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Alkylation of Tricarbonyl(diene)iron Complexes: Model Studies for the Preparation of Protomycinolide IV[1]

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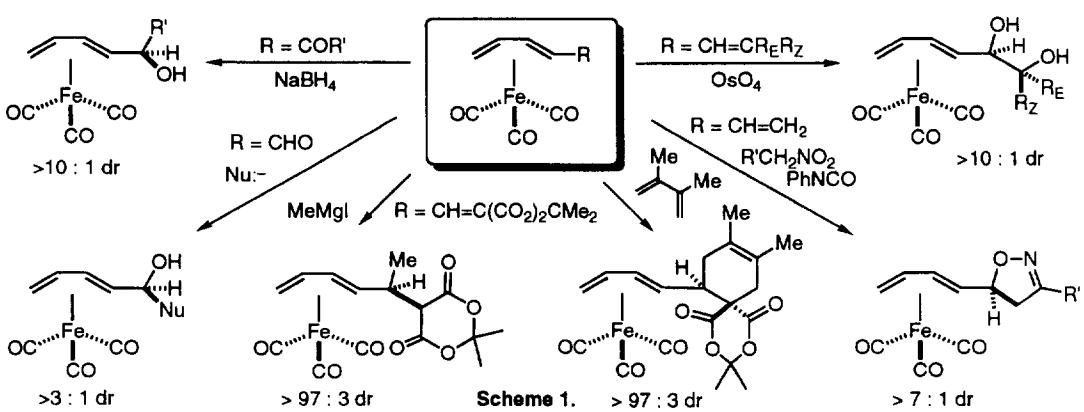
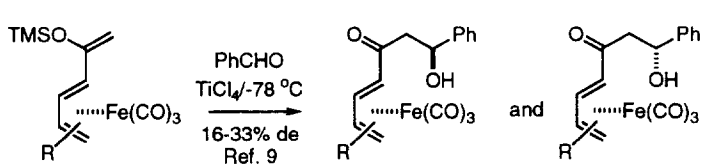
Abstract: The alkylation of (4,6-heptadien-3-one)- and (methyl 3,5-hexadienoate)$Fe(CO)_3$ (**1** and **2**) were examined (0-42% de and 69-92% de respectively). Optically active (methyl 3,5-hexadienoate)$Fe(CO)_3$ (-)-**2** was prepared by resolution of the corresponding carboxylic acid complex with α-methylbenzylamine. © 1997 Elsevier Science Ltd.

Attachment of a (tricarbonyl)iron adjunct to an acyclic diene has been shown to protect the diene against reduction, oxidation, and cycloaddition reactions.[2] 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. For example, ketone reductions,[3] 1,2- and 1,4-nucleophilic additions,[4] cycloadditions,[5] and osmylations[6] occur with modest to excellent diastereoselectivity (Scheme 1). While inter-[7] and intramolecular[8] attack of nucleophiles on the diene ligand has been reported, there are few examples where (diene)$Fe(CO)_3$ complexes serve as the *nucleophilic component* in C-C bond formation. Franck-Neumann, *et al.*, recently reported on the Mukiayama aldol reactions of silyl enol ethers derived from (dienone)$Fe(CO)_3$ complexes (eqn. 1).[9]

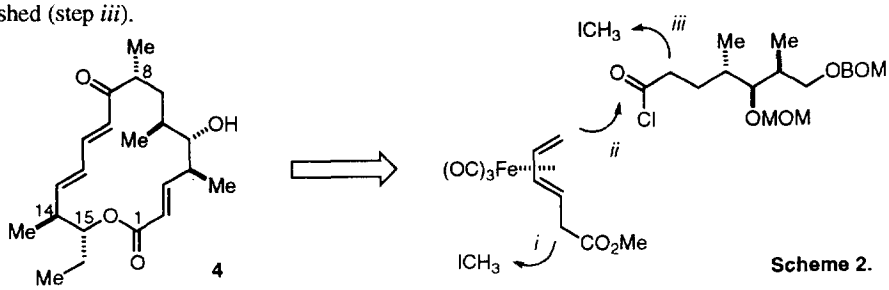


Scheme 1.



(1)

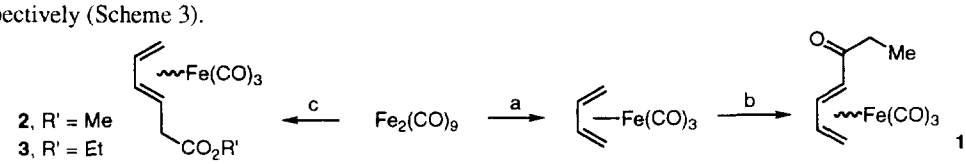
The diastereoselective alkylation of (dienone)- and (4,6-hexadienoate)$Fe(CO)_3$ complexes (**1** and **2/3**) was undertaken. In part, this examination was prompted by interest in the synthesis of the polyene macrolide protomycinolide IV (**4**).[10] The retrosynthetic analysis of **4** (Scheme 2) anticipated that a $Fe(CO)_3$ group attached to the C10-C13 diene portion of **4** could control the stereoselective introduction of the C14 methyl group (step *i*) as well as formation of the C9-C10 dienone bond (step *ii*) via Friedel-Crafts acylation.[11] In addition, it was anticipated that stereoselective alkylation at C8 to affix the C8 methyl group might be accomplished (step *iii*).



Scheme 2.

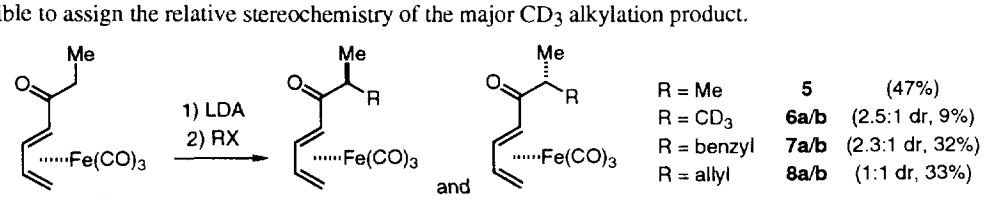
RESULTS AND DISCUSSION[12]

Friedel-Crafts type propionylation[11] of (butadiene)$Fe(CO)_3$, followed by NaOMe catalyzed Z→E isomerization gave the known[13] ethyl ketone **1**. Reaction of methyl or ethyl 3,5-hexadienoate with $Fe_2(CO)_9$ under the influence of ultrasonic agitation, gave methyl or ethyl (3,5-hexadienoate)$Fe(CO)_3$ complexes **2**[14] and **3** respectively (Scheme 3).



Scheme 3. Reagents: a, C_4H_6; b, EtCOCl/$AlCl_3$; EtCOCl (46%); c, 3,5-hexadienoate/EtOAc (51-79%)

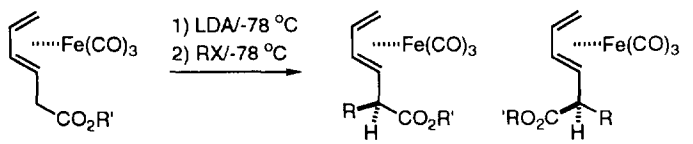
Alkylation of tricarbonyl(4,6-heptadienone)iron (1). Deprotonation of **1** (LDA, -78 °C) followed by treatment with iodomethane gave the isopropyl ketone **5** (47%, Scheme 4). The diastereotopic methyls appear as two distinct doublets in the ^1H NMR spectrum of **5** (δ 1.15 and 1.10 ppm). Alkylation of **1** with d_3-iodomethane gave a mixture of diastereomeric alkylation products **6a/b** in low yield along with minor amounts of dialkylated product and recovered **1**. The diastereomers **6a** and **6b** were determined to be in a 2.4:1 ratio, based on integration of the doublets at δ 1.15 and 1.10 respectively. Treatment of the initially obtained mixture of **6a/b** (2.5:1) with NaOMe/MeOH resulted in the formation of an equimolar mixture of **6a/b** (95% mass recovery), thus indicating that the alkylation diastereoselectivity is the result of kinetic control. Unfortunately, it was not possible to unequivocally assign the doublets to their appropriate CH_3 groups,[15] and thus it is not possible to assign the relative stereochemistry of the major CD_3 alkylation product.



Scheme 4.

In a similar fashion, reaction of the lithium enolate of **1** with benzyl bromide or allyl bromide gave a mixture of diastereomeric alkylation products **7a/b** (32%) and **8a/b** (33%) respectively. Alkylation proceeded with only modest diastereoselectivity for **7a/b** (2.3:1 ratio, based on integration of the methyl doublets and the $H7_{endo}$ signals of each diastereomer) and without any selectivity for **8a/b** (ca. 1:1 ratio). As with **6a/b**, it was not possible to assign the relative stereochemistry of the major product **7a**. Attempted alkylation of **1** with isobutyl bromide led only to the recovery of starting materials. Thus, alkylation of **1** occurs with low diastereoselectivity and in only modest yields for activated electrophiles.

