 Hz, 1H), 3.78 (m, 1H), 3.65 (s, 3H), 1.8–1.2 (m, 7H), 1.11 (d, *J*=6.0 Hz, 3H), 0.97 (dd, *J*=0.9, 8.1 Hz, 1H), 0.88 (s, 9H), 0.05 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 172.6, 87.2, 82.9, 68.3, 65.7, 51.5, 45.6, 39.2, 34.4, 28.2, 25.9, 23.7, 18.1, −4.4, −4.8. The spectral data for (−)-**35** was identical with that provided by Dr Grée.

Tricarbonyl[9-(*t*-butyldimethylsilyl)oxy-2,4-decadien-1-ol]iron [(−)-39]. A solution of (−)-**38** (170 mg, 0.376 mmol) in anhydrous hexanes (7 mL) was cooled to −30°C and a solution of DIBAL (0.76 mL, 1.0 M, 0.76 mmol) in hexanes was added. The reaction was stirred at −30°C for 90 min, and then methanol (1 mL) was cautiously added, followed by saturated aqueous NH_4Cl. The mixture was extracted with ethyl acetate and the combined extracts washed with brine, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (SiO_2, hexanes–ethyl acetate (4:1)) to give (−)-**39** as a yellow oil (130 mg, 81%): $[\alpha]_D$=−23° (*c* 0.22, MeOH); ^{1}H NMR ($CDCl_3$) δ 5.16 (dd, *J*=4.8, 8.4 Hz, 1H), 5.07 (dd, *J*=5.0, 9.0 Hz, 1H), 3.82–3.58 (m, 3H), 1.70–1.15 (m, 9H), 1.11 (d, *J*=6.0 Hz, 3H), 0.88 (s, 9H), 0.05 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 212.0, 85.3, 82.5, 68.3, 65.1, 64.8, 60.3, 39.2, 34.4, 28.3, 25.9, 23.8, 18.1, −4.4, −4.7. The spectral data for (−)-**35** was identical with that provided by Dr Grée.

Tricarbonyl[methyl 9-(*t*-butyldimethylsilyl)oxy-2,4-decadienal]iron [(−)-40]. To a solution of (−)-**39** (150 mg, 0.354 mmol) in THF (10 mL), was added a solution of *n*-propyl magnesium bromide (0.2 mL, 2.0 M, 0.4 mmol) in ether. The solution was stirred at rt for 15 min, and then solid (azodicarbonyl)dipiperidine (103 mg, 0.405 mmol) was added in one portion. The reaction mixture was stirred for 1 h. The reaction mixture was quenched with brine and extracted with ether. The combined ether extracts were washed with brine, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (SiO_2, hexanes–ethyl acetate (9:1)) to give (−)-**40** as a yellow oil (120 mg, 80%): $[\alpha]_D$=−49° (*c* 0.16, MeOH); ^{1}H NMR ($CDCl_3$) δ 9.26 (d, *J*=4.5 Hz, 1H), 5.78 (dd, *J*=4.8, 8.4 Hz, 1H), 5.28 (dd, *J*=5.0, 8.4 Hz, 1H), 3.79 (m, 1H), 1.74–1.36 (m, 7H), 1.26 (ddd, *J*=0.9, 4.5, 8.1 Hz, 1H), 1.12 (d, *J*=6.0 Hz, 3H), 0.88 (s, 9H), 0.05 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 196.0, 88.5, 81.3, 68.2, 66.9, 54.7, 39.2, 34.4, 28.2, 25.9, 23.8, 18.1, −4.4, −4.8. The spectral data for (−)-**35** was identical with that provided by Dr Grée.

Tricarbonyl[10-(*t*-butyldimethylsilyl)oxy-1,3,5-undecatriene]iron [(+)-41]. To magnesium turnings (50 mg, 2.1 mmol) in dry ether (3 mL) was slowly added a solution of chloromethyltrimethylsilane (121 mg, 0.99 mmol) in ether (3 mL). The mixture was stirred at room temperature for 1 h, heated at reflux for 30 min, and then cooled to −78°C. A solution of (−)-**40** (230 mg, 0.545 mmol) in ether (3 mL) 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 (10 mL). To this solution was added 2% aqueous H_2SO_4 (3 drops) and silica gel (60–200 mesh, 1.0 g) and the mixture was stirred overnight at room temperature. The mixture was extracted with ether, the combined extracts were washed with saturated aqueous $NaHCO_3$, followed by water, and then brine, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (SiO_2, hexanes–ethyl acetate (50:1→9:1 gradient)) to give (+)-**41** as a yellow oil (120 mg, 52%) followed by recovered (−)-**40** (30 mg). $[\alpha]_D$=+18° (*c* 0.16, MeOH); IR ($CDCl_3$, cm^{-1}) 2043, 1975; ^{1}H NMR ($CDCl_3$) δ 5.75 (dt, *J*=16.5, 10.2 Hz, 1H), 5.22–5.16 (m, 2H), 5.02 (dd, *J*=5.4, 9.0 Hz, 1H), 4.94 (dd, *J*=1.2, 10.2 Hz, 1H), 3.78 (m, 1H), 1.73 (t, *J*=9.3 Hz, 1H), 1.63–1.20 (m, 7H), 1.12 (s, *J*=6.3 Hz, 3H), 0.89 (s, 9H), 0.05 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 212.1, 139.0, 114.5, 84.3, 81.8, 68.4, 64.0, 61.2, 39.3, 34.4, 28.4, 25.9, 23.8, 18.1, −4.4, −4.7.

