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Stereoselective Synthesis of Macrolactin A Analogues. Part 1: the C_7-C_{20} Fragment

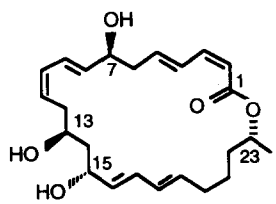
Thierry J. Benvegnu [a] Loïc J. Toupet [b] and René L. Grée [a]*

a) Laboratoire de Synthèses et Activations de Biomolécules, CNRS URA 1467
Ecole Nationale Supérieure de Chimie de Rennes, Avenue du Général Leclerc, 35700 Rennes, France.
Fax: (33) 99 87 13 84 E-mail: Rene.Gree@univ-rennes1.fr

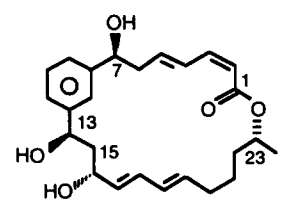
b) Groupe Matière Condensée et Matériaux, associé au CNRS, Université de Rennes,
Avenue du Général Leclerc, 35042 Rennes Cedex, France.

Abstract *: The tricarbonyliron complexed dienoate* ***6*** *corresponding to the C_7-C_{20} fragment of Macrolactin A aromatic analogues was prepared by the aldol reaction of ketone* ***10*** *with aldehyde* ***9****, followed by stereoselective reduction.*

Macrolactin A **1** is the parent aglycone of a small group of bioactive 24-membered macrolides isolated from a deep sea marine bacterium[1] and its stereochemistry has been established recently [2] as 7S, 13S, 15R, 23R. This lactone was found to possess significant antiviral and cancer cell cytotoxic properties.[1] Macrolactin A **1** inhibited B16-F10 marine melanoma cell replication with *in vitro* IC_{50} values of 3.5 µg/mL. Furthermore, it was a potent inhibitor of Herpes simplex type I virus (strain LL), as well as type II (strain G) with IC_{50} values of 5.0 and 8.3 µg/mL respectively. Macrolactin A was also tested by National Cancer Institute for its potential utility on controlling human HIV replication (using human T-lymphoblast cells). Antiviral effects were recorded with maximum protection observed at concentrations of 10 µg/mL. So far total synthesis of this novel natural product has not been achieved, but subunits of the molecule have already been prepared.[3-5] As part of our program dealing with the use of organoiron complexes for the synthesis of biologically active compounds, we designed new structural analogues of Macrolactin A, with a more rigid and more stable skeleton. Our approach was to replace the (E,Z) dienic system corresponding to the C_8-C_{12} part by aromatic rings and then to prepare analogues such as **2** (Figure 1).



Macrolactin A (**1**)