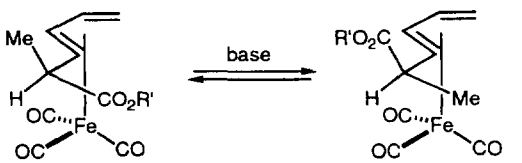
Alkylation of tricarbonyl(4,6-hexadienoate)iron (2/3). In contrast to the results obtained for the alkylation of **1**, deprotonation of either **2** or **3** (LDA, -78 °C) followed by treatment with iodomethane gave the corresponding alkylation products **9a** and **10a** respectively as the major products, in good yields (Scheme 5). In each case, the reaction proceeded with *excellent* diastereoselectivity (**a**:**b**, >20:1 dr) and the major diastereomer could be obtained in pure form after chromatographic separation. Treatment of the initially obtained mixture of **9a/b** (96:4) with NaOMe/MeOH resulted in the formation of a 1.4:1 mixture of **9a/b** with excellent mass recovery (Scheme 6), thus indicating that the alkylation diastereoselectivity is the result of kinetic control. Diastereomer **9a** was eventually assigned the 2R*,3R* relative stereochemistry[16] on the basis of X-ray diffraction analysis of crystalline derivatives (*vide infra*).



2, R' = Me	R' = Me, R = Me	**9a**	**9b**	(96:4 dr, 72-97%)
3, R' = Et	R' = Et, R = Me	**10a**	**10b**	(96:4 dr, 69%)
	R' = Me, R = benzyl	**12a**	**12b**	(8.6:1 dr, 59%)
	R' = Me, R = allyl	**13a**	**13b**	(5.5:1 dr, 48%)

Scheme 5.

Saponification of **9a** gave a separable mixture of **11a** and **11b** (1:7, Scheme 6). The major diastereomer **11b** was isolable by column chromatography and its relative stereochemistry was established as 2S*,3R* by X-ray diffraction analysis.[12,17] Treatment of **11b** with ethereal diazomethane gave **9b**. Thus the relative stereochemistries of **9a** and **9b** are assigned by correspondence to the relative stereochemistry of **11b**. The formation of **11b** as the major product indicates that *epimerization of* **9a** *occurs faster than saponification* under the reaction conditions. Since the relative ratios of **9a/b** at thermodynamic equilibrium under basic conditions was found to be 1.4:1, then the ratio of **11a/b** (1:7) isolated after saponification must be due to the relative rates of hydrolysis of **9a** and **9b**. The difference in the rates of hydrolysis of **9a** (slower) and **9b** (faster) may be attributed to steric hindrance about the methoxycarbonyl group from the $Fe(CO)_3$ group in **9a** which is not present in **9b** (Scheme 6). This steric hindrance could be responsible for slowing the rate of formation of the tetrahedral intermediate in basic hydrolysis. In any event, the above results demonstrate that either diastereomer



slow ⟵ **9a**, R' = Me (1.4 : 1) **9b**, R' = Me ⟶ fast
⟵ **11a**, R' = H (1 : 7) **11b**, R' = H ⟶

Scheme 6.

9a or **9b** may be obtained in good yield; **9a** by direct methylation of **2**, or **9b** by methylation, followed by epimerization/saponification and reesterification.

Deprotonation of **2** (LDA, -78 °C) followed by treatment with either benzyl bromide or allyl bromide gave the alkylation products **12** or **13** respectively (Scheme 5). Alkylation proceeded with good diastereoselectivity (**12a**:**12b**, 8.6:1 dr; **13a**:**13b**, 5.5:1 dr). The ratio of diastereomers **a** and **b** was determined by integration of the ^{1}H NMR signals for methoxycarbonyl groups of each diastereomer. In both cases the major diastereomer was tentatively assigned the 2R*,3R* relative stereochemistry on the basis of the relative ^{1}H NMR chemical shifts of the diastereomeric methoxycarbonyl signals. For **9**, **12**, and **13** the CO_2Me signal for diastereomer **a** appears upfield of that for diastereomer **b**.

The relative diastereoselectivity for alkylation of **1** and **2** may be rationalized in the following fashion. The ester enolate of **2** may exist in an equilibrium between two conformers, *s-trans* and *s-cis* (Figure 1). The *s-cis* conformer should be considerably less stable due to steric interactions present between the enolate and the diene, and thus alkylation should proceed predominantly on the *s-trans* ester enolate. The lower energy transition state for alkylation of the *s-trans* enolate requires approach of the electrophile on the face opposite to the bulky $Fe(CO)_3$ group. Notably, approach of iodomethane via this pathway leads to the formation of the observed major product **9a**. For **1** the situation is less clear. It has been previously reported that TMS enol ethers of (dienone)$Fe(CO)_3$ complexes are almost entirely in the Z-configuration.[9] The Z-enolate of **1** may exist in an equilibrium between two conformers, *s-trans* and *s-cis* (Figure 1). Inspection of molecular models indicates that there should not be a large energy difference between these two conformers. In addition, for the *s-trans* conformer, approach of the electrophile at the β carbon on *either* face of the enolate does not involve significant steric interactions. Thus, the lower diastereoselectivity for alkylation of **1**, compared to alkylation of **2**, may be due to reaction of both the *s-trans* and *s-cis* conformers and to a decrease in the steric influence of the $Fe(CO)_3$ group due to its greater distance from the reactive center.

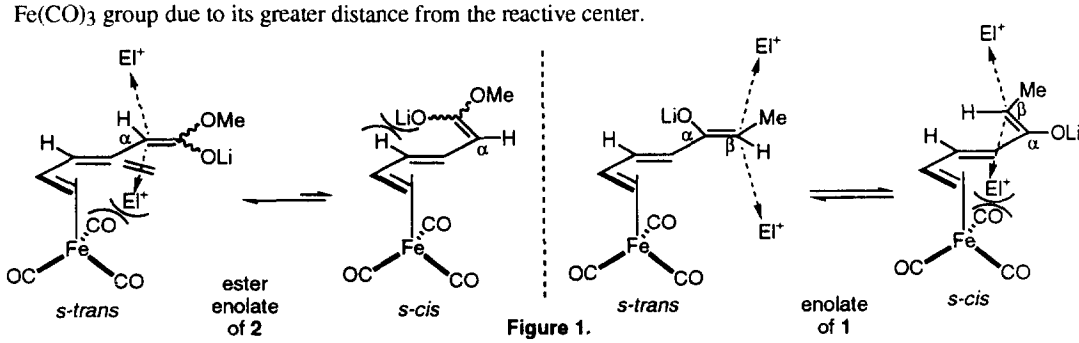
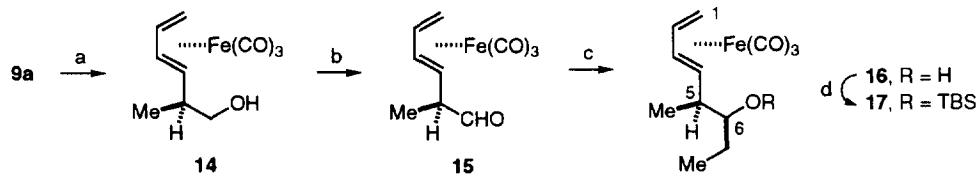


Figure 1.

Model Studies for Synthesis of Protomycinolide IV. With methodology in place for the diastereoselective alkylation of **2** attention was focused on further elaboration of **9a**. As such, reduction of **9a** with DIBAL gave the corresponding 1° alcohol **14** (Scheme 7). Swern oxidation of **14** gave the crude aldehyde **15** as a labile yellow oil. Reaction of freshly prepared **15** with EtMgBr gave **16** as the only isolable product, albeit in low yield (36%).



Scheme 7. Reagents: a, DIBAL (85-91%); b, SO_3:pyr/DMSO/NEt_3 (69%); c, EtMgBr/Et_2O (36%); d, TBSOTf (83%)

While assignment of the relative stereochemistry of **16** on the basis of NMR spectral data was not possible, the corresponding TBS ether (**17**) was a crystalline solid. X-ray diffraction analysis of **17** revealed the relative stereochemistry as shown (Table 1, Figure 2).[18] The bond distances and bond angles of the (diene)Fe(CO)$_3$ portion of **17** are in good agreement with those for complexes reported in the literature.[19] Alcohol **16** results from addition of EtMgBr to the aldehyde **15** via a Felkin-Ahn approach.[20] While the stereochemical outcome is opposite that present in the target **4**, it is anticipated that eventual macrolactonization via an intramolecular Mitsunobo reaction[21] with inversion at the C15 stereocenter will rectify this situation.