Isoxazoline [(−)-42]. To a solution of (+)-**41** (120 mg, 0.284 mmol) and 2-(2-nitroethyl)-1,3-dioxane (90 mg, 0.56 mmol) in benzene (5 mL) was added phenyl isocyanate (65 mg, 0.55 mmol), and triethylamine (55 mg, 0.55 mmol). The mixture was stirred for 24 h after which monitoring by TLC (hexane–ethyl acetate (17:3)) indicated some starting material **41** remaining. Additional 2-(2-nitroethyl)-1,3-dioxane (90 mg, 0.56 mmol), phenyl isocyanate (65 mg, 0.55 mmol), and triethylamine (55 mg, 0.55 mmol) were added and the reaction mixture was stirred for an additional 12 h. Water (10 mL) was added and mixture extracted with ether. The organic layer was washed with water, brine, dried ($MgSO_4$) and concentrated. The white crystalline byproduct formed was washed with hexanes to extract the product. Purification by chromatography (flash SiO_2, hexane–ethyl acetate (17:3)) gave (−)-**42** (96 mg, 60%) as a yellow oil: $[\alpha]_D$=−36° (*c* 0.16, MeOH); IR ($CDCl_3$, cm^{-1}) 2047, 1979; ^{1}H NMR ($CDCl_3$) δ 5.23 (dd, *J*=4.9, 8.2 Hz, 1H), 5.08 (dd, *J*=5.0, 8.8 Hz, 1H), 4.74 (t, *J*=4.8 Hz, 1H), 4.26 (q, *J*=9.3 Hz, 1H), 4.11 (m, 3H), 3.76 (m, 4H), 3.18 (dd, *J*=10.3, 17.6 Hz, 1H), 2.86 (dd, *J*=8.6, 17.6 Hz, 1H), 2.64

(t, *J*=3.9 Hz, 2H), 2.07 (m, 1H), 1.73–1.20 (m, 6H), 1.10 (d, *J*=6.0 Hz, 3H), 1.02 (t, *J*=8.9 Hz, 1H), 0.88 (s, 9H), 0.04 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 155.0, 99.4, 86.3, 83.5, 83.0, 68.2, 66.8, 65.8, 59.6, 45.0, 39.1, 34.3, 33.6, 28.2, 25.8, 25.4, 23.7, 18.0, −4.5, −4.8; HRMS (FAB) *m*/*z* 564.2072 (calcd for $C_{26}H_{42}O_7NSiFe$ $(M+H)^+$ 564.2079).

β-Hydroxyketone (43). To a solution of (−)-**42** (32 mg; 0.056 mmol) in MeOH–H_2O (15:1, 10 mL) in a three-necked flask was added Raney-nickel (ca. 1 mL slurry in H_2O) and $B(OH)_3$ (20 mg). 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 5 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 (SiO_2, hexanes–ethyl acetate (7:3)) to give **43** as a yellow oil (7 mg, 22%): ^{1}H NMR ($CDCl_3$) δ 5.28 (dd, *J*=5.0, 8.3 Hz, 1H), 5.07 (dd, *J*=5.0, 8.7 Hz, 1H), 4.93 (t, *J*=5.2 Hz, 1H), 4.08 (m, 3H), 3.76 (m, 4H), 3.41 (d, *J*=3.4 Hz, OH), 2.97–2.65 (m, 3H), 2.05 (m, 1H), 1.65–1.20 (m, 8H), 1.12 (d, *J*=6.2 Hz, 3H), 0.88 (s, 9H), 0.04 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 208.0, 98.6, 85.5, 82.7, 70.1, 68.4, 66.9, 65.2, 62.3, 51.3, 48.9, 39.2, 34.3, 28.2, 25.8, 25.3, 23.7, 18.0, −4.5, −4.8; LRMS (FAB) *m*/*z* 451.3 (calcd for $C_{20}H_{27}O_8Fe$ $(M-TBS)^+$ 451.1).

2-[12-(*t*-Butyldimethylsilyl)oxy-2,4-dihydroxytridecyl)-1,3-dioxane (44). To a solution of (−)-**42** (50 mg; 0.089 mmol) in MeOH–H_2O (15:1, 10 mL) in a three-necked flask was added Raney-nickel (ca. 1 mL slurry in H_2O) and $B(OH)_3$ (30 mg). 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 48 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 (SiO_2, hexanes–ethyl acetate (7:3)) to give **44** as a pale oil (14 mg, 36%): ^{1}H NMR ($CDCl_3$) δ 4.79 (dd, *J*=4.8, 5.6 Hz, 1H), 4.28 (m, 1H), 4.13 (m, 3H), 3.95–3.70 (m, 5H), 2.10 (m, 1H), 1.87 (m, 1H), 1.60 (m, 2H), 1.45–1.20 (m, 16H), 1.10 (d, *J*=6.3 Hz, 3H), 0.88 (s, 9H), 0.03 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 101.6, 69.0, 68.6, 66.9, 66.8, 66.0, 42.5, 41.5, 41.4, 39.7, 37.5, 29.6, 25.9, 25.7, 25.6, 23.8, 18.1, −4.4, −4.7; HRMS (FAB) *m*/*z* 455.3176 (calcd for $C_{23}H_{48}O_5SiNa$ $(M+Na)^+$ 455.3169).

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