Conjugate Reduction Vicinal to Butadiene Tricarbonyl Iron Complexes. Application to the Synthesis of (±)-6,7-Dihydro-LTB$_4$ Methyl Ester

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Received December 26, 1991

The conjugate reduction of enones vicinal to butadiene tricarbonyl iron complexes was best performed using Red-Al/CuBr/2-butanol in THF. This reaction was applied to α,β-unsaturated ketone **13** for the synthesis of three possible metabolites of LTB$_4$ (as their methyl esters **4a**, **4b**, **4c**) generated via a 6,7-reductase pathway. Ketone **13** was synthesized in five steps starting from the organometallic complex **5**. Conjugate reduction of **13** selectively saturated the 6,7 double bond to give ketone **14**. Potassium borohydride reduction of **16** yielded a mixture of diols **17** which upon decomplexation using CAN afforded (±)-6,7-dihydro-LTB$_4$ methyl ester **4a** along with its 5-epimer **4b**. The 5-keto derivative **4c** was also prepared by direct decomplexation of **16**.

Introduction

In the past several years, the lipoxygenase-derived metabolites of arachidonic acid have been the subject of extensive research. Among these biologically active compounds, leukotriene B$_4$ (LTB$_4$) **1**, which is formed by polymorphonuclear leukocytes (PMNL) and monocytes, is one of the most potent chemotactic agents produced[2] and therefore may play a major role in inflammation and acute hypersensitivity.[3] Though a great deal of interest has been focused on the biological properties of LTB$_4$, it is also important to understand its metabolic fate. In human PMNL, LTB$_4$ has been found to be rapidly transformed into more polar, and generally biologically less active products, such as 20- and 19-hydroxy-LTB$_4$ (**2a** and **2b**) and 20-carboxy-LTB$_4$ (**2c**).[4] More recently another metabolic route of LTB$_4$ in various rat cells (rat PMNL, mouse bone marrow-derived macrophages and T-lymphocytes, rat mesangial and fibroblast tumor cells), probably involving a reductase, was independently elucidated by Powell and Kaever.[5] On the basis of spectroscopic data (UV absorbance at about 230 nm indicating a conjugated diene chromophore and mass spectra), these new, less polar, metabolites were identified as 10,11-dihydro-LTB$_4$ (**3a**) and 10,11-dihydro-12-oxo-LTB$_4$ (**3b**) (Figure 1).

Thereafter, dihydro-LTB$_4$ was also identified in human tissues by König et al.[6] Subsequently, Powell et al. evidenced 10,11-dihydro-12-*epi*-LTB$_4$ (**3c**) as a third major metabolite. The formation of **3c** proved to be consistent with a reversible reduction of **3b** as suggested by studies using 12-^{3}H-labeled 10,11-dihydro-LTB$_4$.[7] **3a** and its 12-*epi* analog **3c** were enantiospecifically synthesized by Falck et al.[8] However, it was also found that other LTB$_4$ isomers, generated by human PMNL (6-*trans*-LTB$_4$ and 12-*epi*-6-*trans*-LTB$_4$), were transformed into dihydro compounds in which the dienic system was not only shifted to the 6,8-position but also to the 7,9-position.[9] It has been also proposed that a 10,11-dihydro-12-oxo metabolite and another dihydro-5-oxo isomer are readily formed from 6-*trans*-LTB$_4$ and 12-*epi*-6-*trans*-LTB$_4$ with porcine leucocytes.[9b] More recently, Kaever et al. reported that human monocytes[10] and human glomerular mesangial cells[11] mainly metabolize LTB$_4$ to two undetermined dihydro isomers. In order to elucidate their structure, it seems helpful to have synthetic standards. As an extension of our program[12,13] concerning the application of butadiene tricarbonyl iron complexes for the stereocontrolled synthesis of polyenic systems, we chose to prepare 6,7-dihydro-LTB$_4$ methyl ester **4a**, its 5-*epi* analog **4b**, and the 5-oxo derivative **4c** in racemic form.[14] The preparation

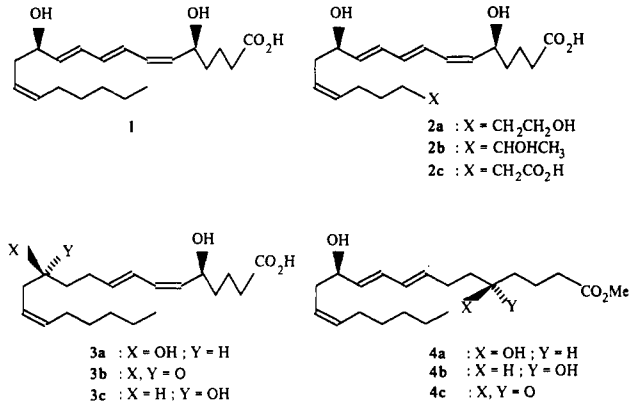

Figure 1.

(1) (a) Universität Erlangen-Nürnberg. (b) ENSCR.

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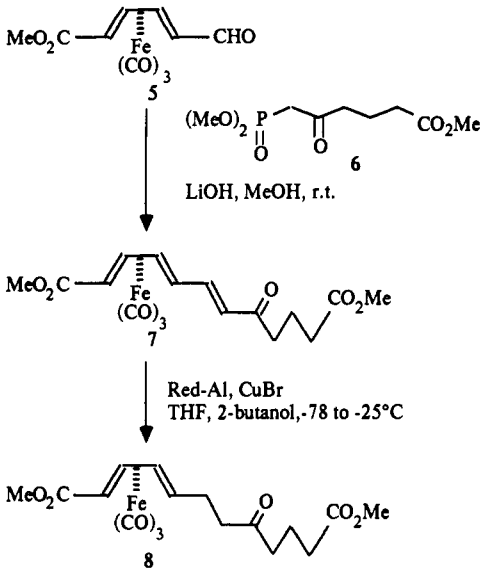
Scheme I



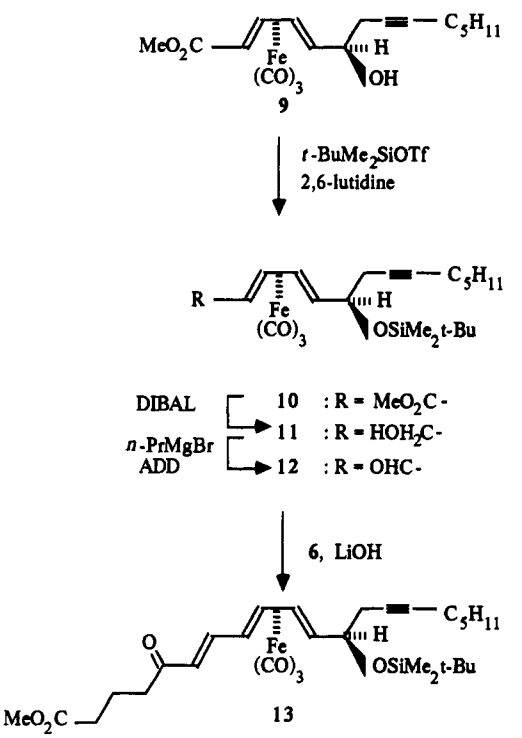
of **4c** was motivated by the fact that **3b** is a key intermediate in the reversible interconversion of **3a** to its 12-epimer **3c**. By analogy, it is possible that 6,7-dihydro-5-oxo-LTB_4 is a key intermediate in the reversible interconversion of 6,7-dihydro-LTB_4 to 6,7-dihydro-5-*epi*-LTB_4, utilizing a 6,7-reductase pathway for LTB_4.

In our synthetic plan, the saturation of the 6,7 double bond was envisaged by 1,4-reduction of an α,β-unsaturated ketone vicinal to a butadiene tricarbonyl iron complex to give the corresponding saturated ketone.[15] In this case, the butadiene unit is temporarily protected by the organometallic moiety, thus allowing the regioselective reduction of the uncomplexed $\Delta_{6,7}$ double bond.