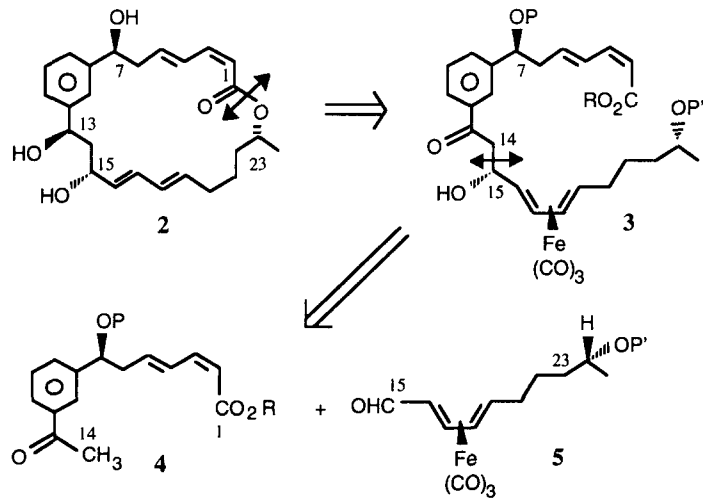


2

Fig. 1

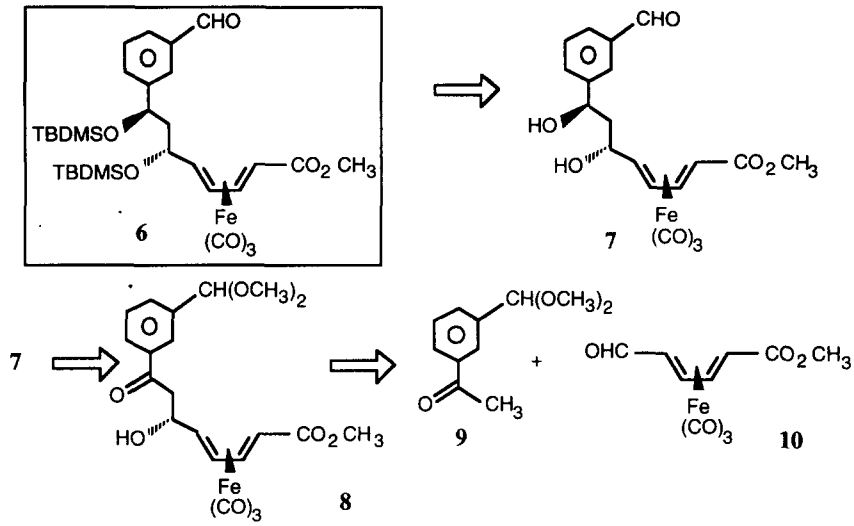
SYNTHETIC PLAN

Scheme 1 summarizes our strategy for the construction of analogue **2**. Inspection of **2** revealed two main disconnections in the retrosynthesis, namely the lactone linkage and the C_{14}-C_{15} bond. The macrocyclic ring could be formed by macrolactonization of the seco-acid corresponding to **3**. We planned a highly convergent aldol-based route for the synthesis of the key organometallic complex **3**. This aldol approach involved two fragments: ketone **4** and aldehyde **5** which reproduce respectively the C_1-C_{14} and C_{15}-C_{23} parts. The tricarbonyliron system plays here a key role: it should protect efficiently and temporarily the 1,3 diene and furthermore it should afford the chirality for a stereochemical control at the C_{15} position.[3] The synthesis of aldehyde **5**, in optically pure form, has already been described[3] and the preparation of type **4** functionalized ketones will be reported in the following publication.



Scheme 1

The cornerstone of our strategy is a stereocontrolled aldolization to establish the (R) absolute configuration at C_{15} followed by a reduction at C_{13} to the desired anti 1,3-diol. Thus, the purpose of this publication is to describe model studies towards this goal: the preparation of **6** *via* the retrosynthetic analysis described, in Scheme 2 allowed us to determine the proper conditions for these reactions.[6]

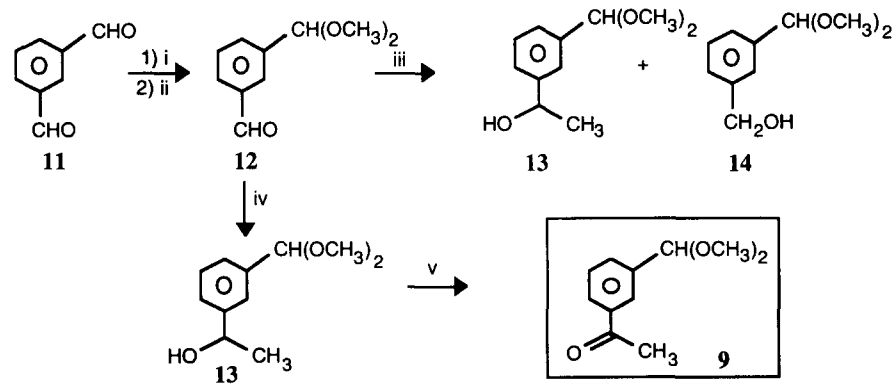


Scheme 2

SYNTHESES OF KETONE 9 AND TRICARBONYLIRON COMPLEXED DIENAL 10

The starting complex **10** was easily available both in racemic and in optically pure form.[7] The ketone component **9** required for the aldol reaction was prepared in five steps and 52% overall yield from isophtaldehyde **11**. As shown in Scheme 3, synthesis of **9** began with the bisacetalization of **11** followed by monodeacetalization under mild acidic conditions to afford monoaldehyde **12**.[8]

Reaction of methyl Grignard with **12** gave a 1:1 mixture of the desired product **13** and the primary alcohol **14**, while reaction of methyl lithium produced **13** in a 95% yield. Oxidation of **13** with pyridinium dichromate (PDC) in the presence of 4Å molecular sieves gave the required ketone **9** (Scheme 3).