Table 1. Final atomic coordinates and displacement parameters (Å). U(eq) is defined as 1/3 of the trace of the orthogonalized U_{ij} tensor.

Atom	*x*	*y*	*z*	U_{eq}
Fe(1)	0.5577(1)	0.7075(1)	0.0388(2)	4.0(1)
C(1)	0.6024(6)	0.6346(8)	-0.084(1)	4(1)
C(2)	0.5521(7)	0.679(1)	-0.122(1)	5(1)
C(3)	0.5504(6)	0.768(1)	-0.112(1)	4.1(9)
C(4)	0.5978(6)	0.8088(9)	-0.055(1)	3.9(8)
C(5)	0.5950(6)	0.9021(9)	-0.024(1)	4.0(9)
C(6)	0.6384(6)	0.9225(8)	0.070(1)	4(1)
C(7)	0.6354(7)	1.0150(9)	0.105(1)	5(1)
C(8)	0.5740(8)	1.046(1)	0.140(1)	8(2)
C(9)	0.6088(7)	0.9557(8)	-0.128(1)	6(1)
C(10)	0.5045(8)	0.773(1)	0.104(1)	6(1)
C(11)	0.6191(7)	0.710(1)	0.133(1)	5(1)
C(12)	0.5205(7)	0.615(1)	0.083(1)	5(1)
C(14)	0.8122(7)	0.835(1)	0.024(2)	5(1)
C(15)	0.7879(7)	0.743(1)	0.028(1)	8(1)
C(16)	0.8175(8)	0.857(1)	-0.098(2)	8(2)
C(17)	0.8750(7)	0.836(1)	0.076(2)	10(1)
C(18)	0.7897(6)	1.0172(8)	0.087(1)	6(1)
C(19)	0.7549(7)	0.8804(8)	0.245(1)	6(1)
O(6)	0.6970(4)	0.8987(5)	0.0374(8)	4.2(5)
O(10)	0.4696(5)	0.8166(8)	0.145(1)	7.6(8)
O(11)	0.6598(4)	0.7102(7)	0.1901(8)	5.2(6)
O(12)	0.4980(6)	0.5533(7)	0.112(1)	8.6(9)
Si(13)	0.7615(2)	0.9087(3)	0.0978(4)	4.3(2)

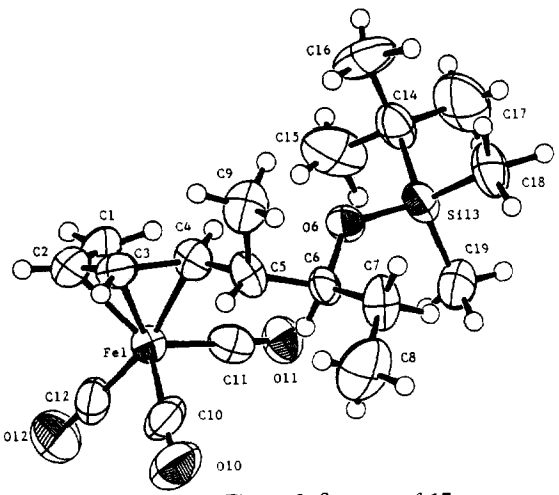
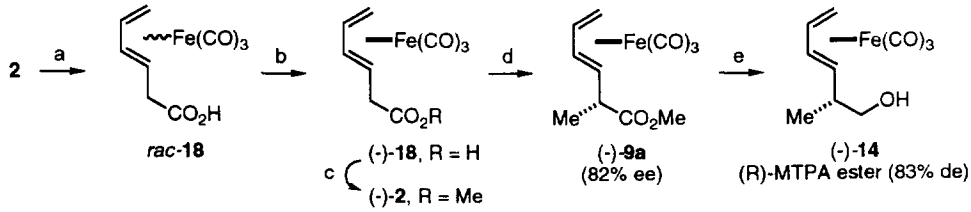


Figure 2. Structure of **17**

Selected bond distances (Å) and bond angles (deg)

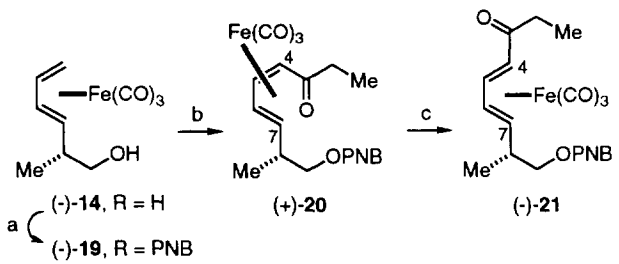
Fe-C1	2.13(1)	C1-C2	1.47(7)
Fe-C2	2.02(2)	C2-C3	1.42(8)
Fe-C3	2.07(1)	C3-C4	1.33(6)
Fe-C4	2.15(1)	C4-C5	1.52(2)
C1-C2-C3	119(1)	C10-Fe-C11	102.6(7)
C2-C3-C4	118(1)	C11-Fe-C12	100.5(7)
C3-C4-C5	122(1)	C10-Fe-C12	91.2(8)

In order for the above diastereoselective alkylation to be translated into enantioselective synthesis, the precursor **2** must be obtained in optically active form. Saponification (LiOH/aq. THF) of *rac*-**2** gave the carboxylic acid *rac*-**18** (Scheme 8). Resolution of **18** was accomplished by preparation and fractional recrystallization (acetone-pentane) of the diastereomeric (R)-α-methylbenzylammonium salts.[22] Fractions with rotation ≤ -30.7° (MeOH) were pooled and treated with acid to give (-)-**18**. Esterification of (-)-**18** with trimethylsilyldiazomethane in methanol gave (-)-**2**. Examination of *rac*-**2** by ^{1}H NMR spectroscopy in the presence of Eu(tfc)$_3$ (d_6-acetone, $CDCl_3$, or C_6D_6) failed to give satisfactory separation of signals for the two enantiomers, thus the optical purity of (-)-**2** was not assessed. Methylation of (-)-**2** gave the optically active product (-)-**9a**. Examination of *rac*-**9a** by ^{1}H NMR spectroscopy in the presence of Eu(tfc)$_3$ (0.3 equiv, C_6D_6) indicated separation of the methoxycarbonyl signals. By this method, (-)-**9a** was determined to be 82% ee. Reduction of (-)-**9a** gave (-)-**14**. Analysis of the ^{1}H NMR spectra (C_6D_6) of the diastereomeric (R)-MTPA esters[23] of *rac*-**14** indicated clear separation in their methylene proton signals (δ 4.17 and 4.00 vs. 4.43 and 3.79 ppm). By this method, the (R)-MTPA ester of (-)-**14** was determined to be 83% de.



Scheme 8. Reagents: a, LiOH/THF (78%); b, (R)-α-methylbenzylamine; HCl/EtOAc; c, $TMSCHN_2$/MeOH (86%); d, LDA/-78°C; MeI/-78°C (73%); e, DIBAL/THF (67%)

For 1-substituted (diene)$Fe(CO)_3$ complexes bearing an electron withdrawing substituent, the 1(*R*)-enantiomers exhibit a negative $[\alpha]_D$ rotation.[24] Thus, to assign the *absolute* stereochemistry of (-)-**18**, (-)-**2**, (-)-**9a**, and (-)-**14**, it was necessary to convert the latter complex into a dienone complex via Friedel-Crafts type acylation.[11] In order to accomplish this task, a suitable protecting group for the hydroxyl substituent was attached. It was anticipated that a PNB group would be unreactive toward the acylation reaction conditions. Reaction of (-)-**14** with p-nitrobenzoyl chloride gave (-)-**19** (Scheme 9). Reaction of (-)-**19** with propionyl chloride/$AlCl_3$ gave the ethyl ketone (+)-**20**. Treatment of (+)-**20** with excess propionyl chloride effected Z→E isomerization to give the dienone complex (-)-**21**. The diene stereochemistry of (+)-**20** and (-)-**21** (Z,E- and E,E- respectively) were assigned on the basis of their ^1H NMR spectral data. In particular, the signals for H4 of (+)-**20** and (-)-**21** appear at δ 3.10 and 1.27-1.18 ppm respectively. These chemical shifts are characteristic of *cis*- and *trans*-dienone iron complexes.[11] The *absolute* stereochemistry of (+)-**20** and (-)-**21** is assigned as 4*S*- and 4*R* respectively by comparison of the sign of their rotations with those of the (diene)iron complexes (+)-**22** and (-)-**23** of known absolute stereochemistry (Figure 3).[25] Since it has been previously established that racemization of (diene)$Fe(CO)_3$ complexes does not occur under the acylation conditions,[25] then the *absolute* stereochemistry of (-)-**18**, (-)-**2**, (-)-**9a**, (-)-**14**, and (-)-**19** is assigned as indicated (Schemes 8 and 9). Thus, for the preparation of natural **4** via diastereoselective alkylation, the desired dienoate complex **2** would require the opposite absolute stereochemistry.