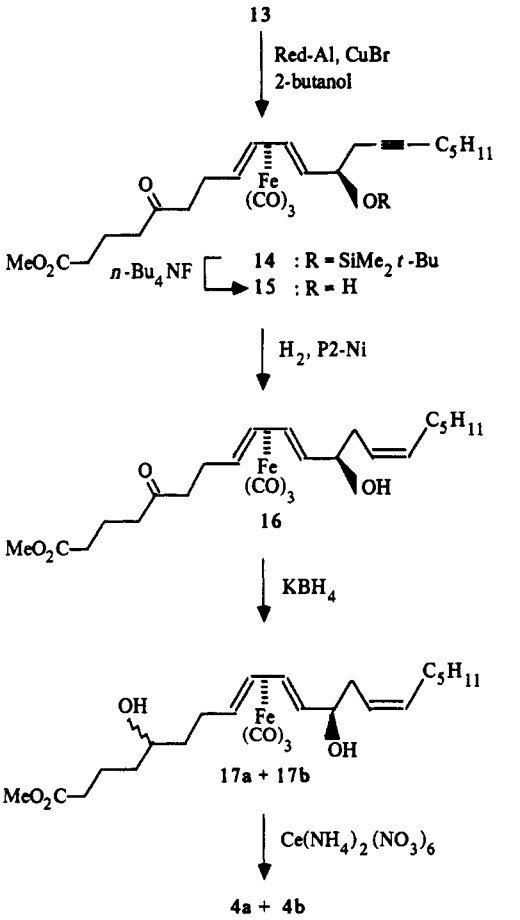
Results and Discussion

In order to test the crucial 1,4-reduction vicinal to a butadiene tricarbonyl iron moiety, model enone **7** was prepared; it was readily available by Horner–Wadsworth–Emmons condensation of aldehyde **5**[16] and β-keto phosphonate **6**[17] ((Scheme I). Whereas little 1,4-reduction of

Scheme II

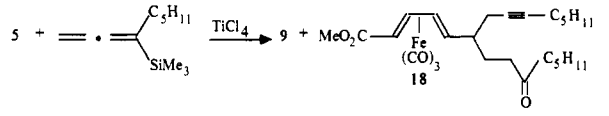


Scheme III



7 was obtained using sodium hydrotelluride,[18] the use of either lithium tri-*tert*-butoxyaluminium hydride or Red-Al in the presence of cuprous bromide (4 equiv of each, THF)

(13) During the preparation of **9** by reaction of **5** with 3-(trimethylsilyl)octa-1,2-diene in the presence of $TiCl_4$,[12] a ketone **18** was isolated as major byproduct (20%).



The structure attributed to **18** was proposed on the basis of spectroscopic data (see supplementary material). The mechanism of the formation of **18** has not been established. The initial step might be a nucleophilic attack, by the terminal carbon of the allenylsilane, on a pentadienyl-tricarbonyliron cation generated in situ by reaction of alcohol **9** with the Lewis acid ($TiCl_4$).

(14) For clarity, in all representations the absolute configuration of starting **5** was chosen to be 2(*R*),5(*S*) [(−)-**5**], consequently leading to **4a** in optically active form, i.e., methyl 5(*S*),12(*R*)-dihydroxyeicosa-8(*E*),10(*E*),14(*Z*)-trienoate and its 5*R*-*epi* analog **4b**. Although we worked with racemic compounds, it should be noted that the starting complex **5** can be resolved (see Monpert, A.; Grée, R.; Carrié, R. *Tetrahedron Lett.* **1981**, *22*, 1961).

(15) Saturation of the 6,7 double bond was not envisaged by catalytic hydrogenation since until now, double bonds vicinal to a butadiene tricarbonyl iron complex had not been reduced, except with difficulty in the case of allylic alcohols. See ref 16, pp 351–2.

(16) Grée, R. *Synthesis* **1989**, 341 and references cited therein.

(17) Dimethyl 5-(methoxycarbonyl)-2-oxopentylphosphonate (**6**) was prepared by reaction of 2 equiv of dimethyl lithiomethylphosphonate with glutaric anhydride in anhydrous ether at −90 to −5 °C followed by quenching with oxalic acid, filtration, and esterification with ethereal diazomethane: Delamarche, I.; Mosset, P. To be published.

(18) Yamashita, M.; Kato, Y.; Suemitsu, R. *Chem. Lett.* **1980**, 847.

and 2-butanol (15 equiv), as reported by Semmelhack et al.,[19] successfully afforded the reduced ketone **8** in, respectively, 50 and 59% yield. As described later, this conjugate reduction was also applied to enone **13** then leading to 6,7-dihydro-LTB$_4$.

Protection of secondary alcohol **9**[12,13] by *tert*-butyldimethylsilyl trifluoromethanesulfonate in the presence of 2,6-lutidine[20] afforded the corresponding silyl ether **10** in 93% yield (Scheme II). Conversion of methyl ester **10** to aldehyde **12**[21] was achieved by subsequent reduction of **10** using diisobutylaluminium hydride (DIBAL) and oxidation of the resulting primary alcohol **11** using *n*-propylmagnesium bromide and 1,1'-(azodicarbonyl)dipiperidine (ADD) in 89% overall yield.[22] This oxidation method proved to be especially suitable in the presence of a Fe(CO)$_3$ group since other oxidants tried (PCC, PDC, SO_3·Py, DMSO–oxalyl chloride) constantly gave lower yields and competitive decomplexation. The reaction of **12** with β-keto phosphonate **6** and lithium hydroxide in methanol afforded α,β-unsaturated ketone **13** in 89% yield. The *E* stereochemistry of the newly created double bond was confirmed by ^{1}H NMR ($J_{6,7}$ = 15.5 Hz).

Application of the conjugate reduction conditions detailed above (Red-Al/CuBr/2-butanol) to enone **13** afforded ketone **14** and starting enone **13** in, respectively, 47 and 23% yield after chromatography on silica gel (Scheme III). Desilylation of **14** using a solution of tetra-*n*-butylammonium fluoride in THF gave homopropargylic alcohol **15** in 81% yield. **15** was catalytically partially hydrogenated using P2–Ni in ethanol[23] to afford the homoallylic alcohol **16** in 89% yield. The *Z* stereochemistry of the $\Delta_{14,15}$ double bond was confirmed by ^{1}H NMR ($J_{14,15}$ = 10.9 Hz). Ketone **16** was reduced by potassium borohydride in methanol/water (10:3) to afford two 5-epimeric diols **17a** and **17b** (ca. 55:45) in 96% yield.[24] We failed to separate these epimers on a preparative scale. However, a partial separation was obtained by normal-phase HPLC on an analytical scale (hexane/THF 3:1). Proton NMR spectra of the two epimeric diols **17a** and **17b** clearly differ only by the signals of H-C$_9$; their ^{13}C NMR spectra exhibit different signals only for C$_3$ to C$_9$.

Decomplexation of **17a** and **17b** using ceric ammonium nitrate (CAN) in methanol afforded (±)-6,7-dihydro-LTB$_4$ methyl ester **4a** along with its 5-epimer: (±)-6,7-dihydro-5-*epi*-LTB$_4$ methyl ester **4b** in 94% yield. The two diastereoisomers **4a** and **4b** could not be separated by TLC on silica gel and were spectroscopically indistinguishable. The 5-oxo derivative **4c** was also prepared as its methyl ester by decomplexation of **16** using CAN in methanol in 69% yield. These three compounds would constitue useful chemical standards in order to check the actual occurrence of the 6,7-reductase pathway.

Conclusion

Red-Al in the presence of CuBr/2-butanol efficiently performs the 1,4-reduction of enones adjacent to a butadiene tricarbonyl iron moiety, thus leading to the corresponding saturated ketones. Noteworthy is that Fe(CO)$_3$ acts as an excellent protecting group thus allowing the regioselective reduction of the α-double bond of a conjugated trienic system. The usefulness of such an organometallic group is further enhanced by its easy removal by decomplexation. Butadiene–Fe(CO)$_3$ complexation thus enables the synthesis of elaborated polyenic systems such as compounds **4a**, **4b**, and **4c** described in this study. Their corresponding optically active[14] free acids are possible metabolites of LTB$_4$, which could be formed via a 6,7-reductase pathway. Comparison of such synthetic standards with biological materials would clarify the question of their actual occurrence. Additionally, it would be interesting to study the biological profile of these new potential metabolites.

Experimental Section

General. Nuclear magnetic resonance spectra were obtained in $CDCl_3$ solution. Mass spectra (MS) and high-resolution mass spectra (HRMS) were recorded under electronic impact at 70 eV.