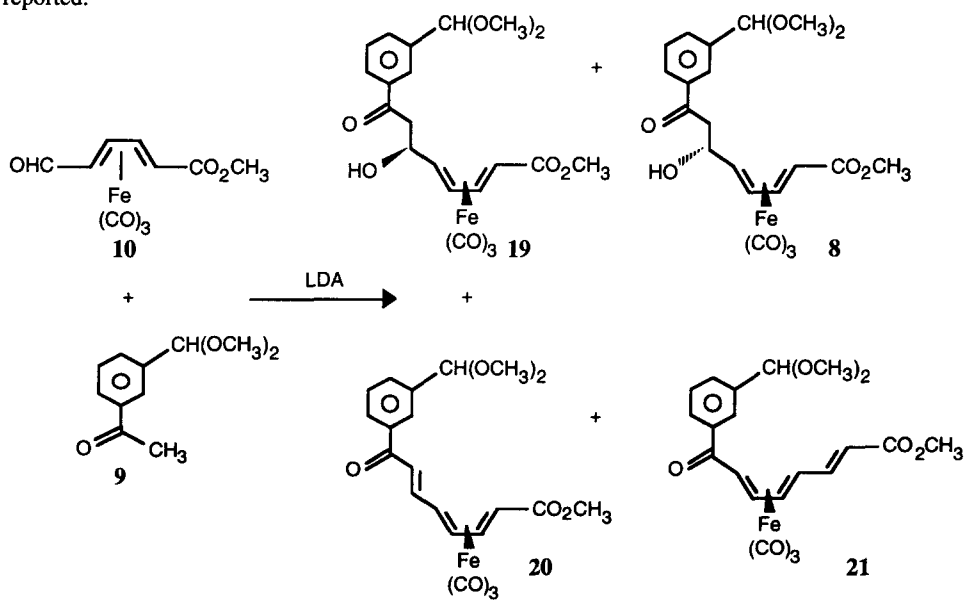
i: $HC(OCH_3)_3$, APTS, MeOH-CH_2Cl_2, 93%; ii: SiO_2, 1% H_2SO_4, CH_2Cl_2, 88%;
iii: CH_3MgI, THF, -40°C, 72% overall yield; iv: CH_3Li, THF/Et_2O, -80°C, 95%;
v: PDC, 4Å Molecular sieves, CH_2Cl_2, 83%.

Scheme 3

DIASTEREOSELECTIVE ALDOL CONDENSATION WITH TRICARBONYLIRON COMPLEXED DIENAL 1

Aldol condensation is one of the most frequently used C-C bond forming reactions and it has also been successfully applied in asymmetric synthesis.[9] Transition metal carbonyl complexes of unsaturated compounds have already found many applications in organic synthesis[10] but their use in aldol type reactions was developed only more recently. The reactivity of α,β-unsaturated aldehydes can be improved by complexation as shown, for instance, with aldol reactions on cobalt complexed alkynals.[11] Furthermore, most of these complexes have a planar chirality which can strongly influence the diastereoselectivity of these reactions. Several recent examples have described highly stereoselective aldol condensation of enolates with unsaturated aldehydes complexed to cobalt[11] or chromium[12] and noteworthy also are the allylboronate reactions described by Roush.[13] Reactions of enolates vicinal to transition metal carbonyl complexes have been reported in the case of chromium[14] and recently with iron derivatives.[15] However, to the best of our knowledge, few aldolization reactions of dienals complexed to tricarbonyliron complexes have been described until now. Preliminary studies from our group have shown the possibility to use aldol reactions to prepare stereoselectively β-hydroxycarbonyl systems vicinal to an organoiron complex.[16]

In the case of the lithium enolate from ketone **9** the reaction gave the aldol adducts **19** and **8**, together with the complexed trienes **20** and **21** (Scheme 4). The diastereoisomers **19** and **8** are easily separated by chromatography; the Ψ-exo structure is attributed to the more polar isomer **8** by analogy with literature data[17] and this was confirmed later by the X-ray crystallographic analysis of **6**. The trienes **20** and **21** are isolated as a mixture and thus a bond-shift isomerization is observed in the case of **21**. Such shifts of the $Fe(CO)_3$ moiety are not common with acyclic conjugated polyenes but a few cases, involving basic reaction conditions, have already been reported.[18]



Scheme 4

A systematic study to focus experimental conditions (reagents concentration) was achieved to optimize both yields and diastereoselectivities. As shown in Table 1, aldolization proceeded in satisfactory overall yield in every case. However, the relative ratio of products was strongly dependent upon the concentration of reagents: high concentration favoured the elimination products **20** and **21**. In agreement with preceding results,[16] a good selectivity in Ψ-exo isomer **8** was observed offering a promising entry into the required (R)-C_{15} alcohol when starting from optically pure organoiron complexes.