Scheme 9. Reagents: a, PNBCl/pyr (90%); b, EtCOCl/$AlCl_3$ (43%); c, EtCOCl (93%)

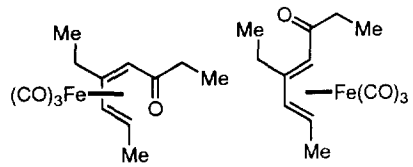


Figure 3.

Summary

The present results demonstrate that the $Fe(CO)_3$ group can serve as a stereodirecting adjunct for alkylation at the carbon α to a complexed diene (e.g. **2**). Preparation of the optically active dienone complex (-)-**21** demonstrates that the $Fe(CO)_3$ group may be used for the stereoselective introduction of the C14 methyl group and for facilitating formation of the C9-C10 dienone bond of protomycinolide IV. Attempts to prepare **4** via acylation of (+)-**19** with a C3-C9 acyl chloride are planned. Since alkylation of (dienone)$Fe(CO)_3$ at the β position (e.g. **1**) proceeds with only modest to non-existent stereoselectivity, introduction of the C8 methyl group of **4** will rely on the stereodirecting effects inherent in a macrocyclic ring.[26]

EXPERIMENTAL SECTION

General Data: Spectrograde solvents were used without purification with the exception of tetrahydrofuran which was distilled from the sodium benzophenone ketyl. Dichloromethane and DMSO used were Aldrich sure-seal solvents and were used without further purification. Methyl iodide was filtered through basic alumina prior to use. Column chromatography was performed on silica gel 60 (0.04-0.063 mm, E. Merck or 60-200 mesh, Aldrich) and "flash" chromatography was performed on silica gel 60 (230-400 mesh).

All ^1H NMR and ^{13}C NMR spectra were recorded at 300 and 75 MHz respectively. Melting points were obtained on a Mel-Temp melting point apparatus and are uncorrected. Elemental analyses were obtained from either Midwest Microlabs, Ltd., Indianapolis, IN; Robertson Microlit Laboratories, Inc., Madison, NJ or by the analytical department of Abbott Laboratories, North Chicago, IL, and high resolution mass spectra were obtained from the Nebraska Center for Mass Spectrometry.

Tricarbonyl(4E,6-heptadien-3-one)iron (1). Aluminum chloride (9.7 g, 73 mmol) was slurried in CH_2Cl_2 (180 mL) at 0°C and neat propionyl chloride (9.3 mL, 110 mmol) was slowly added to the reaction mixture. The mixture was stirred for 20 min, and then a solution of (butadiene)$Fe(CO)_3$ (12.2 g, 62.9 mmol in CH_2Cl_2 (85 mL) was added by cannula transfer under N_2 pressure. After stirring for 15 min, the yellow slurry was poured over concentrated NH_4OH (240 mL) and ice (ca. 300 g). The red-brown slurry was diluted with water (1 L) and extracted with CH_2Cl_2. The combined organic phases were washed with water, dried ($MgSO_4$), and concentrated. The residue was purified by flash chromatography (CH_2Cl_2) to give a mixture of *cis*- and *trans*-dienone complexes. This mixture was dissolved in methanol (15 mL) and added to a freshly prepared methanolic sodium methoxide solution (2.4 g Na/105 mL MeOH). The mixture was stirred for 30 min and then poured over CH_2Cl_2/H_2O and the layers separated. The aqueous layer was extracted with CH_2Cl_2 and the combined CH_2Cl_2 phases were washed with brine, dried ($MgSO_4$), and concentrated. The residue was purified by flash chromatography (CH_2Cl_2-hexanes (1:1)) to give **1** as an orange oil which solidified upon storing in the freezer (7.2 g, 46%): mp 37-39 °C; R_f 0.50 (CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 5.97 (tdd, J = 1.0, 5.0, 8.2 Hz, 1H), 5.43 (dddd, J = 0.9, 5.0, 6.9, 9.3 Hz, 1H), 2.41 (dq, J = 3.0, 7.4 Hz, 2H), 2.00 (ddd, J = 1.2, 2.7, 6.9 Hz, 1H), 1.24 (dd, J = 1.1, 8.1 Hz, 1H), 1.08 (t, J = 7.4 Hz, 3H), 0.69 (ddd, J = 1.1, 2.6, 9.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 205.9, 85.9, 85.0, 53.8, 41.1, 35.7, 8.5; MS (CI/NH_3) *m/z* 251 $(M+H)^+$, 268 $(M+NH_4)^+$; Anal. Calcd for $C_{10}H_{10}O_4Fe$: C, 48.03; H, 4.03. Found: C, 48.12; H, 3.99.

Tricarbonyl(methyl 3,5-hexadienoate)iron (2). Methyl 3,5-hexadienoate (5.35 g, 42.5 mmol) was taken up in ethyl acetate (30 mL) and agitated in an ultrasonic bath under argon for 15 min. To this solution was added $Fe_2(CO)_9$ (16.97 g, 46.7 mmol) and agitation was continued for an additional 48 h after which the solvents were evaporated. The resulting dark oil was kugelrohr distilled under vacuo (0.200-1 mm Hg). The product fraction which distilled at a bath temperature between 80-100 °C was further purified by column chromatography (hexanes-ethyl acetate (19:1)) to afford **2** as a golden oil (5.85 g, 51%): R_f 0.25 (hexanes-ethyl acetate (9:1)); IR (neat) 2048, 1973, 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.22-5.31 (m, 2H), 3.73 (s, 3H), 2.70 (dd, J = 7.5, 15 Hz, 1H), 2.55 (dd J = 7.5, 15.0 Hz, 1H), 1.78-1.80 (m, 1H), 1.11 (q, J = 7.5 Hz, 1H), 0.39 (dd, J = 2.7, 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 171.7, 87.7, 82.3, 54.1, 51.9, 40.1, 38.8; Anal. Calcd for $C_{10}H_{10}O_5Fe$: C, 45.15; H, 3.79. Found C, 45.48; H, 4.01.

Tricarbonyl(ethyl 3,5-hexadienoate)iron (3) was prepared from ethyl 3,5-hexadienoate using the same procedure as for the preparation of **2**. **3**: ^1H NMR ($CDCl_3$) δ 5.28 (m, 2H), 4.18 (m, 2H), 2.68 (dd, J = 7.5, 16.5, 1H), 2.53 (dd, J = 7.5, 16.5, 1H), 1.77 (m, 1H), 1.28 (t, J = 7.5, 3H), 2.23 (dd, J = 4.5, 7.5, 1H), 0.30 (dd, J = 2.7, 8.7, 1H); ^{13}C NMR ($CDCl_3$) δ 211.2, 171.3, 87.8, 82.3, 60.9, 54.4, 40.2, 39.1, 14.2. Anal. Calcd for $C_{11}H_{12}O_5Fe$: C, 47.17; H, 4.32. Found C, 46.91; H, 3.96.

Tricarbonyl(2-methyl-4,6-heptadien-3-one)iron (5). To a solution of diisopropylamine (45 μL, 0.30 mmol) in THF (1 mL) at 0 °C was added dropwise a solution of n-butyl lithium (2.5 M, 120 μL, 0.30 mmol) in hexane. The mixture was stirred at 0 °C for 10 min, and then cooled to -78 °C and a solution of **1** (69 mg, 0.28

mmol) in THF (1 mL) was added followed by iodomethane (25 μL, 0.42 mmol). The reaction mixture was warmed to rt and stirred for 2 h. The reaction mixture was diluted with saturated aqueous NH_4Cl (2 mL) and the phases separated. The aqueous layer was diluted with brine and extracted with CH_2Cl_2. All of the organic layers were combined, dried ($MgSO_4$) and concentrated. The residue was purified by flash chromatography (hexanes-ethyl acetate (20:1)) to give **5** as a yellow oil which solidified upon storing in the freezer (35 mg, 47%): mp 44-44.5 °C; ^1H NMR ($CDCl_3$) δ 5.97 (tdd, J = 1.0, 4.8, 8.2 Hz, 1H), 5.47 (dddd, J = 0.9, 4.8, 6.9, 9.3 Hz, 1H), 2.59 (hept, *J* = 7.0 Hz, 1H), 2.02 (ddd, *J* = 1.3, 2.7, 6.9 Hz, 1H), 1.28 (dd, *J* = 1.1, 8.0 Hz, 1H), 1.15 (d, *J* = 7.0 Hz, 3H), 1.10 (d, *J* = 7.0 Hz, 3H), 0.69 (ddd, *J* = 1.1, 2.6, 9.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 209.5, 86.6, 85.2, 52.6, 41.0, 40.8, 19.2, 18.9; MS (CI/NH_3) *m/z* 265 $(M+H)^+$, 282 $(M+NH_4)^+$; Anal. Calcd for $C_{11}H_{12}O_4Fe$: C, 50.03; H, 4.58. Found C, 50.38; H, 4.52.