(2*E*,4*E*,6*E*)-Tricarbonyliron [Dimethyl (η^4-2,3,4,5)-8-Oxododeca-2,4,6-trienedioate] (7). To a solution of dimethyl 5-(methoxycarbonyl)-2-oxopentylphosphonate (**6**) (400 mg, 1.27 mmol, 1.18 equiv, purity ca. 80%) in anhydrous methanol (10 mL) was added while stirring LiOH·H$_2$O (60 mg, 1.4 mmol, 1.3 equiv) followed by aldehyde **5** (300 mg, 1.07 mmol). After 50 min of reaction at rt, the reaction mixture was diluted with 25% aqueous NH_4Cl and extracted three times with ether. Drying ($MgSO_4$), concentration, and chromatography on silica gel using ether/petroleum ether (1:1 and then 7:3) as eluent afforded enone **7** as a red oil (385 mg, 88%, R_f = 0.27 with ether/petroleum ether (7:3)).

IR (neat): 2060 (C≡O), 1990 (C≡O), 1735 (C$_1$=O and C$_{12}$=O), 1690 (C$_8$=O), 1665 (C=C), 1605 (C=C) cm^{-1}. ^{1}H NMR (400 MHz): δ 6.73 (dd, 1 H, *J* = 15.4, 10.4 Hz, H-C$_6$), 6.25 (d, 1 H, *J* = 15.4 Hz, H-C$_7$), 5.92 (ddd, 1 H, *J* = 8.1, 5.0, 0.6 Hz, H-C$_3$), 5.62 (broad dd, 1 H, *J* = 8.7, 5.0 Hz, H-C$_4$), 3.69 (s, 3 H, CH_3OC$_1$), 3.67 (s, 3 H, CH_3OC$_{12}$), 2.58 (td, 2 H, *J* = 7.3, 2.0 Hz, H-C$_9$); 2.37 (t, 2 H, *J* = 7.0 Hz, H-C$_{11}$), 1.94 (broad dd, 1 H, *J* = 10.4, 8.7 Hz, H-C$_5$), 1.93 (tt, 2 H, *J* = 7.3, 7.0 Hz, H-C$_{10}$), 1.41 (broad d, 1 H, *J* = 8.1 Hz, H-C$_2$). ^{13}C NMR (100 MHz): δ 198.42 (C$_8$), 173.65 (C$_{12}$), 172.08 (C$_1$), 145.72 (C$_6$), 128.11 (C$_7$), 86.61 (C$_4$), 85.35 (C$_3$), 57.83 (C$_5$), 51.91 (CH_3OC$_1$), 51.56 (CH_3OC$_{12}$), 46.68 (C$_2$), 39.50 (C$_9$), 33.03 (C$_{11}$), 19.26 (C$_{10}$). MS: *m*/*z* 378 (M – CO)$^{\bullet+}$, 375 (M – OCH$_3$)$^{\bullet+}$, 350 (M – 2 CO)$^{\bullet+}$, 322 (M – 3 CO)$^{\bullet+}$, 291 (M – 3 CO – OCH$_3$)$^{\bullet+}$. Anal. Calcd for C$_{17}$H$_{18}$FeO$_8$: C, 50.27; H, 4.47. Found: C, 50.53; H, 4.68.

(2*E*,4*E*)-Tricarbonyliron [Dimethyl (η^4-2,3,4,5)-8-Oxododeca-2,4-dienedioate] (8). The conjugate reduction of enone **7** (84 mg, 0.21 mmol) was performed using the same procedure as described below for that of enone **13**. Chromatography on silica gel using ether/petroleum ether (1:1 and then 7:3) as eluent afforded ketone **8** as an orange oil (50 mg, 59%, R_f = 0.40 with ether/petroleum ether (7:3)).

IR (neat): 2060 (C≡O), 1980 (C≡O), 1740 (C$_1$=O and C$_{12}$=O), 1710 (C$_8$=O) cm^{-1}. ^{1}H NMR (400 MHz): δ 5.79 (ddd, 1 H, *J* = 8.1, 5.0, 1.1 Hz, H-C$_3$), 5.28 (broad dd, 1 H, *J* = 8.8, 5.0 Hz, H-C$_4$), 3.67 (s, 3 H, CH_3OC$_{12}$), 3.65 (s, 3 H, CH_3OC$_1$), 2.57 (t, 2 H, *J* = 7.2 Hz, H-C$_7$), 2.51 (t, 2 H, *J* = 7.2 Hz, H-C$_9$), 2.35 (t, 2 H, *J* = 7.2 Hz, H-C$_{11}$), 2.11 (ddt, 1 H, *J* = 14.0, 7.3, 7.2 Hz, H-C$_6$), 1.91 (tt, 1 H, *J* = 7.2, 7.2 Hz, H-C$_{10}$), 1.75 (dtd, 1 H, *J* = 14.0, 7.2, 7.0 Hz, H-C$_6$), 1.31 (dddd, 1 H, *J* = 8.8, 7.3, 7.0, 0.7 Hz, H-C$_5$), 0.98 (dd, 1 H, *J* = 8.1, 0.9 Hz, H-C$_2$). ^{13}C NMR (100 MHz): δ 208.42 (C$_8$), 173.56 (C$_{12}$), 172.52 (C$_1$), 87.37 (C$_4$), 83.29 (C$_3$), 63.78 (C$_5$), 51.67 (CH_3OC$_{12}$), 51.59 (CH_3OC$_1$), 45.95 (C$_2$), 44.16 (C$_7$), 41.56 (C$_9$), 32.97 (C$_{11}$), 27.84 (C$_6$), 18.78 (C$_{10}$). MS: *m*/*z* 377 (M – OCH$_3$)$^{\bullet+}$, 352 (M – 2 CO)$^{\bullet+}$, 324 (M – 3 CO)$^{\bullet+}$, 293 (M – 3 CO – OCH$_3$)$^{\bullet+}$. Anal. Calcd for C$_{17}$H$_{20}$FeO$_8$: C, 50.02; H, 4.94. Found: C, 50.30; H, 5.04.

(2*R*,5*S*,6*R*)- and (2*S*,5*R*,6*S*)-(2*E*,4*E*)-Tricarbonyliron [Methyl (η^4-2,3,4,5)-6-[(*tert*-Butyldimethylsilyl)oxy]tadeca-2,4-dien-8-ynoate] (10). To a solution of alcohol **9** (2.20 g, 5.64 mmol) in anhydrous THF (33 mL), cooled at −15 °C, was

(19) Semmelhack, M. F.; Stauffer, R. D.; Yamashita, A. *J. Org. Chem.* **1977**, *42*, 3180.

(20) Corey, E. J.; Cho, H.; Rücker, C.; Hua, D. H. *Tetrahedron Lett.* **1981**, *22*, 3455.

(21) Attempted direct reductions of an ester group vicinal to a butadiene tricarbonyl iron complex into an aldehyde were, until now, not synthetically useful. Mixtures of ester, alcohol, and aldehyde were obtained in each case.

(22) Narasaka, K.; Morikawa, A.; Saigo, K.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 2773.

(23) Brown, C. A.; Ahuja, V. K. *J. Chem. Soc., Chem. Commun.* **1973**, 553.

(24) Although this stategy did not enable, at present, a convenient control of C5 stereochemistry, it is important to point out that both 6,7-dihydro-LTB$_4$ and its 5-epimer would exist if such a 6,7-reductase pathway of LTB$_4$ actually occurs.

added, under N_2 and stirring, 2,6-lutidine (1.32 mL, 11.3 mmol, 2 equiv) and then over 2 min *tert*-butyldimethylsilyl trifluoromethanesulfonate (1.95 mL, 8.4 mmol, 1.5 equiv). After 15 min at −15 °C, anhydrous methanol (3 mL) was added to the reaction mixture which was left at −15 °C for a further 10 min. After addition to 1 M aqueous $NaHCO_3$ (50 mL) and ether (50 mL) and partitioning, the aqueous layer was again extracted with ether. Combined organic extracts were washed with water, dried ($MgSO_4$), and concentrated. Flash chromatography on silica gel using ether/petroleum ether (1:19) as eluent afforded the silyl ether **10** as a fairly stable orange oil (2.64 g, 93%, R_f = 0.48 with ether/petroleum ether (1:4)).