	8	**19**	Ψ-exo/Ψ-endo	**20** +**21**	Overall yield*
a	61	8	7.3	19	88
b	42	8	5.3	17	67
c	10	4	2.5	56	70

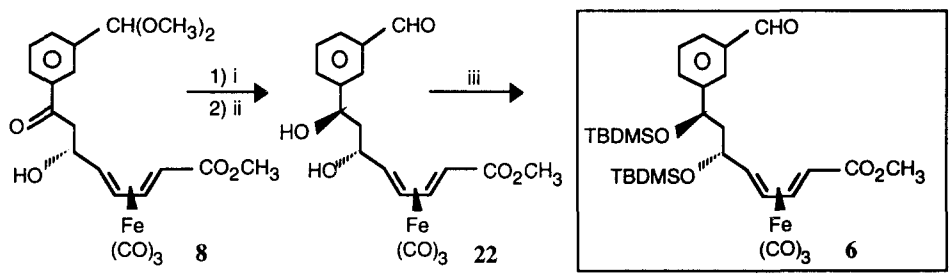
a: **10** $[\mathbf{10}]_{t=0}$= 0.11 M; b: **10** $[\mathbf{10}]_{t=0}$= 0.03 M; c: **10** $[\mathbf{10}]_{t=0}$= 0.28 M

* in every case, a small amount (<10%) of starting materials was also isolated.

Table 1 : Isolated yields of reaction products

1,3 DIASTEREOSELECTIVE REDUCTION OF β-HYDROXY KETONE 8

We next examined the reduction of the ketone **8** to the anti-1,3-diol **22**. The methodology developed by Evans[19] proved to be very efficient also in our case both in terms of yield and selectivity. Since the slightly acidic reaction conditions induced a partial deacetalization, an acidic treatment of the crude product allowed the total transformation into the 1,3-diol **22** (Scheme 5). NMR studies revealed an excellent diastereoselectivity (>95%) on behalf of the anti diol **22**. The last stage in the sequence involved the protection of C_{13}-C_{15} hydroxyl groups as silylethers by using tert-butyldimethylsilyl triflate and 2,6-lutidine in THF at -40°C.



i: $Me_4NHB(OAc)_3$, AcOH/CH_3CN, -40°C, 16 h.; ii: SiO_2, 1%, H_2SO_4, CH_2Cl_2;
iii: $CF_3SO_3SiMe_2tBu$, 2,6-lutidine, THF, -40°C.

Scheme 5

A purification step by preparative chromatography on SiO_2 gave the anti-diol **6** in a 82% overall yield in addition to a mixture of syn 1,3-diol and decomplexed dienes in very small amounts (< 5%). An X-ray analysis of the major compound was found to be in agreement with the anti and Ψ-exo stereochemistries of the target compound **6** (Figure 2).