*Tricarbonyl(1,1,1-d_3-2-methyl-4,6-heptadien-3-one)iron (**6a/b**).* To a solution of diisopropylamine (0.78 mL, 5.6 mmol) in THF (5 mL) at 0 °C was added dropwise a solution of n-butyl lithium (1.6 *M*, 3.7 mL, 5.9 mmol) in cyclohexane. The mixture was stirred at 0 °C for 10 min, and then cooled to -100 °C and a solution of **1** (1.00 g, 4.0 mmol) in THF (3 mL) was added followed by d_3-iodomethane (1.0 g, 6.9 mmol). The reaction mixture was warmed to rt and stirred for 2 h. The reaction mixture was diluted with saturated aqueous NH_4Cl and the phases separated. The aqueous layer was diluted with brine and extracted with ethyl acetate. All of the organic layers were combined, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (hexanes-ethyl acetate (20:1)) to give dialkylated ketone (50 mg, 4%), followed by **6a/b** (90 mg, 9%) and unreacted **1** (70 mg) all as yellow oils: dialkylated ketone: ^1H NMR ($CDCl_3$) δ 5.96 (dd, *J* = 5.1, 8.1 Hz, 1H), 5.49 (m, 1H), 2.01 (ddd, *J* = 0.9, 2.4, 6.7 Hz, 1H), 1.40 (d, *J* = 8.1 Hz, 1H), 1.15 (s, 3H), 0.67 (dd, *J* = 1.8, 9.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 211.4, 87.8, 85.2, 49.3, 43.0, 40.9, 27.0. **6a/b**: ^1H NMR ($CDCl_3$) δ 5.95 (dd, *J* = 5.2, 7.8 Hz, 1H), 5.46 (m, 1H), 2.55 (br q, *J* = 6.9 Hz, 1H), 2.00 (dd, *J* = 1.5, 6.9 Hz, 1H), 1.27 (d, *J* = 8.0 Hz, 1H), 1.15 (d, *J* = 7.0 Hz, 2.1H), 1.10 (d, *J* = 7.0 Hz, 0.9H), 0.68 (dd, *J* = 1.8, 9.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 210.2, 86.5, 85.2, 52.5, 41.1, 40.5, 19.1 (18.7); EI-HRMS *m/z* 239.0321 (calcd for $C_{10}H_9D_3O_3Fe$ (M - CO) 239.0324).

*Tricarbonyl(2-methyl-1-phenyl-4,6-heptadien-3-one)iron (**7a/b**).* To a solution of diisopropylamine (445 μL, 3.18 mmol) in THF (11.5 mL) at 0 °C was added dropwise a solution of n-butyl lithium (2.5 *M*, 1.30 mL, 3.18 mmol) in hexane. The mixture was stirred at 0 °C for 10 min, and then cooled to -100 °C and a solution of **1** (763 mg, 2.89 mmol) in THF (11.5 mL) was precooled to -78 °C and added followed by benzyl bromide (2.1 mL, 17.3 mmol). The reaction mixture was stirred at -100 °C for 2 h, and then warmed to rt and stirred for 18 h. The reaction mixture was diluted with saturated aqueous NH_4Cl and the phases separated. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layers were dried ($MgSO_4$) and concentrated. The residue was purified by flash chromatography (hexanes-ether (20:1)) to give **7a/b** as a yellow oil (319 mg, 32%): ^1H NMR ($CDCl_3$) δ 7.39-7.12 (m, 5H), 5.98-5.91 (m, 1H), 5.47-5.38 (m, 1H), 3.06-2.92 (m, 1H), 2.83-2,76 (m, 1H), 2.60-2.52 (m, 1H), 2.00-1.96 (m, 1H), 1.12-1.03 (m, 4H), 0.68-0.57 (m, 1H); EI-HRMS *m/z* 284.0496 (calcd for $C_{15}H_{16}O_2Fe$ (M - 2CO) 284.0500).

*Tricarbonyl(6-methyl-1,3,8-nonatrien-5-one)iron (**8a/b**).* To a solution of diisopropylamine (435 μL, 3.10 mmol) in THF (11.5 mL) at 0 °C was added dropwise a solution of n-butyl lithium (2.5 *M*, 1.25 mL, 3.10 mmol) in hexane. The mixture was stirred at 0 °C for 10 min, and then cooled to -100 °C and a solution of **1** (745 mg, 2.82 mmol) in THF (11.5 mL) was precooled to -78 °C and added followed by allyl bromide (1.5 mL, 17 mmol). The reaction mixture was stirred at -100 °C for 2 h, and then warmed to rt and stirred for 18 h. The reaction mixture was diluted with saturated aqueous NH_4Cl and the phases separated. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layers were dried ($MgSO_4$) and concentrated. The residue was purified by flash chromatography (hexanes-ether (30:1)) to give **8a/b** as a yellow oil (270 mg, 33%): ^1H NMR ($CDCl_3$) δ 6.02 (dd, *J* = 5.2, 8.1 Hz, 1H), 5.81-5.64 (m, 1H), 5.51-5.43 (m, 1H), 5.11-4.98 (m, 2H), 2.62-2.35 (m, 2H), 2.13-1.99 (m, 2H), 1.25-1.22 (m, 1H), 1.14 and 1.09 (2 x d, *J* = 7.0 Hz and *J* = 7.0 Hz, 3H), 0.72-0.67 (m, 1H); MS (CI/NH_3) *m/z* 291 $(M+H)^+$, 308 $(M+NH_4)^+$; Anal. Calcd for $C_{13}H_{14}O_4Fe$: C, 53.82; H, 4.68. Found: C, 54.00; H, 4.93.

Tricarbonyl[methyl (2R,3R*)-2-methyl-3,5-hexadienoate]iron (9a).* To a solution of diisopropylamine (6.85 mL, 48.9 mmol) in THF (100 mL) at 0 °C was added a solution of n-butyl lithium (19.57 mL, 2.5 *M* in THF, 48.9 mmol). After 10 min, the reaction was cooled to -78 °C followed by the dropwise addition of **2** (12.39 g, 46.6 mmol) in THF (5 mL). The reaction was maintained at this temperature for 20 min followed by the addition of methyl iodide (10 mL). The reaction was allowed to come to room temperature over 1h after which it was quenched into saturated aqueous NH_4Cl solution. The product was extracted with ethyl acetate (3 x 50 mL). The combined organic layers were washed with 1 N H_3PO_4 (2 x 40 mL), saturated aqueous $NaHCO_3$ (1 x 40 mL), dried ($MgSO_4$) and concentrated. The resultant oil was purified by chromatography (hexanes-ethyl acetate (19:1)) to give **9a** as a yellow solid (9.46 g, 72%): mp 43-44 °C; R_f 0.53 (hexane-ethyl acetate (9:1)); ^1H NMR ($CDCl_3$) δ 5.18-5.28 (m, 2H), 3.77 (s, 3H), 2.38 (dq, *J* = 6.8, 10.2 Hz, 1H), 1.72-1.74 (m, 1H), 1.33 (d, *J* = 6.75 Hz, 3H), 1.04 (dd, *J* = 7.5, 10.5 Hz, 1H), 0.34 (dd, *J* = 3.0, 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 211.0, 174.7, 86.5, 82.1, 63.3, 51.8, 45.2, 39.9, 21.4; MS (CI/NH_3) *m/z* 298 $(M+NH_4)^+$; Anal. Calcd for $C_{11}H_{12}O_5Fe$: C, 47.17; H, 4.32. Found C, 47.29; H, 4.32.