IR (neat): 2060 (C≡O), 1975 (C≡O), 1720 (C═O) cm^{-1}. ^1H NMR (300 MHz): δ 5.81 (broad dd, 1 H, J = 8.0, 5.1 Hz, H-C_3), 5.43 (broad dd, 1 H, J = 8.9, 5.1 Hz, H-C_4), 4.09 (ddd, 1 H, J = 9.1, 4.7, 3.4 Hz, H-C_6), 3.66 (s, 3 H, CO_2CH_3), 2.52 (ddt, 1 H, J = 16.3, 4.7, 2.3 Hz, H-C_7), 2.33–2.08 (m, 3 H: H-C_7, ddt at 2.20 ppm, J = 16.3, 9.1, 2.3 Hz and H-C_{10}, pseudo tt at 2.17 ppm, J = 6.9, 2.3 Hz), 1.75 (broad dd, 2 H, J = 8.9, 3.4 Hz, H-C_5), 1.50 (broad tt, 2 H, J = 7.0, 6.9 Hz, H-C_{11}), 1.44–1.22 (m, 4 H, H-$C_{12,13}$), 0.91 (H-C_2), 0.90 (s, 9 H, *t*-Bu and t, 3 H, J = 6.8 Hz, H-C_{14}), 0.13 (s, 3 H, $SiCH_3$), 0.09 (s, 3 H, $SiCH_3$). ^{13}C NMR (22.5 MHz): δ 209.5 (C≡O), 172.67 (C_1), 83.76 (C_9), 83.30 (C_3), 82.17 (C_4), 75.71 (C_8), 71.26 (C_6), 69.99 (C_5), 51.49 (OCH_3), 45.30 (C_2), 31.52 (C_7), 31.17 (C_{12}), 28.60 (C_{11}), 25.80 ($C(CH_3)_3$), 22.24 (C_{13}), 18.80 (C_{10}), 18.15 ($C(CH_3)_3$), 13.94 (C_{14}), −4.44 ($SiCH_3$), −4.89 ($SiCH_3$). MS: m/z 476 (M − CO)$^{\bullet+}$, 473 (M − OCH_3)$^{\bullet+}$, 448 (M − 2 CO)$^{\bullet+}$, 420 (M − 3 CO)$^{\bullet+}$, 363 (M − 3 CO − *t*-Bu)$^{\bullet+}$. Anal. Calcd for $C_{24}H_{36}FeO_6Si$: C, 57.14; H, 7.20. Found: C, 57.18; H, 7.07.

(2*R*,5*S*,6*R*)- and (2*S*,5*R*,6*S*)-(2*E*,4*E*)-Tricarbonyliron [(η⁴-2,3,4,5)-6-[(*tert*-Butyldimethylsilyl)oxy]butadeca-2,4-dien-8-yn-1-ol] (11). To a solution of methyl ester **10** (2.64 g, 5.23 mmol) in anhydrous ether (35 mL; −45 °C, nitrogen) was added dropwise while stirring a 1 M solution of diisobutylaluminium hydride in hexanes (12.1 mL, 2.3 equiv). After 20 min of reaction at −45 °C, the reaction mixture was quenched by the addition of water (10 mL) and warmed to rt. Saturated aqueous potassium sodium tartrate (60 mL) and ether (50 mL) were added, and the resulting mixture was stirred until it became clear. After separation of the ethereal layer, the aqueous layer was extracted twice with ether. Combined organic extracts were washed with brine and then with water. After drying ($MgSO_4$) and concentration, flash chromatography on silica gel using ether/petroleum ether (1:4) as eluent afforded alcohol **11** as a yellow oil (2.454 g, 98%, R_f = 0.11 with ether/petroleum ether (1:4)).

IR (neat): 3355 (broad, OH), 2050 (C≡O), 1965 (C≡O) cm^{-1}. ^1H NMR (300 MHz): δ 5.29 (broad dd, 1 H, J = 8.8, 5.0 Hz, H-C_4, ddd after irradiation of H-C_6, J = 8.8, 5.0, 0.9 Hz), 5.19 (broad dd, 1 H, J = 8.3, 5.0 Hz, H-C_3), 4.04 (ddd, 1 H, J = 8.8, 4.6, 3.8 Hz, H-C_6), 3.75 (broad dd, 1 H, H-C_1, dd after addition of D_2O, J = 11.9, 5.6 Hz), 3.64 (broad dd, 1 H, H-C_1, dd after addition of D_2O, J = 11.9, 7.5 Hz), 2.48 (ddt, 1 H, J = 15.9, 4.6, 2.4 Hz, H-C_7), 2.20 (ddt, 1 H, J = 15.9, 8.8, 2.4 Hz, H-C_7), 2.14 (tt, 2 H, J = 7.2, 2.4 Hz, H-C_{10}), 1.60 (broad s, OH + H_2O), 1.56 (ddd, 1 H, J = 8.8, 3.8, 0.8 Hz, H-C_5), 1.53–1.43 (m, 2 H, H-C_{11}), 1.43–1.24 (m, 4 H, H-$C_{12,13}$), 1.04 (dddd, 1 H, J = 8.3, 7.5, 5.6, 0.9 Hz, H-C_2), 0.91 (s, 9 H, *t*-Bu), 0.90 (t, 3 H, J = 7.1 Hz, H-C_{14}), 0.13 (s, 3 H, $SiCH_3$), 0.08 (s, 3 H, $SiCH_3$). ^{13}C NMR (22.5 MHz): δ 211.40 (m, C≡O), 83.28 (m, C_9), 82.05 (dm, J = 167.5 Hz, C_4), 81.48 (dm, J = 169.8 Hz, C_3), 76.17 (q, J = 3.5 Hz, C_8), 71.55 (dm, J = 142 Hz, C_6), 69.35 (dm, J = 158 Hz, C_5), 64.52 (tm, J = 143 Hz, C_1), 59.71 (dm, J = 159 Hz, C_2), 31.62 (broad t, J = 132 Hz, C_7), 31.26 (tm, J = 125–126 Hz, C_{12}), 28.74 (C_{11}), 25.88 (qp, J = 125.1, 5.6 Hz, $C(CH_3)_3$), 18.88 (tm, J = 130 Hz, C_{10}), 18.20 (m, $C(CH_3)_3$), 14.03 (qm, J = 125 Hz, C_{14}), −4.42 (qd, J = 118.2, 1.4 Hz, $SiCH_3$), −4.90 (qd, J = 118.5, 2 Hz, $SiCH_3$). MS: m/z 420 (M − 2 CO)$^{\bullet+}$, 392 (M − 3 CO)$^{\bullet+}$, 375 (M − 3 CO − OH)$^{\bullet+}$, 335 (M − 3 CO−*t*Bu)$^{\bullet+}$. Anal. Calcd for $C_{23}H_{36}FeO_5Si$: C, 57.98; H, 7.62. Found: C, 57.76; H, 7.88.

(2*R*,5*S*,6*R*)- and (2*S*,5*R*,6*S*)-(2*E*,4*E*)-Tricarbonyliron [(η⁴-2,3,4,5)-6-[(*tert*-Butyldimethylsilyl)oxy]butadeca-2,4-dien-8-ynal] (12). A solution of *n*-propylmagnesium bromide in THF (10 mL) was prepared by reacting magnesium turnings (92.1 mg, 3.75 mmol, 1.25 equiv) with 1-bromopropane (0.358 mL, 3.9 mmol, 1.3 equiv). This Grignard reagent was added dropwise to a stirred solution of alcohol **11** (1.444 g, 3.0 mmol) in anhydrous THF (12 mL), cooled at 0 °C. After 10 min at 0 °C, a solution of 1,1′-(azodicarbonyl)dipiperidine (918 mg, 3.6 mmol, 1.2 equiv) in anhydrous THF (8 mL) was subsequently added. After 20 min of further reaction at 0 °C, the resulting black solution was quenched by addition of brine and extracted twice with ether. Combined organic layers were washed with 1 M aqueous $NaHCO_3$ and then with water. Drying ($MgSO_4$), concentration, and flash chromatography on silica gel using ether/petroleum ether (1:9) as eluent afforded aldehyde **12** as an orange oil (1.306 g, 91%, R_f = 0.50 with ether/petroleum ether (1:4)).