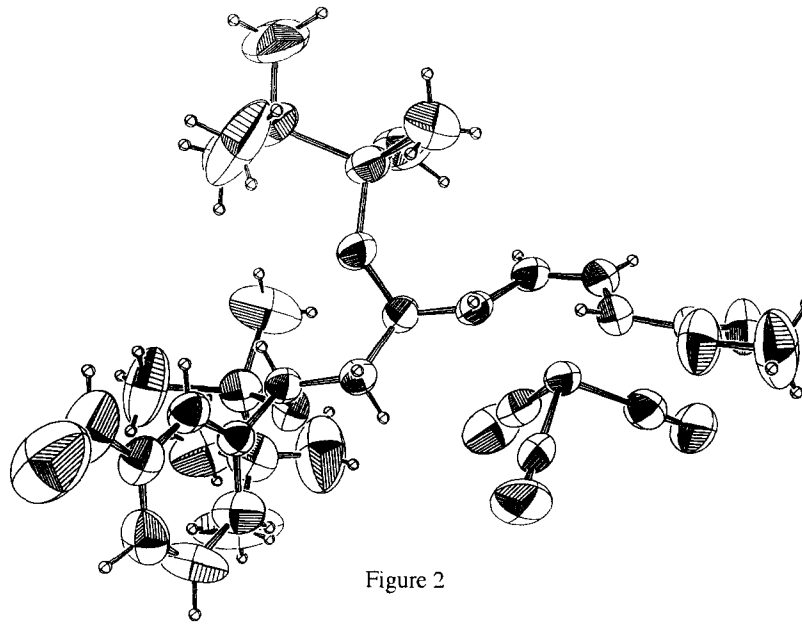


Figure 2

CONCLUSION

In summary, the synthesis of a C_7-C_{20} organoiron complexed segment for analogue **2** has been achieved. The asymmetric aldol coupling/1,3 reduction methodology was very successful in providing the necessary stereocenters in C_{13}-C_{15} positions. These studies demonstrate the use of aldolization reaction to prepare a β-hydroxycarbonyl system vicinal to the organoiron complex, with high diastereofacial selectivity. This new route is of interest not only for the preparation of aromatic analogues of Macrolactin A but could be used more generally in the synthesis of polyenic type macrolides.

ACKNOWLEDGEMENTS

We wish to thank Institut de Recherches Servier and Mrs J. Roc-Schneider for a student fellowship. We also thank the IdRS analytical service, Drs J.P. Volland and M. Amm for performing microanalyses, and Dr Y. Rolland for very fruitful discussions.

EXPERIMENTAL SECTION

General. Melting points (m.p.) were obtained using a Kofler hotbench. Infrared spectra were recorded on Nicolet 205 Fourier Transform spectrometer. Nuclear magnetic resonance spectra were obtained on a JEOL FX90Q or a Bruker AM 300 instrument, in $CDCl_3$ solution. Chemical shifts were referenced to Me_4Si . High-resolution mass spectra (HRMS) were recorded on a Varian Mat 311 spectrometer at the Centre Régional de Mesures Physiques de l'Ouest (Rennes). Elemental analyses were performed at the Institut de Recherches Servier.

2-(3'-dimethoxymethyl)phenyl-ethan-2-ol **(13)**

A solution of monoaldehyde **12** [8] (3.70, 20.5 mmol) in a mixture of anhydrous diethylether (50 mL) and tetrahydrofuran (70 mL) was cooled to -90°C under nitrogen and methyllithium (23 mL of a 2.24 M solution in diethylether) was added dropwise under stirring. The resulting mixture was stirred for 2 hours at the same temperature before being quenched by the addition of methanol (50 mL), water (50 mL) and diethyl ether. The organic layer was separated and washed with saturated aqueous brine, dried ($MgSO_4$), filtered and concentrated in vacuo. Flash chromatography of the residue on silica gel using ether/ petroleum ether 3:7 + 1% Et_3N afforded alcohol **13** as a colorless oil (3.8 g, 95%, R_F= 0.26 with ether/petroleum ether 1:1). IR (neat): 3419 (OH) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 7.42-7.32 (m, 4H), 5.35 (s, 1H), 4.86 (q, 1H, J= 6.4 Hz), 3.30 (s, 6H), 2.46 (broad s, 1H), 1.46 (d, 3H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 146.1, 137.8, 127.9, 125.3, 123.6 (aromatic C), 102.9 [$\underline{C}H(OCH_3)_2$], 69.6 (C_2); 52.3 [$CH(O\underline{C}H_3)_2$], 24.9 (C_1). Anal. Calcd. for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.34; H, 8.26.

2-(3'-dimethoxymethyl)phenyl-ethan-1-one **(9)**

To a stirred solution of pyridinium dichromate (16.5 g, 43.8 mmol) in anhydrous methylene chloride (150 mL) containing 4Å powdered dried molecular sieves (10 g) was added under nitrogen a solution of alcohol **13** (3.62 g, 18.6 mmol) in anhydrous methylene chloride (20 mL). The mixture was stirred for 2 hours before being filtered through silica gel and concentrated in vacuo. Flash chromatography on silica gel using ether/ petroleum ether 2:3 + 1% Et_3N afforded ketone **9** as a colorless oil (3 g, 83%, R_F= 0.58 with ether/petroleum ether 1:1). IR (neat): 1690 (C=O) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 8.03-7.29 (m, aromatic 4H), 5.43 (s,1H), 3.34 (s, 6H), 2.62 (s, 3H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 196.5 (C=O), 138.4, 136.6, 130.6, 127.7, 127.6, 125.9 (aromatic C), 101.7 [$\underline{C}H(OCH_3)_2$], 51.7 [$CH(O\underline{C}H_3)_2$], 25.7 ($CO\underline{C}H_3$). Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 67.95; H, 7.13.