Tricarbonyl[ethyl (2R,3R*)-2-methyl-3,5-hexadienoate]iron (10a)* was prepared by generation of the lithium anion of **3** (0.241 g, 0.866 mmol) at -78 °C for 15 min, followed by addition of methyl iodide (1.1 equiv.). The reaction mixture was allowed to warm to rt over 1 h and worked up in a similar manner to compound **9a**. The residue was purified by column chromatography (hexanes-ethyl acetate (19:1)) to give **10a** as a clear yellow oil (0.176g, 69%): ^1H NMR ($CDCl_3$) δ 5.18-5.28 (m, 2H), 4.12-4.33 (m, 2H), 2.45 (dq, *J* = 6.75, 9.75, 1H), 1.72 (m, 1H), 1.32 (m, 6H), 1.07 (dd, *J* = 7.5, 10.5, 1H), 0.34 (dd, *J* = 3.0, 9.0, 1H); ^{13}C NMR ($CDCl_3$) δ 174.4, 86.6, 82.2, 63.4, 60.8, 45.3, 39.9, 21.5, 14.0; MS (CI/NH_3) *m/z* 295 $(M+H)^+$, 312 $(M+NH_4)^+$; Anal. Calcd for $C_{12}H_{14}O_5Fe$: C, 49.01; H, 4.80. Found C, 49.24; H, 4.67.

Tricarbonyl[(2S,3R*)-2-methyl-3,5-hexadienoic acid]iron (11b).* To a solution of **9a** (0.266 g, 0.95 mmol) in THF (4 mL) was added $LiOH{\cdot}H_2O$ (0.044 g, 1.0 mmol) under argon. The reaction was heated to 50 °C for 48 h after which it was cooled, acidified with 1 N H_3PO_4 and extracted with ethyl acetate (3 x 40 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$) and evaporated to yield a mixture of **11a/b** (1:7) as a white solid. The major diastereomer, **11b** (0.21 g, 81%), could be obtained pure upon chromatography (hexane-ethyl acetate (2:1)). The minor diastereomer, **11a**, was only characterized as a mixture with **11b**. **11a:** ^{13}C NMR ($CDCl_3$) δ 211.0, 181.2, 86.4, 82.2, 62.1, 45.1, 39.9, 21.3.
11b: ^1H NMR ($CDCl_3$) δ 5.41 (dd, *J* = 5.0, 8.5 Hz, 1H), 5.23-5.31 (m, 1H), 2.31 (dq, *J* = 6.0, 9.0 Hz, 1H), 1.81 (dd, *J* = 1.5, 6.7 Hz, 1H), 1.35 (d, *J* = 6.0, 3H), 0.95 (t, *J* = 9.0, 1H), 0.38 (dd, *J* = 2.7, 9.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 211.0, 181.2, 87.2, 82.4, 63.0, 44.0, 40.5, 19.0; MS (CI/NH_3) *m/z* 267 $(M+H)^+$, 284 $(M+NH_4)^+$; Anal. Calcd for $C_{10}H_{10}O_5Fe{\cdot}0.5H_2O$: C, 43.67; H, 4.03. Found: C, 43.62; H, 3.78. A sample suitable for X-ray diffraction analysis[10] was obtained by recrystallization from hexanes-ethyl acetate.

Tricarbonyl[methyl (2S,3R*)-2-methyl-3,5-hexadienoate]iron (9b).* To 50% KOH (10 mL) and ether (5 mL) at 0 °C was added 1-methyl-3-nitro-1-nitrosoguanidine (0.53 g, 3.6 mmol). After 5 min the ether layer was separated and added to an ether solution (5 mL) containing **11b** (0.096 g, 0.36 mmol). The reaction was stirred for 30 min after which the solvent was evaporated. The residue was purified by chromatography (hexane-ethyl acetate (97:3)) to give **9b** as a clear yellow oil (0.081g, 81%): R_f 0.42 (hexanes-ethyl acetate (9:1)): ^1H NMR ($CDCl_3$) δ 5.42-5.33 (m, 1H), 5.19-5.30 (m, 1H), 3.70 (s, 3H), 2.31 (dq, *J* = 10.5, 7.5 Hz, 1H), 1.78 (dd, *J* = 3.0, 7.5 Hz, 1H), 1.32 (d, *J* = 7.5 Hz, 3H), 0.98 (t, *J* = 9.0 Hz, 1H), 0.38 (dd, *J* = 9.0, 3.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 174.9, 87.2, 82.2, 64.0, 52.0, 44.1, 40.4, 19.3.

Tricarbonyl[methyl (2R,3R*)-2-benzyl-3,5-hexadienoate]iron (12)* was prepared by generation of the lithium anion of **2** (0.298 g, 1.12 mmol) at -78 °C for 15 min, followed by addition of benzyl bromide (1.5 equiv). The reaction mixture was warmed to 0 °C and worked up in a manner similar to that for the preparation of **9**. The residue was purified by chromatography (hexane-ethyl acetate (9:1)) to give a mixture of diastereomers **12a** and **12b** (8.6 : 1), along with a minor amount of dibenzylated product, as a golden oil (0.235 g, 59%): ^1H NMR ($CDCl_3$) δ 7.27 (m, 3H), 7.12 (m, 2H), 5.12 (m, 1H), 4.79 (dd, *J* = 9.0, 5.2 Hz, 1H),

3.61 and 3.73 (2 x s, 3H combined, ratio of 1: 8.6), 3.11 (dd, J = 13.5, 7.5 Hz, 1H), 2.79 (dd, J = 13.5, 8.2 Hz, 1H), 2.48 (dt, J = 10.5, 7.5 Hz, 1H), 1.72 (d, J = 7.5 Hz, 1H), 0.98 (t, J = 9.0 Hz, 1H), 0.34 (br d, J = 9.3 Hz,1H); ^{13}C NMR ($CDCl_3$) δ 210.8, 173.6, 137.2, 129.2, 128.4, 126.6, 87.1, 81.8, 60.7, 53.4, 51.8, 41.9, 39.9; MS (CI/NH_3) *m/z* 357 $(M+H)^+$, 374 $(M+NH_4)^+$; Anal. Calcd for $C_{17}H_{16}O_5Fe$: C, 57.30; H, 4.49. Found: C, 59.19; H, 4.83.

Tricarbonyl[methyl (2R,3R*)-2-allyl-3,5-hexadienoate]iron (13)* was prepared by generation of the lithium anion of **2** (0.301 g, 1.13 mmol) at -78 °C for 15 min, followed by addition of allyl bromide (1.2 equiv.). The reaction mixture was warmed to 0 °C and worked up in a manner similar to that for the preparation of **9**. The residue was purified by chromatography (hexane-ethyl acetate (9:1)) to give a mixture of diastereomers **13a** and **13b** (5.5 : 1 ratio) as a yellow oil (0.166 g, 48%): ^{1}H NMR ($CDCl_3$) δ 5.63- 5.84 (m, 1H), 5.22 (m, 2H), 5.06 (m, 2H), 3.69 and 3.77 (2 x s, 3H combined, 1 : 5.5 ratio), 2.51 (m, 1H), 2.32 (m, 2H), 1.74 (m, 1H), 0.96 (dd, J = 7.5, 9.7 Hz,1H), 0.34 (dd, J = 2.6, 8.5 Hz, 1H); MS (CI/NH_3) *m/z* 307 $(M+H)^+$, 324 $(M+NH_4)^+$; Anal. Calcd for $C_{13}H_{14}O_5Fe$: C, 51.01, H, 4.61. Found: C, 51.22, H, 4.77.

Tricarbonyl[(2R,3R*)-2-methyl-3,5-hexadien-1-ol)iron (14).* To a solution of **9a** (0.90 g, 3.4 mmol) in THF (10 mL) at 0 °C was added DIBAL (8.0 mL, 1.0 *M* in toluene, 8.0 mmol). The reaction mixture was maintained at 0 °C for 2 h after which methanol (1 mL) was added. The reaction was then quenched into cold 1N H_3PO_4 (25 mL) and the extracted with ethyl acetate (3 x 10 mL). The combined organic phases were dried ($MgSO_4$), concentrated and dried in vacuo to give **14**, as light yellow crystals (0.74 g, 91%): mp 73-73.5 °C; ^{1}H NMR ($CDCl_3$) δ 5.28-5.32 (m, 2H), 3.71 (dd, J = 4.0, 10.6 Hz, 1H), 3.48 (dd, J = 6.6, 10.3 Hz, 1H), 1.73 (m, 1H), 1.55 (m, 1H), 1.46 (t, J = 5.4 Hz, OH), 1.17 (d, J = 6.6 Hz, 3H), 0.91 (dd, J = 8.1, 9.6 Hz, 1H), 0.29 (dd, J = 2.6, 8.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 211.9, 87.1, 81.7, 68.7, 66.9, 40.8, 39.9, 20.5; MS (CI/NH_3) *m/z* 253 $(M+H)^+$, 270 $(M+NH_4)^+$; Anal. Calcd for $C_{10}H_{12}O_4Fe$: C, 47.62; H, 4.76. Found: C, 47.77; H, 4.90. Use of $LiAlH_4$ in place of DIBAL gave **14** in 23% yield.