IR (neat): 2760 (CH of CHO), 2060 (C≡O), 1980 (C≡O), 1685 (C═O) cm^{-1}. ^1H NMR (300 MHz): δ 9.30 (d, 1 H, J = 4.4 Hz, *CHO*), 5.81 (ddd, 1 H, J = 8.1, 5.1, 0.9 Hz, H-C_3), 5.50 (broad dd, 1 H, J = 9.0, 5.1 Hz, H-C_4), 4.14 (ddd, 1 H, J = 9.2, 5.0, 3.6 Hz, H-C_6), 2.56 (ddt, 1 H, J = 16.1, 5.0, 2.4 Hz, H-C_7), 2.21 (ddt, 1 H, J = 16.1, 9.2, 2.4 Hz, H-C_7), 2.17 (tt, 2 H, J = 7.0, 2.4 Hz, H-C_{10}), 2.04 (ddd, 1 H, J = 9.0, 3.6, 0.9 Hz, H-C_5), 1.50 (broad tt, 2 H, J = 7.0, 6.9 Hz, H-C_{11}), 1.42–1.24 (m, 4 H, H-$C_{12,13}$), 1.18 (ddd, 1 H, J = 8.1, 4.4, 0.8 Hz, H-C_2), 0.90 (s, 9 H, *t*-Bu and *t*, 3 H, J = 7.0 Hz, H-C_{14}), 0.14 (s, 3 H, $SiCH_3$), 0.10 (s, 3 H, $SiCH_3$). ^{13}C NMR (100 MHz): δ 196.33 (C_1), 84.61 (C_3), 83.99 (C_9), 80.51 (C_4), 75.46 (C_8), 71.11 (C_6), 71.04 (C_5), 54.28 (C_2), 31.50 (C_{12}), 31.12 (C_7), 28.55 (C_{11}), 25.74 ($C(CH_3)_3$), 22.22 (C_{13}), 18.72 (C_{10}), 18.11 ($C(CH_3)_3$), 14.01 (C_{14}), −4.46 ($SiCH_3$), −4.92 ($SiCH_3$). MS: m/z 418 (M − 2 CO)$^{\bullet+}$, 390 (M − 3 CO)$^{\bullet+}$, 335 (M − 3 CO − *t*Bu)$^{\bullet+}$. Anal. Calcd for $C_{23}H_{34}FeO_5Si$: C, 58.22; H, 7.23. Found: C, 58.27; H, 7.19.

(8*R*,11*S*,12*R*)- and (8*S*,11*R*,12*S*)-(6*E*,8*E*,10*E*)-Tricarbonyliron [Methyl (η⁴-8,9,10,11)-12-[(*tert*-Butyldimethylsilyl)oxy]-5-oxoeicosa-6,8,10-trien-14-ynoate] (13). To a solution of phosphonate **6** (1.2 g, 3.8 mmol, 1.6 equiv, purity ca. 80%) in anhydrous methanol (25 mL) was added while stirring $LiOH·H_2O$ (300 mg, 7.1 mmol, 2.9 equiv) followed by a solution of aldehyde **12** (1.151 g, 2.42 mmol) in anhydrous methanol (25 mL). After 60 min of reaction at rt, the reaction mixture was worked up as described for the enone **7**. Chromatography on silica gel using ether/petroleum ether (1:4) as eluent afforded methyl ester **13** as a red oil (1.303 g, 89%, R_f = 0.50 with ether/petroleum ether (1:1)).

IR (neat): 2050 (C≡O), 1985 (C≡O), 1745 (C_1═O), 1690 (C_5═O), 1665 (C═C), 1605 (C═C) cm^{-1}. ^1H NMR (300 MHz): δ 6.74 (dd, 1 H, J = 15.5, 10.3 Hz, H-C_7), 6.13 (d, 1 H, J = 15.5 Hz, H-C_6), 5.44 (broad dd, 1 H, J = 8.4, 5.2 Hz, H-C_9), 5.36 (broad dd, 1 H, J = 8.5, 5.1 Hz, H-C_{10}), 4.09 (ddd, 1 H, $J_{12,13}$ = 9.0 and 5.0 Hz, $J_{11,12}$ = 3.5 Hz, H-C_{12}), 3.67 (s, 3 H, CO_2CH_3), 2.57 (pseudo t, 2 H, J = 7.2 Hz, H-C_4), 2.52 (ddt, 1 H, $J_{13,13}$ = 16.6 Hz, $J_{12,13}$ = 5.0 Hz, $J_{13,16}$ = 2.4 Hz, H-C_{13}), 2.36 (t, 2 H, J = 7.2 Hz, H-C_2), 2.21 (ddt, 1 H, $J_{13,13}$ = 16.6 Hz, $J_{12,13}$ = 9.0 Hz, $J_{13,16}$ = 2.4 Hz, H-C_{13}), 2.18 (tt, 2 H, $J_{16,17}$ = 7.0 Hz, $J_{13,16}$ = 2.4 Hz, H-C_{16}), 1.93 (tt, 2 H, J = 7.2, 7.1 Hz, H-C_3), 1.89 (broad dd, 1 H, J = 8.5, 3.5 Hz, H-C_{11}), 1.58–1.44 (m, 3 H, H-$C_{8,17}$ with H-C_8 broad d at 1.545 ppm, J = 8.4 Hz), 1.44–1.26 (m, 4 H, H-$C_{18,19}$), 0.91 (t, 3 H, J = 7.1 Hz, H-C_{14}), 0.90 (s, 9 H, *t*-Bu), 0.13 (s, 3 H, $SiCH_3$), 0.09 (s, 3 H, $SiCH_3$). ^{13}C NMR (100 MHz): δ 198.65 (C_5), 173.71 (C_1), 147.62 (C_7), 126.84 (C_6), 83.64 (C_{15}), 82.38 (C_9 and C_{10}), 75.84 (C_{14}), 71.22 (C_{12}), 69.73 (C_{11}), 55.81 (C_8), 51.53 (OCH_3), 39.06 (C_4), 31.49 (C_{18}), 31.09 (C_{13}), 28.57 (C_{17}), 25.76 ($C(CH_3)_3$), 22.24 (C_{19}), 19.39 (C_3), 18.73 (C_{16}), 18.11 ($C(CH_3)_3$), 14.04 (C_{20}), −4.45 ($SiCH_3$), −4.93 ($SiCH_3$). MS: m/z 569 (M − OMe)$^{\bullet+}$, 544 (M − 2 CO)$^{\bullet+}$, 516 (M − 3 CO)$^{\bullet+}$. Anal. Calcd for $C_{30}H_{44}FeO_7Si$: C, 59.99; H, 7.39. Found: C, 60.09; H, 7.27.

(8*R*,11*S*,12*R*)- and (8*S*,11*R*,12*S*)-(8*E*,10*E*)-Tricarbonyliron [Methyl (η⁴-8,9,10,11)-12-[(*tert*-Butyldimethylsilyl)oxy]-5-oxoeicosa-8,10-dien-14-ynoate] (14). To a solution of CuBr (1.34 g, 9.3 mmol, 4.0 equiv) in anhydrous THF (25 mL), stirred and cooled at −5 °C, was added dropwise under N_2 a 3.4 M solution of Red-Al in toluene (2.75 mL, 9.3 mmol, 4.0 equiv). The resulting black suspension was further stirred for 30 min at 0 °C and then cooled to −78 °C (dry ice/acetone bath). Sieve-dried 2-butanol (3.21 mL, 35 mmol, 15 equiv) was added followed 4 min later by a solution of α,β-unsaturated ketone **13** (1.40 g, 2.33 mmol) in anhydrous THF (20 mL). After 10 min at −78 °C, the reaction mixture was warmed at −25 °C and left stirring at −25 °C for 1.1 h. After addition of water (20 mL), it was poured to 25% aqueous NH_4Cl (100 mL) and extracted three times with ether. Combined organic extracts were washed with 1 M aqueous $NaHCO_3$ and

dried ($MgSO_4$). After concentration and column chromatography on silica gel under air*, gradient elution using ether/petroleum ether (1:9, 1:4, and 1:1) sequentially afforded some *tert*-butyldimethylsilanol, ketone **14** as a yellow oil (655 mg, 47%) and unreduced starting ketone **13** (319 mg, 23%).

*When the chromatography was performed under N_2, little starting ketone was recovered but instead a highly polar red oil (R_f = 0.10 with ether/petroleum ether (1:1)) which was oxidized by air contact to the starting ketone with formation of a brown mineral. This may be due to competing formation of a cuprous and/or aluminium enolate of the starting ketone.