(2R,5S) and (2S,5R)-(2E,4E,6E)-Tricarbonyliron [methyl (η^4-2,5)-8-oxo-8-(3'-dimethoxymethyl)phenyl-octa-2,4,6-trien-oate] **(20)** */ (4R,7S) and (4S,7R)-(2E,4E,6E)-Tricarbonyliron [methyl (η^4-4,7)-8-oxo-8-(3'-dimethoxymethyl)phenyl-octa-2,4,6-trien-oate]* **(21)** *mixture ; (2R,5S,6S) and (2S,5R,6R)-(2E,4E)-Tricarbonyliron [methyl (η^4-2,5)-8-oxo-8-(3'-dimethoxymethyl)phenyl-6-hydroxy-octa-2,4-dien-oate]* **(19)**; *(2R,5S,6R) and (2S,5R,6S)-(2E,4E)-Tricarbonyliron [methyl (η^4-2,5)-8-oxo-8-(3'-dimethoxymethyl)phenyl-6-hydroxy-octa-2,4-dien-oate]* **(8)**

A solution of diisopropylamine (0.18 mL, 1.28 mmol) in 2 mL of anhydrous tetrahydrofuran was cooled under nitrogen to 0°C and a solution of n-butyllithium in hexane (0.75 mL, 1.28 mmol) was added slowly by syringe. After 10 minutes at 0°C the solution was cooled to -70°C and ketone **9** (1.03 mmol) in 3 mL of THF was added with a syringe over 5 minutes with rapid stirring. After 30 minutes, complex **10** (215 mg, 0.77 mmol) in 2 mL of THF was added in one fraction. The mixture was stirred for 45 minutes at -70°C and an aqueous saturated NH_4Cl solution (10 mL) was added followed by diethyl ether (100 mL). The resulting mixture was allowed to warm up to room temperature in 30 minutes. The organic phase was washed, dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography on silica gel successively using ether/ petroleum ether 1:9, 2:3, 1:1

and then ether as eluents sequentially afforded a 3/1 mixture of the trienes **20** and **21** (67 mg, 19%, R_F= 0.51 with ether/ petroleum ether 1:1) then the Ψ-endo (30 mg, 8%, R_F= 0.47 with ether/ petroleum ether 1:1) and Ψ-exo (223 mg, 61%, R_F= 0.27 with ether/ petroleum ether 1:1) isomers **19** and **8** as orange oils.

Mixture of trienes (**20, 21**). IR (neat): 2061 and 1996 (C≡O), 1708 and 1687 (C=O), 1630 (C=C) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.04-7.49 (m, aromatic 4H), 7.09 [d, 1H, J= 15.0 Hz, (**21**)], 6.99 [dd, 1H, J= 10 Hz, (**21**)], 6.90 [dd, 1H, J= 15.3, 10.5 Hz, (**20**)], 6.20 [ddd, 1H, J= 8.1, 5.2, 0.9 Hz, (**20**)], 6.09 [d, 1H, (**20**)], 5.94 [ddd, 1H, J= 8.2, 5.1, 0.9 Hz, (**21**)], 5.73 [dd, 1H, J= 8.8 Hz, (**20**)], 5.69 [dd, 1H, J= 8.8 Hz, (**21**)], 5.46 [s, 1H, (**20**)], 5.44 [s, 1H, (**21**)], 3.75 [s, 3H, (**20**)], 3.70 [s, 3H, (**21**)], 3.6 and 3.35 [2s, 6H, (**20**)], 3.35 and 3.34 [2s, 6H, (**21**)], 2.34 [d, 1H, (**20**)], 2.28 [t, 1H, (**20**)], 2.09 [t, 1H, (**21**)], 1.46 [d, 1H, (**21**)]; ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 207.7 (C≡O), 194.6 [C=O (**20**)], 189.2 [C=O (**21**)], 172.1 [CO_2CH_3 (**21**)], 166.7 [CO_2CH_3 (**20**)], 148.0, 124.2 [C_2, C_3, (**21**)], 147.6, 120.0 [C_7, C_6, (**20**)], 139.0, 137.1 [ipso C, (**20**)], 131.5, 128.8, 128.5, 126.1 [aromatic C (**20**)], 131.2, 128.7, 128.5, 126.8 [aromatic C, (**21**)], 102.6 [$CH(OCH_3)_2$], 87.5, 84.8 [C_3, C_4, (**20**)], 86.9, 85.4 [C_5, C_6, (**21**)], 58.5 [C_4 (**21**)], 57.6 [C_5 (**20**)], 52.9 [$CH(OCH_3)_2$ (**21**)], 52.8 [$CH(OCH_3)_2$ (**20**)], 51.9 [CO_2CH_3 (**21**)], 51.7 [CO_2CH_3 (**20**)], 50.6 [C_2, (**20**)], 46.7 [C_7 (**21**)].