Tricarbonyl[(2R,3R*)-2-methyl-3,5-hexadienal)iron (15).* To a solution containing **14** (0.50 g, 2.0 mmol), DMSO (0.43 mL, 6.0 mmol) and triethylamine (0.83 mL, 6.0 mmol) in CH_2Cl_2 (10 mL) at 0 °C under argon was added SO_3-pyridine complex (0.955 g, 6.0 mmol). The temperature was maintained at 0 °C for 30 min then warmed to 25 °C over 30 min. The reaction was quenched into cold H_2O and extracted with ethyl acetate. The combined organic phases were washed with 1 N H_3PO_4 (3 x 50 mL), saturated $NaHCO_3$ (2 x 50 mL), brine (50 mL) dried ($MgSO_4$) and the solvent evaporated to yield **15** as a labile yellow oil which was used in the next step without further purification (0.348 g, 69%): ^{1}H NMR ($CDCl_3$) δ 9.64 (s, 1H), 5.21-5.41(m, 2H), 2.31 (m, 1H), 1.83 (d, J = 7.0 Hz, 1H), 1.25 (d, J = 6.75 Hz, 3H), 0.68 (t, J = 9.0 Hz, 1H), 0.35 (dd, J = 1.5, 9.0 Hz, 1H); MS (CI/NH_3) *m/z* 251 $(M+H)^+$, 268 $(M+NH_4)^+$.

Tricarbonyl[(3S,4R*,5R*)-4-methyl-5,7-octadien-3-ol]iron (16).* To a solution **15** (238 mg, 0.952 mmol) in THF (10 mL) at -78 °C was added ethyl magnesium bromide (0.95 mL, 2.0 M in THF, 1.9 mmol). The reaction was warmed to rt, stirred for 1h, and stored at 0 °C overnight. The mixture was poured into cold 0.5 M H_3PO_4, extracted with ethyl acetate (3 x 50 mL) and the combined organic phases were washed with saturated $NaHCO_3$ (2 x 50 mL), brine (1 x 40 ml), dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (hexanes-ethyl acetate (19:1)) to give **16** as a yellow oil (95 mg, 36%): ^{1}H NMR ($CDCl_3$) δ 5.21-5.30 (m, 2H), 3.57 (m, 1H), 1.73 (m, 1H), 1.53 (m, 1H), 1.32-1.47 (m, 4H), 1.02 (d, J = 7.5 Hz, 3H), 0.93 (t, J = 7.5 Hz, 3H), 0.36 (dd, J = 2.0, 9.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 212.1, 87.6, 81.4, 77.6, 70.0, 41.9, 39.9, 38.2, 15.5, 10.4; MS (CI/NH_3) *m/z* 281 $(M+H)^+$; Anal. Calcd for $C_{12}H_{16}O_4Fe$: C, 51.45; H, 5.76. Found C, 51.24; H, 5.53.

Tricarbonyl[(3S,4R*,5R*)-O-(t-butyldimethylsilyl)-4-methyl-5,7-octadien-3-ol]iron (17).* To a solution containing the alcohol **16** (60 mg, 0.215 mmol) and 2,6 lutidine (50 mL, 0.429 mmol) in CH_2Cl_2 (2 mL) was added of t-butyldimethylsilyl triflate (148 mL, 6.44 mmol) under an atmosphere of argon. Following the disappearance of the starting material the reaction was transfered with additional CH_2Cl_2 to a separatory

funnel and washed with 1 N H_3PO_4, saturated $NaHCO_3$, brine, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (hexanes) to yield **17** as a yellow oil (70 mg, 83%): ^1H NMR ($CDCl_3$) δ 5.25 (m, 2H), 3.63 (m, 1H), 1.69 (m, 1H), 1.34-1.66 (m, 4H), 1.34-1.66 (m, 4H), 1.34-1.66 (m, 4H), 0.86 (s, 9H), 0.79 (t, *J* = 7.5 Hz, 3H), 0.26 (dd, *J* = 2.7, 8.25 Hz, 1H), 0.09 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 212.2, 87.2, 81.2, 77.8, 70.9, 40.5, 39.5, 28.0, 26.0, 15.3, 10.0, -3.8, -4.5; MS (CI/NH_3) *m/z* 395 $(M+H)^+$, 412 $(M+NH_4)^+$. A sample of **17** suitable for for X-ray diffraction analysis[18] was obtained by crystallization from $CHCl_3$.

*Tricarbonyl(3,5-hexadienoic acid)iron (rac-**18**).* To a solution of *rac*-**2** (5.75 g, 21.6 mmol) in THF (80 mL) was added LiOH·H_2O (1.44 g, 34.3 mmol) under N_2. The reaction was heated to 50 °C for 48 h after which it was cooled, acidified with 1 N H_3PO_4 (70 mL) and extracted with ethyl acetate (6 x 80 mL). The combined organic solution was washed with brine (90 mL), dried ($MgSO_4$) and evaporated to give a yellow solid (5.12 g). Recrystallization (hexanes-ethyl acetate) gave *rac*-**18** as golden yellow crystals (4.23 g, 78 %): mp 107-109 °C; ^1H NMR ($CDCl_3$) δ 5.35-5.25 (m, 2H), 2.72 (dd, *J* = 7.0, 16.3 Hz, 1H), 2.61 (dd, *J* = 6.6, 16.2 Hz, 1H), 1.78 (dd, *J* = 2.4, 8.1 Hz, 1H), 1.09 (q, *J* = 7.2 Hz, 1H), 0.40 (dd, *J* = 2.4, 8.4 Hz, 1H); Anal. Calcd for $C_9H_8O_5Fe$: C, 42.90; H, 3.20. Found: C, 42.42; H, 2.96.

Resolution of tricarbonyl(3,5-hexadienoic acid)iron. To a solution of *rac*-**18** (4.43 g, 17.6 mmol) in acetone (40 mL) was added dropwise (R)-α-methylbenzylamine (Fluka*brand*™, 1.02 mL, 0.96 g, 7.9 mmol). The reaction mixture was allowed to stand at rt for ca. 3 h. The yellow crystals which formed during this time were collected (2.61 g, $[\alpha]_D$ -25.2°, c = 0.515, MeOH). Diffusion controlled recrystallization (acetone-pentane) gave yellow needles (1.36 g, $[\alpha]_D$ -30.7°, c = 0.515, MeOH). It was found that further recrystallizations did not significantly increase the magnitude of the rotation. The fractions from various resolutions with rotation ≤ -30.7° were pooled (2.33 g), suspended in ethyl acetate (200 mL) and treated with 10% aqueous HCl (100 mL). After 15 min, the organic layer was separated, dried (MgSO4) and evaporated. The yellow solid was recrystallized (ethyl acetate-pentane) to give two crops: A, 0.42 g, $[\alpha]_D$ -78°, c = 0.50, MeOH; B, 1.05 g, $[\alpha]_D$ -75.0°, c = 0.504, MeOH, mp 93-95 °C. The ^1H NMR spectrum of carboxylic acid obtained in this fashion was identical to that of *rac*-**18**.

*(-)-Tricarbonyl(methyl 3,5-hexadienoate)iron ((-)-**2**).* To a solution of (-)-**18** (1.39 g, 5.51 mmol) in THF (20 mL) and anhydrous methanol (20 mL) was slowly added, via syringe, a solution of trimethylsilyldiazomethane (2.0 *M* in hexane, 8.27 mL, 16.5 mmol). The reaction mixture was stirred for 3 h and then concentrated. The residue was purified by column chromatography (hexanes-ether (20:1)) to give (-)-**2** as a yellow oil (1.26 g, 86%); $[\alpha]_D$ -79°, c = 0.57, MeOH; $[\alpha]_D$ -66°, c = 0.53, $CDCl_3$. The ^1H NMR spectrum of (-)-**2** was identical to that of *rac*-**2**.

*(-)-Tricarbonyl[methyl (2S,3S)-2-methyl-3,5-hexadienoate)iron ((-)-**9a**).* The preparation of (-)-**9a** from (-)-**2** (1.22 g, 4.58 mmol) was carried out in the same fashion as for the preparation of *rac*-**9a** (0.92 g, 73%); $[\alpha]_D$ -75°, c = 0.74, MeOH; $[\alpha]_D$ -84°, c = 0.81, $CDCl_3$. All the spectral data were identical with those of *rac*-**9a**. Analysis by ^1H NMR specroscopy in the presence of a chiral shift reagent (Eu[tfc]$_3$, C_6D_6) indicated that the product was 82% ee.