IR (neat): 2040 (C≡O), 1975 (C≡O), 1740 (C_1=O), 1715 (C_5=O) cm^{-1}; ^{1}H NMR (300 MHz): δ 5.23 (broad dd, 1 H, J = 8.9, 5.1 Hz, ddd after irradiation of H-C_{12}, J 7.1, 2.3 8.8, 5.1, 0.8 Hz, H-C_{10}), 5.07 (broad dd, 1 H, J = 8.6, 5.1 Hz, ddd after irradiation of H-C_6, J = 8.6, 5.1, 0.5 Hz, H-C_9), 3.98 (ddd, 1 H, J = 8.6, 5.0, 3.7 Hz, H-C_{12}), 3.67 (s, 3 H, CO_2CH_3), 2.52 (broad t, 2 H, J = 6.9 Hz, H-C_6), 2.49 (t, 2 H, J = 7.1 Hz, H-C_4), 2.44 (ddt, 1 H, J = 15.9, 5.0, 2.3 Hz, H-C_{13}), 2.34 (t, 2 H, J = 7.2 Hz, H-C_2), 2.19 (ddt, 1 H, J = 15.9, 8.6, 2.3 Hz, H-C_{13}), 2.15 (tt, 2 H, J = 7.1, 2.3 Hz, H-C_{16}), 2.095 (dtd, 1 H, J = 14.6, 6.9, 6.3 Hz, H-C_7), 1.895 (tt, 2 H, J = 7.2, 7.1 Hz, H-C_3), 1.67 (ddt, 1 H, J = 14.6, 7.7, 6.9 Hz, H-C_7), 1.49 (pseudo tt, 2 H, J = 7.2, 6.9 Hz, H-C_{17}), 1.42–1.24 (m, 5 H: H-$C_{18,19}$ and H-C_{11} ddd at 1.36 ppm, J = 8.9, 3.7, 0.6 Hz), 0.90 (s, 9 H, *t*-Bu and m, 1 H, H-C_8, and t, 3 H, J = 7.0 Hz, H-C_{20}), 0.12 (s, 3 H, CH_3-Si), 0.07 (s, 3 H, CH_3-Si). ^{13}C NMR (100 MHz): δ 208.82 (C_5), 173.60 (C_1), 83.21 (C_{15}), 83.14 (C_9 or C_{10}), 80.36 (C_9 or C_{10}), 76.23 (C_{14}), 71.48 (C_{12}), 68.72 (C_{11}), 61.49 (C_8), 51.58 (OCH_3), 44.57 (C_4), 41.52 (C_6), 33.03 (C_2), 31.45 (C_{13}), 31.12 (C_{18}), 28.58 (C_{17}), 28.01 (C_7), 25.77 ($C(CH_3)_3$), 22.24 (C_{19}), 18.81 (C_3), 18.75 (C_{16}), 18.12 ($C(CH_3)_3$), 14.03 (C_{20}), −4.42 ($SiCH_3$), −4.93 ($SiCH_3$). MS: m/z 545 (M − *t*-Bu)$^{\bullet+}$, 518 (M − 3 CO)$^{\bullet+}$. Anal. Calcd for $C_{30}H_{46}FeO_7Si$: C, 59.79; H, 7.70. Found: C, 59.67; H, 7.62.

(8*R*,11*S*,12*R*)- and (8*S*,11*R*,12*S*)-(8*E*,10*E*)-Tricarbonyliron [Methyl (η^4-8,9,10,11)-12-Hydroxy-5-oxoeicosa-8,10-dien-14-ynoate] (15). To a solution of silyl ether **14** (535 mg, 0.89 mmol) in anhydrous THF (5.5 mL) was added a 1 M solution of tetra-*n*-butylammonium fluoride in THF (5.5 mL, 6.2 equiv). After 45 h of stirring at room temperature in darkness, brine was added and the resulting mixture was extracted three times with ether. Combined organic extracts were washed with water, dried ($MgSO_4$), and concentrated. Chromatography on silica gel with gradient elution using ether/petroleum ether (1:9, 1:4, and 1:1) afforded alcohol **15** as a yellow oil (351 mg, 81%, R_f = 0.26 with ether/petroleum ether (1:1)).

IR (neat): 3500 (broad, OH), 2040 (C≡O), 1970 (C≡O), 1740 (C_1=O), 1720 (C_5=O) cm^{-1}. ^{1}H NMR (300 MHz): δ 5.24 (broad ddd, ddd after irradiation of H-C_{12}, J = 8.5, 5.0, 0.9 Hz, 1 H, H-C_{10}), 5.11 (broad dd, broad ddd after irradiation of H-C_{12}, J = 8.7, 5.0, 0.5 Hz, 1 H, H-C_9), 3.67 (s, 3 H, CO_2CH_3), 3.62 (broad ddd, 1 H, $J_{11,12}$ = 7.0 Hz, $J_{12,13}$ = 6.7, 5.8 Hz, H-C_{12}), 2.53 (broad t, 2 H, J = 7.2 Hz, H-C_6), 2.50 (t, 2 H, J = 7.3 Hz, H-C_4), 2.45–2.38 (m, 2 H, H-C_{13} [1 H, ddt at 2.42 ppm, J = 16, 5.8, 2.4 Hz, and 1 H, ddt at 2.40 ppm, J = 16, 6.7, 2.4 Hz]), 2.34 (t, 2 H, J = 7.2 Hz, H-C_2), 2.17 (tt, 2 H, J = 7.0, 2.4 Hz, H-C_{16}), 2.12 (dtd, 1 H, J = 14.3, 7.2, 7.2 Hz, H-C_7), 1.97 (broad, 1 H, OH), 1.90 (tt, 2 H, J = 7.2, 7.2 Hz, H-C_3), 1.67 (dtd, 1 H, J = 14.3, 7.2, 6.9 Hz, H-C_7), 1.56–1.45 (m, 2 H, H-C_{17}), 1.43–1.25 (m, 4 H, H-$C_{18,19}$), 1.005 (dddd, 1 H, J = 8.7, 7.2, 6.9, 0.7 Hz, H-C_8), 1.00 (ddd, 1 H, J = 8.5, 7.0, 0.9 Hz, H-C_{11}), 0.90 (t, 3 H, J = 7.1 Hz, H-C_{20}). ^{13}C NMR (100 MHz): δ 208.75 (C_5), 173.60 (C_1), 84.32 (C_9 or C_{10}), 83.83 (C_{15}), 81.25 (C_9 or C_{10}), 75.53 (C_{14}), 72.05 (C_{12}), 66.35 (C_{11}), 62.54 (C_8), 51.59 (OCH_3), 44.41 (C_4), 41.53 (C_6), 33.02 (C_2), 31.10 (C_{18}), 30.30 (C_{13}), 28.60 (C_{17}), 27.88 (C_7), 22.21 (C_{19}), 18.79 (C_3), 18.72 (C_{16}), 14.01 (C_{20}). MS: m/z 404 (M − 3 CO)$^{\bullet+}$, 386 (M − 3 CO − H_2O)$^{\bullet+}$. Anal. Calcd for $C_{24}H_{32}FeO_7$: C, 59.02; H, 6.61. Found: C, 59.20; H, 6.34.

(8*R*,11*S*,12*R*)- and (8*S*,11*R*,12*S*)-(8*E*,10*E*,14*Z*)-Tricarbonyliron [Methyl (η^4-8,9,10,11)-12-Hydroxy-5-oxoeicosa-8,10,14-trienoate] (16). For this hydrogenation, ultrasound degassed 95% ethanol was used as solvent. In a 25-mL flask filled with hydrogen, a 0.1 M ethanolic solution of sodium borohydride (1.28 mL, 0.2 equiv) was added to a vigorously stirred 0.05 M ethanolic solution of nickel acetate tetrahydrate (2.56 mL, 0.2 equiv). A black precipitate of P2–Ni catalyst was immediately formed. To this suspension was added a 0.1 M ethanolic solution of ethylenediamine (1.60 mL, 0.25 equiv) followed by a solution of the acetylenic alcohol **15** (312 mg, 0.64 mmol) in ethanol (2 mL). Transfer of the alkyne was completed using ethanol (0.5 mL). The reaction flask was stoppered after the hydrogen pressure had risen to 2 bar. After 44 h of stirring at room temperature in darkness, the reaction mixture was diluted with ether and filtered over silica gel. After rinsing with ether, and concentration, chromatography on silica gel afforded the ethylenic alcohol **16** as a yellow oil (278 mg, 89%, R_f = 0.26 with ether/petroleum ether (1:1)).