Ψ-endo isomer (**19**). IR (neat): 3472 (OH), 2059, 1971 (C≡O), 1708, 1683 (C=O ketone and ester) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.04-7.45 (m, aromatic 4H), 5.86 (ddd, 1H, J= 8.9, 5.1, 0.8 Hz), 5.58 (dd, 1H, J= 8.7 Hz), 5.45 (s, 1H), 4.32 (m, 1H), 3.67 (s, 3H), 3.35 (s, 6H), 3.30 (m, 2H), 1.71 (broad s, 1H), 1.37 (t, 1H), 1.05 (dd, 1H, J= 0.7 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 208.2 (C≡O), 199.8 (C=O), 172.7 (CO_2CH_3), 139.2, 136.4 (ipso C), 132.3, 128.8, 128.1, 126.6 (aromatic C), 102.3 [$CH(OCH_3)_2$], 83.6, 83.0 (C_3, C_4); 67.8 (C_6); 68.0 (C_5), 52.8 ($CH(OCH_3)_2$), 51.7 (CO_2CH_3), 46.3, 46.2 (C_2, C_7). Anal. Calcd. for $C_{21}H_{22}O_9Fe$: C, 53.19; H, 4.68. Found: C, 53.26; H, 4.86.

Ψ-exo isomer (**8**). IR (neat): 3464 (OH), 2060 and 1972 (C≡O), 1708 and 1636 (C=O ketone and ester) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.05-7.48 (m, aromatic 4H), 5.88 (ddd, 1H, J= 8.1, 5.1, 0.8 Hz), 5.64 (ddd, 1H, J= 8.6, 1.0 Hz), 5.45 (s, 1H), 4.18 (m, 1H), 3.67 (s, 3H), 3.35 (s, 6H), 3.32 (m, 2H), 1.37 (dd, 1H), 1.07 (dd, 1H, J= 0.9 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 208.9 (C≡O), 199.8 (C=O), 172.4 (CO_2CH_3); 139.2, 136.4 (ipso C), 132.2, 128.8, 128.1, 126.6 (aromatic C), 102.3 [$CH(OCH_3)_2$], 85.1, 84.1 (C_3, C_4); 68.9 (C_6), 64.9 (C_5), 52.8 [$CH(OCH_3)_2$], 51.7 (CO_2CH_3), 46.3, 46.2 (C_2, C_7). Anal. Calcd. for $C_{21}H_{22}O_9Fe$: C, 53.19; H, 4.68. Found:C, 53.18; H, 4.81.

(2R,5S,6S,8S) and (2S,5R,6R,8R)-(2E,4E)-Tricarbonyliron [methyl (η^4-2,5)-8-hydroxy-8-(3'-oxymethyl) phenyl-6-hydroxy-octa-2,4-dien-oate] (**22**)

A solution of $Me_4NBH(OAc)_3$ (3.1 g, 11.8 mmol) in dry acetonitrile (6.6 mL) and dry acetic acid (6.6 mL) was stirred at room temperature for 30 minutes, cooled to -40°C under nitrogen and to this stirred solution, was added a solution of **8** (0.7 g, 1.47 mmol) in dry acetonitrile (5.8 mL). The mixture was stirred at -40°C for 24 h. and then quenched with 10 mL of 1N aqueous disodium tartrate solution and 10 mL of acetone. The mixture was allowed to warm slowly to room temperature, the acetone was removed in vacuo, and the residue was poured into