*(-)-Tricarbonyl[(2S,3S)-methyl-3,5-hexadien-1-ol)iron ((-)-**14**).* The preparation of (-)-**14** from (-)-**9a** (0.91 g, 3.2 mmol) was carried out in the same fashion as the preparation of *rac*-**14** (0.54 g, 67%); $[\alpha]_D$ -20°, c = 0.50, MeOH; mp 53-55 °C. All the spectral data were identical with those of *rac*-**14**.

*(R)-MTPA ester of rac-**14**.* To a solution of *rac*-**14** (50 mg, 0.20 mmol) in dry THF (5 mL) was added (R)-methoxytrifluoromethylphenylacetic acid (150 mg, 0.64 mmol), DCC (130 mg) and DMAP (15 mg). The reaction mixture was stirred at rt for 2 h, and then water (2 mL) was added. The mixture was extracted with ether, and the combined ethereal extracts washed with 3% aqueous HCl, water, and brine, dried ($MgSO_4$) and evaporated. The residue was purified by column chromatography (hexane-ethyl acetate (9:1)) to give a mixture

of diastereomers as a yellow oil (0.91 mg, 97 %): ^{1}H NMR (C_6D_6) δ 7.4-7.45 (m, 2H), 6.9-7.15 (m, 3H), 4.52 (m), 4.43 (m), 4.17 (dd, *J* = 3.3, 10.8 Hz, 1H), 4.00 (dd, *J* = 6.8, 10.8 Hz, 1H), 3.40 (s, 3H), 1.36 (m, 1H), 1.26 (br d, *J* = ca. 7 Hz, 1H), 0.80 (d, *J* = 6.7 Hz, 3H), 0.49 (t, *J* = 8.8 Hz, 1H), -0.14 (m, 1H). For the spectral data for the diastereomer, see below.

*(R)-MTPA ester of (-)-**14**.* The preparation of the (R)-MTPA ester of (-)-**14** was carried out in the same fashion as the preparation of the diastereomeric (R)-MTPA ester of *rac*-**14** (96%). Analysis by ^{1}H NMR specroscopy (C_6D_6) indicated that the product was 83% de. ^{1}H NMR (C_6D_6) δ 7.4-7.45 (m, 2H), 6.9-7.15 (m, 3H), 4.52 (m, 1H), 4.43 (dd, *J* = 5.1, 8.8 Hz, 1H), 4.39 (dd, *J* = 3.6, 10.8 Hz, 1H), 3.79 (dd, *J* = 6.8, 10.8 Hz, 1H), 3.40 (s, 3H), 1.36 (m, 1H), 1.26 (ddd, *J* = 1.0, 2.4, 6.9 Hz, 1H), 0.77 (d, *J* = 6.6 Hz, 3H), 0.49 (t, *J* = 8.8 Hz, 1H), -0.15 (ddd, *J* = 0.7, 2.4, 9.3 Hz, 1H).

*(-)-Tricarbonyl[(2S,3S)-O-(4'-nitrobenzoyl)-2-methyl-3,5-hexadien-1-ol]iron ((-)-**19**).* To a solution of (-)-**14** (0.45 g, 1.8 mmol) in pyridine (5 mL) at rt was added 4-nitrobenzoyl chloride (0.67 g, 3.6 mmol). The mixture was stirred at rt for 3 h, poured into water (10 mL) and extracted with ether (3 x 20 mL). The combined ethereal extracts were washed with saturated aqueous $NaHCO_3$, brine, dried ($MgSO_4$) and concentrated. Yellow-green crystals of product formed during the concentration. Trace amounts of pyridine were removed by the addition of toluene and co-evaporation, to give (-)-**19** as pale yellow crystals (0.65 g, 90%): mp 74-76 °C; $[\alpha]_D$ -41°, c = 0.55, MeOH; ^{1}H NMR ($CDCl_3$) δ 8.26 (AA'BB', J_{AB} = 9.0 Hz, 4H), 5.32-5.25 (m, 2H), 4.40 (dd, *J* = 5.0, 11.0 Hz, 1H), 4.19 (dd, *J* = 6.4, 11.0 Hz, 1H), 1.90 (m, 1H), 1.78 (m, 1H), 1.23 (d, *J* = 6.9 Hz, 3H), 0.86 (dd, *J* = 7.5, 9.9 Hz, 1H), 0.30 (dd, *J* = 2.4, 8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 164.6, 150.5, 135.6, 130.6, 123.5, 86.8, 82.2, 71.0, 65.3, 40.2, 37.9, 21.2; Anal. Calcd for $C_{17}H_{15}NO_7Fe$: C, 50.90; H, 3.77; N, 3.49. Found C; 51.09; H, 3.86; N, 3.55.

*(+)-Tricarbonyl[9-(4'-nitrobenzoyloxy)-8(S),7(S)-8-methyl-4Z,6E-nonadien-3-one]-iron ((+)-**20**).* Aluminum chloride (0.20 g, 1.5 mmol) was slurried in CH_2Cl_2 (5 mL) at 0 °C and neat propionyl chloride (0.14 g, 1.5 mmol) was added. The mixture was stirred for 20 min, and then a solution of (-)-**19** (0.30 g, 0.75 mmol) in CH_2Cl_2 (5 mL) was added. The mixture was stirred at 0 °C for 50 min, warmed to rt, and stirred for an additional 2h. The yellow-brown reaction mixture was poured over concentrated NH_4OH (5 mL) and ice (8 g). The slurry was diluted with water (10 mL) and extracted with ether (5 x 15 mL). The combined organic phases were washed with water (2 x 35 mL), brine (2 x 15 mL), dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (hexanes-ether (1:1)) to give (+)-**20** as a viscous yellow-orange oil (0.15 g, 43 %): $[\alpha]_D$ +269°, c = 0.62, MeOH; IR (CH_2Cl_2) 2056, 1990, 1726, 1664, 1529, 1276 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.26 (AA'BB', J_{AB} = 9.0 Hz, 4H), 5.48 (dd, *J* = 5.4, 9.0 Hz, 1H), 5.34 (t, *J* = 6.0 Hz, 1H), 4.45 (dd, *J* = 3.9, 10.8 Hz, 1H), 4.20 (dd, *J* = 5.4, 10.8 Hz, 1H), 3.10 (d, *J* = 6.3 Hz, 1H), 2.6-2.2 (m, 3H), 1.95 (m, 1H), 1.38 (d, *J* = 6.9 Hz, 3H), 0.97 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 205.7, 164.6, 150.5, 135.4, 130.7, 123.6, 94.6, 82.6, 70.6, 55.8, 38.6, 35.5, 29.6, 21.0, 8.7; Anal. Calcd for $C_{20}H_{19}NO_8Fe$: C, 52.54; H, 4.19; N, 3.06. Found C; 52.82; H, 4.31; N, 3.12.

*(-)-Tricarbonyl(9-p-nitrobenzoyloxy-8(S),7(S)-8-methyl-4E,6E-nonadien-3-one)iron ((-)-**21**).* A sample of (+)-**20** (0.14 g, 0.31 mmol) was dissolved in propionyl chloride (1.0 mL). After 30 min, TLC (hexanes-ether (1:1)) indicated consumption of starting material. The reaction mixture was poured into ice/water (30 mL), and extracted with ether (2 x 50 mL). The combined ethereal extracts were washed with saturated aqueous $NaHCO_3$ (2 x 20 mL), brine (2 x 10 mL), dried ($MgSO_4$) and concentrated to give (-)-**21** as a viscous yellow oil (0.13 g, 93%): $[\alpha]_D$ -201°, c = 0.70, MeOH; IR (CH_2Cl_2) 2048, 1975, 1736, 1637 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.27 (AA'BB', J_{AB} = 9.3 Hz, 4H), 5.90 (ddd, *J* = 1.2, 5.1, 8.4 Hz, 1H), 5.34 (dd, *J* = 5.4, 9.0 Hz, 1H), 4.43 (dd, *J* = 5.1, 11.1 Hz, 1H), 4.23 (dd, *J* = 6.6, 11.1 Hz, 1H), 2.40 (q, *J* = 7.5 Hz, 2H), 1.95 (m, 1H), 1.29 (d, *J* = 6.6 Hz, 3H), 1.27-1.18 (m, 2H), 1.07 (t, *J* = 7.5 Hz, 3H); HRMS (EI) *m/z* 401.0560 (calcd for $C_{18}H_{19}NO_6Fe$ (M - 2CO) 401.0562).

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