IR (neat): 3450 (broad, OH), 2040 (C≡O), 1965 (C≡O), 1740 (C_1=O), 1720 (C_5=O) cm^{-1}. ^{1}H NMR (300 MHz): δ 5.59 (dtt, 1 H, $J_{14,15}$ = 10.9 Hz, $J_{15,16}$ = 7.3 Hz, $J_{13,15}$ = 1.3 Hz, H-C_{15}), 5.38 (dddt, 1 H, $J_{14,15}$ = 10.9 Hz, $J_{13,14}$ = 8.3 and 6.7 Hz, $J_{14,16}$ = 1.4 Hz), 5.18 (broad dd, 1 H, J = 8.8, 5.1 ($J_{9,10}$) Hz, ddd after irradiation of H-C_{12}, J = 8.5, 5.0, 0.9 Hz, H-C_{10}), 5.10 (broad dd, 1 H, J = 8.5, 5.1 Hz, H-C_9), 3.67 (s, 3 H, CO_2CH_3), 3.51 (ddd, 1 H, $J_{11,12}$ = 7.4 Hz, $J_{12,13}$ = 7.1 and 5.4 Hz, H-C_{12}), 2.52 (t, 2 H, J = 7.3 Hz, H-C_6), 2.50 (t, 2 H, J = 7.3 Hz, H-C_4), 2.36 (broad ddd, 1 H, $J_{13,13}$ = 14.1 Hz, $J_{13,14}$ = 8.3 Hz, $J_{12,13}$ = 7.1 Hz, H-C_{13}), 2.34 (t, 2 H, J = 7.2 Hz, H-C_2), 2.26 (broad ddd, 1 H, $J_{13,13}$ = 14.1 Hz, $J_{13,14}$ = 6.7 Hz, $J_{12,13}$ = 5.4 Hz), 2.13 (dtd, 1 H, $J_{7,7}$ = 13.8 Hz, $J_{6,7}$ = 7.3 Hz, $J_{7,8}$ = 6.8 Hz, H-C_7), 2.03 (broad dt, 2 H, $J_{15,16}$ = 7.3 Hz, $J_{16,17}$ = 7.0 Hz, H-C_{16}), 1.90 (tt, 2 H, $J_{3,4}$ = 7.3 Hz, $J_{2,3}$ = 7.2 Hz, H-C_3), 1.66 (ddt, 1 H, $J_{7,7}$ = 13.8 Hz, $J_{6,7}$ = 8.5 Hz, $J_{7,8}$ = 6.9 Hz, H-C_7), 1.46–1.18 (m, 6 H, H-$C_{17,18,19}$), 1.03 (ddd, 1 H, J = 8.5, 7.1, 0.7 Hz, H-C_{11}), 1.01 (broad ddd, 1 H, J = 8.8, 6.9, 6.8 Hz, H-C_8), 0.88 (t, 3 H, J = 6.8 Hz, H-C_{20}). ^{13}C NMR (100 MHz): δ 208.79 (C_5), 173.60 (C_1), 134.24 (C_{15}), 124.18 (C_{14}), 84.21 (C_9 or C_{10}), 81.16 (C_9 or C_{10}), 73.18 (C_{12}), 68.06 (C_{11}), 62.57 (C_8), 51.59 (OCH_3), 44.41 (C_4), 41.55 (C_6), 37.99 (C_{13}), 33.02 (C_2), 31.50 (C_{18}), 29.28 (C_{17}), 27.88 (C_7), 27.37 (C_{16}), 22.54 (C_{19}), 18.79 (C_3), 14.06 (C_{20}). MS: m/z 434 (M − 2 CO)$^{\bullet+}$, 406 (M − 3 CO)$^{\bullet+}$, 388 (M − 3 CO − H_2O)$^{\bullet+}$. Anal. Calcd for $C_{24}H_{34}FeO_7$: C, 58.78; H, 6.99. Found: C, 58.86; H, 7.07.

(5(*R*,*S*),8*R*,11*S*,12*R*)- and (5(*R*,*S*),8*S*,11*R*,12*S*)-(8*E*,10*E*,14*Z*)-Tricarbonyliron [Methyl (η^4-8,9,10,11)-5,12-Dihydroxyeicosa-8,10,14-trienoate] (17a, 17b). To a solution of ketone **16** (85 mg, 0.173 mmol) in anhydrous methanol (1.5 mL), cooled at 0 °C, was added a freshly prepared solution of KBH_4 (270 mg, 5 mmol) in methanol (10 mL) and water (3 mL). After 15 min of reaction at 0 °C, the reaction mixture was diluted with brine and extracted three times with ether. Combined organic extracts were washed with water, dried ($MgSO_4$), and concentrated. Chromatography on silica gel using ether/petroleum ether (1:1) as eluent afforded a mixture ca. 55:45 of two inseparable diastereoisomeric diols **17a, 17b** as a yellow oil (82 mg, 96%, R_f = 0.22 with ether/petroleum ether (7:3)).

IR (neat): 3420 (broad, OH), 2040 (C≡O), 1965 (C≡O), 1735 (C=O), 1720 (C=O) cm^{-1}. ^{1}H NMR (300 MHz): δ 5.59 (broad dtt, 1 H, J = 10.8, 7.3, 1.4 Hz, H-C_{15}), 5.40 (broad dddt, 1 H, J = 10.8, 8.4, 6.7, 1.4 Hz, H-C_{14}), 5.185 (broad dd, 1 H, J = 8.6, 5.1 Hz, H-C_{10}: ddd after irradiation of H-C_{12}, J = 8.6, 5.1, 0.6 Hz), 5.09 (broad dd, 0.6 H, J = 8.6, 5.1 Hz, H-C_9 of the major diastereoisomer), 5.075 (broad dd, 0.4 H, H-C_9 of the minor diastereoisomer), 3.68 (s, 3 H, CO_2CH_3), 3.66–3.55 (m, 1 H, H-C_5), 3.51 (ddd, 1 H, $J_{11,12}$ = 6.7 Hz, $J_{12,13}$ = 7.8 and 5.4 Hz, H-C_{12}), 2.44–2.20 (4 H, H-$C_{2,13}$: 1 H of H-C_{13} broad ddd at 2.37 ppm, $J_{13,13}$ = 14.1 Hz, $J_{13,14}$ = 8.4 Hz, $J_{12,13}$ = 7.8 Hz; 2 H of H-C_2 t at 2.355 ppm, J = 7.3 Hz; 1 H of H-C_{13} broad ddd at 2.27 ppm, $J_{13,13}$ = 14.1 Hz, $J_{13,14}$ = 6.7 Hz, $J_{12,13}$ = 5.4 Hz), 2.035 (broad dt, 2 H, $J_{15,16}$ = 7.3 Hz, $J_{16,17}$ = 6.7 Hz, H-C_{16}), 1.98–1.40 (m, 10 H, H-$C_{3,4,6,7}$ and 2 OH with H-C_3 tt at 1.71 ppm, J = 7.6, 7.3 Hz), 1.40–1.16 (m, 6 H, H-$C_{17,18,19}$), 1.04 (broad dd, 1 H, $J_{10,11}$ = 8.6 Hz, $J_{11,12}$ = 6.7 Hz, H-C_{11}), 1.08–0.95 (m, 1 H, H-C_8), 0.88 (t, 3 H, J = 6.8 Hz, H-C_{20}). ^{13}C NMR (22.5 MHz): common signals to the two diastereoisomers δ 212.04 (C≡O), 174.16 (C_1), 134.09 (C_{15}), 124.24 (C_{14}), 81.10 (C_{10}), 73.34 (C_{11}), 67.85 (C_{12}), 51.56 (OCH_3), 37.96 (C_{13}), 33.79 (C_7), 31.51 (C_{18}), 29.28 (C_{17}), 27.40 (C_{16}), 22.54 (C_{19}), 14.03 (C_{20}); major diastereoisomer δ 84.23 (C_9), 70.41 (C_5); 63.74 (C_8), 39.52 (C_6), 36.97 (C_4), 30.02 (C_7), 20.94 (C_3); minor diastereoisomer δ 84.07 (C_9), 71.06 (C_5); 64.03 (C_8), 39.87 (C_6), 36.72 (C_4), 30.44 (C_7), 20.87 (C_3). MS: m/z 408 (M − 3 CO)$^{\bullet+}$, 390 (M − 3 CO − H_2O)$^{\bullet+}$, 376 (M − 3 CO − MeOH)$^{\bullet+}$, 358 (M − 3 CO − MeOH − H_2O)$^{\bullet+}$; loss of MeOH gives formation of a δ-lactone. Anal. Calcd for $C_{24}H_{36}FeO_7$: C, 58.54; H, 7.37. Found: C, 58.72; H, 7.30.