15 mL of saturated aqueous sodium bicarbonate solution. The aqueous layer was extracted with 3x20 mL of dichloromethane. The combined organic layers were dried ($MgSO_4$), filtered and concentrated in vacuo. The crude product was dissolved in dichloromethane (60 mL) before adding silica gel (7 g) and 20 drops of an 1% aqueous sulfuric acid solution. The mixture was stirred for 1 hour before being filtered and concentrated in vacuo. Flash chromatography on silica gel using ether afforded aldehyde **22** (4.75 mg, 75%, R_F=0.27 with ether) as an orange oil. IR (neat): 3430 (OH), 2066 and 1996 (C≡O), 1687 (CHO and CO_2CH_3) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.02 (s, 1H), 7.92-7.51 (m, 4H), 5.85 (dd, 1H, J= 7.5, 5.1 Hz), 5.47 (dd, 1H, J=7.8 Hz), 5.24 (m, 1H), 3.82 (m, 1H), 3.67 (s, 3H), 2.09 (m, 2H), 1.35 (t, 1H), 1.10 (dd, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 192.5 (CHO), 172.2 (CO_2CH_3), 145.1, 136.6 (ipso C), 131.7, 129.3, 129.2, 126.4 (aromatic C), 85.5, 84.5 (C_3, C_4), 71.4, 71.2 (C_8, C_6), 65.8 (C_5), 51.8 (CO_2CH_3), 46.3 (C_2), 45.2 (C_7). EIHRMS: the intensity of the molecular ion (m/z 430 for $C_9H_{18}O_8Fe$) was too low to be measured accurately; for $[M-2CO]^+$ calc. 374.0453 and $[M-3CO]^+$ calc. 346.0503. Found 374.0450 and 346.0511.

(2R,5S,6R,8S) and (2S,5R,6S,8R)-(2E,4E)-Tricarbonyliron [methyl (η^4-2,5)-6,8-t-butyldimethylsilyloxy-8-(3'-oxymethyl)phenyl-octa-2,4-dien-oate] (**6**)

To a stirred solution of diol **22** (453 mg, 1.05 mmol) in 30 mL anhydrous THF, cooled to -40°C, was added under nitrogen, 2,4-lutidine (0.491 mL, 422 mmol) and 5 minutes later tert-butyldimethylsilyl trifluoromethane sulfonate (0.594 mL, 3.38 mmol). The mixture was stirred at -40°C for 30 minutes before it was quenched with 10 mL of aqueous saturated ammonium chloride solution. The aqueous layer was extracted with 3x20 mL of diethylether. The combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was chromatographed on preparative silica gel plate by using a 1/9 mixture of ether/ petroleum ether as eluent to afford the major anti 1,3-diol **6** (564 mg, 86%, R_F= 0.56 with ether/petroleum ether 1:1) as yellow orange crystals (mp: 88°C). Small amounts (30 mg) of syn 1,3-diol and decomplexed dienes were also isolated. **6** IR (neat): 2064 and 2003 (C≡O), 1715 and 1702 (CO_2CH_3 and CHO) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.03 (s, 1H), 7.81-7.48 (m, 4H), 5.81 (dd, 1H, J= 8.2, 5.4 Hz), 5.41 (dd, 1H, J= 8.9, 5.3 Hz), 4.94 (dd, 1H, J= 9.2, 1.6 Hz), 3.81 (td, 1H, J= 9.4, 1.8 Hz), 3.65 (s, 3H), 2.03 and 1.82 (m, 2H), 1.23 (t, 1H), 0.95 and 0.82 (m, 9H), 0.23 to -0.11 (m, 12H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 208.4 (C≡O), 192.3 (CHO), 172.3 (CO_2CH_3), 147.1, 136.1 (ipso C), 132.2, 129.1, 128.8, 127.2 (aromatic C), 86.7, 83.4 (C_3, C_4), 72.7, 71.4 (C_8, C_6), 67.3 (C_5), 51.9 (C_7), 51.7 (CO_2CH_3), 46.5 (C_2), 26.0, 25.7 [$C(CH_3)_2$], 18.3, 18.1 [$C(CH_3)_3$], -1.8 to -4.6 ($CH_3)_2$. Anal. Calcd. for $C_{31}H_{46}O_8FeSi_2$: C, 56.53; H, 7.04. Found: C, 56.87; H, 7.10.

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