(12(*R*,*S*))-(8*E*,10*E*,14*Z*)-Methyl 12-Hydroxy-5-oxoeicosa-8,10,14-trienoate [(±)-6,7-Dihydro-5-oxo-LTB$_4$ Methyl Ester] (4c). To a solution of complex **16** (69 mg, 0.14 mmol) in anhydrous methanol (2.5 mL, O °C) was added ceric ammonium nitrate (270 mg, 0.49 mmol, 3.5 equiv) portionwise over 20 min while stirring (CO formation). After 10 min further reaction at 0 °C, the reaction mixture was diluted with brine and extracted three times with ether. Combined organic extracts were washed with water, dried ($MgSO_4$) and concentrated. Chromatography on silica gel using ether/petroleum ether (1:1) as eluent afforded hydroxy ketone **4c** as a colorless oil (34 mg, 69%, R_f = 0.16 with ether/petroleum ether (1:1)).

IR (neat): 3450 (broad, OH), 1735 (C_1=O), 1715 (C_5=O) cm^{-1}. ^{1}H NMR (300 MHz): δ 6.18 (ddd, 1 H, J = 15.0, 10.4, 0.9 Hz, H-C_{10}), 6.04 (broad ddt, 1 H, J = 15.0, 10.5, 1.3 Hz, H-C_9), 5.66 (dt, 1 H, J = 14.9, 6.9 Hz, H-C_8), 5.62 (dd, 1 H, J = 15.0, 6.5 Hz, H-C_{11}), 5.56 (dtt, 1 H, J = 10.9, 7.3, 1.4 Hz, H-C_{15}), 5.37 (dtt, 1 H, J = 10.9, 7.4, 1.5 Hz, H-C_{14}), 4.16 (broad dt, 1 H, J = 6.5, 6.2 Hz, H-C_{12}), 3.67 (s, 3 H, CO_2CH_3), 2.50 (pseudo t, 2 H, J = 7.0 Hz, H-C_6), 2.475 (t, 2 H, J = 7.1 Hz, H-C_4), 2.41–2.22 (m, 6 H, H-$C_{2,7,13}$ with H-C_2, t at 2.335 ppm, J = 7.2 Hz), 2.04 (broad dt, 2 H, J = 7.3, 6.7 Hz, H-C_{16}), 1.895 (tt, 2 H, J = 7.3, 7.2 Hz, H-C_3), 1.56 (broad s, O*H* + H_2O), 1.43–1.20 (m, 6 H, H-$C_{17,18,19}$), 0.88 (t, 3 H, J = 6.7 Hz, H-C_{20}). ^{13}C NMR (100 MHz): δ 209.21 (C_5), 173.63 (C_1), 133.86 (CH=), 133.65 (CH=), 132.92 (C_{15}), 130.46 (CH=), 130.36 (CH=), 124.29 (C_{14}), 72.01 (C_{12}), 51.58 (OCH_3), 42.11 (C_6), 41.62 (C_4), 35.34 (C_{13}), 33.03 (C_2), 31.51 (C_{18}), 29.28 (C_{17}), 27.41 (C_{16}), 26.70 (C_7), 22.56 (C_{19}), 18.82 (C_3), 14.06 (C_{20}). HRMS: m/z (rel intensity) 350 (0.6, $M^{\bullet+}$), 332 (5, $M^{\bullet+} - H_2O$), 239 (13, $M^{\bullet+} - C_8H_{15}$), 221 (17, $C_{13}H_{17}O_3^{\bullet+}$), 207 (33, $C_{12}H_{15}O_3^{\bullet+}$), 189 (99, $C_{12}H_{13}O_2^{\bullet+}$), 129 (69, $C_6H_9O_3^{\bullet+}$), 28 (100); exact mass m/e 332.2336 ($M^{\bullet+} - H_2O$), calcd for $C_{21}H_{32}O_3$ 332.2351. UV (CH_3CN): $\lambda_{max}(\epsilon)$ 230 (26 000) nm.

(5*R*,12*S*)- and (5*S*,12*R*)-(8*E*,10*E*,14*Z*)-Methyl 5,12-Dihydroxyeicosa-8,10,14-trienoate [(±)-6,7,-Dihydro-LTB$_4$ Methyl Ester] (4a) and (5*S*,12*S*)- and (5*R*,12*R*)-(8*E*,10*E*,14*Z*)-Methyl 5,12-Dihydroxyeicosa-8,10,14-trienoate [(±)-6,7-Dihydro-5-*epi*-LTB$_4$ Methyl Ester] (4b). Using the same procedure as described for the preparation of ketone **4c**, decomplexation of the diastereoisomeric mixture of diols **17a**, **17b** (85 mg, 0.17 mmol) afforded after purification by chromatography on silica gel using ether/petroleum ether (7:3) as eluent a spectroscopically indistinguishable mixture of diols **4a** and **4b** epimeric on C_5 (57 mg, 94%, colorless oil, R_f = 0.24 with ether/petroleum ether (7:3)).

IR (neat): 3400 (broad, OH), 1740 and 1720 (Fermi resonance of C=O) cm^{-1}. ^{1}H NMR (300 MHz): δ 6.20 (ddd, 1 H, J = 15.0, 10.3, 0.8 Hz, H-C_{10}), 6.06 (ddt, 1 H, J = 14.9, 10.5, 1.3 Hz, H-C_9), 5.70 (dt, 1 H, J = 14.9, 7.0 Hz, H-C_8), 5.62 (dd, 1 H, J = 15.0, 6.1 Hz, H-C_{11}), 5.57 (dtt, 1 H, J = 10.9, 7.3, 1.5 Hz, H-C_{15}), 5.38 (dtt, 1 H, J = 10.9, 7.4, 1.5 Hz, H-C_{14}), 4.16 (broad tdd, 1 H, J = 6.5, 6.1, 0.7 Hz, H-C_{12}), 3.67 (s, 3 H, CO_2CH_3), 3.61 (tt, 1 H, J = 7.5, 4.8 Hz, H-C_5), 2.35 (t, 2 H, J = 7.3 Hz, H-C_2), 2.41–2.24 (m, 2 H, H-C_{13}, nonequivalent protons at 2.34 and 2.29 ppm, J_{gem} = 14.0 Hz), 2.27–2.11 (m, 2 H, H-C_7), 2.04 (broad dtd, 2 H, J = 7.3, 6.7, 1.5 Hz, H-C_{16}), 1.84–1.63 (m, 2 H, H-C_3, nonequivalent protons at 1.78 and 1.69 ppm), 1.61 (broad s, 2 O*H* + H_2O), 1.59–1.42 (m, 4 H, H-$C_{4,6}$), 1.42–1.20 (m, 6 H, H-$C_{17,18,19}$), 0.885 (t, 3 H, J = 6.8 Hz, H-C_{20}). ^{13}C NMR (100 MHz): δ 174.25 (C_1), 134.49 (CH=), 133.42 (2 C: C_{15} and another olefinic carbon*), 130.60 (CH=), 129.98 (CH=), 124.42 (C_{14}), 72.07 (C_{12}), 70.73 (C_5), 51.58 (OCH_3), 36.73 (2 C: C_4 and C_6*), 35.35 (C_{13}), 33.85 (C_2), 31.50 (C_{18}), 29.28 (C_{17}), 28.27 (C_7), 27.41 (C_{16}), 22.56 (C_{19}), 20.93 (C_3), 14.07 (C_{20}). HRMS: m/z (rel intensity) 352 (0.4, $M^{\bullet+}$), 334 (5, $M^{\bullet+} - H_2O$), 302 (14, $M^{\bullet+}$ – MeOH – H_2O), 241 (13, $M^{\bullet+} - C_8H_{15}$), 223 (40, $M^{\bullet+}$ – MeOH – C_7H_{13}), 209 (90, $M^{\bullet+}$ – MeOH – C_8H_{15}), 191 (81, $M^{\bullet+}$ – MeOH – H_2O – C_8H_{15}), 173 (100, $C_{12}H_{13}O^{\bullet+}$), 131 (60, $C_6H_{11}O_3^{\bullet+}$), 79 (70), 67 (94); exact mass m/e 334.2487 ($M^{\bullet+} - H_2O$), calcd for $C_{21}H_{34}O_3$ 334.2508. UV (CH_3CN): $\lambda_{max}(\epsilon)$ 230 (23 000) nm. *The signals of these two carbons were distinguished in C_6D_6.

Acknowledgment. This work was supported by the Ministère des Affaires Etrangères Deutschen Akademischen Austauschdienst (MAE/DAAD) within the framework of project-oriented promotion of the scientific exchange between France and Germany (PROCOPE fellowship for K.N and P.M). K.N. thanks the Freistaat Bayern for a study grant.

Supplementary Material Available: Characterization data for **9** and **18** (1 page). Ordering information is given on any current masthead page.