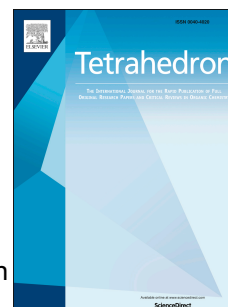# Accepted Manuscript

Reactivity of acyclic (pentadienyl)iron(1+) cations with phosphonate stabilized nucleophiles: Application to the synthesis of oxygenated metabolites of carvone

Do W. Lee, Charles F. Manful, Jayapal Reddy Gone, Yuzhi Ma, William A. Donaldson

Please cite this article as: Lee DW, Manful CF, Gone JR, Ma Y, Donaldson WA, Reactivity of acyclic (pentadienyl)iron(1+) cations with phosphonate stabilized nucleophiles: Application to the synthesis of oxygenated metabolites of carvone, *Tetrahedron* (2016), doi: 10.1016/j.tet.2015.12.035.

Graphical Abstract

To create your abstract, type over the instructions in the template box below.
Fonts or abstract dimensions should not be changed or altered.

Reactivity of acyclic (pentadienyl)iron(1+) cations with phosphonate stabilized nucleophiles: Application to the synthesis of oxygenated metabolites of carvone

Leave this area blank for abstract info.
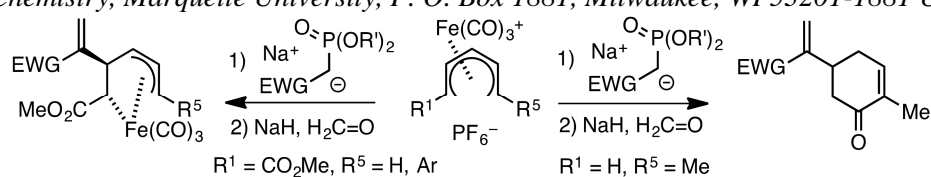
Do W. Lee, Charles F. Manful, Jayapal Reddy Gone, Yuzhi Ma and William A. Donaldson*

Department of Chemistry, Marquette University, P. O. Box 1881, Milwaukee, WI 53201-1881 USA

Tetrahedron

journal homepage: www.elsevier.com

Reactivity of acyclic (pentadienyl)iron(1+) cations with phosphonate stabilized nucleophiles: Application to the synthesis of oxygenated metabolites of carvone

Do W. Lee, Charles F. Manful, Jayapal Reddy Gone, Yuzhi Ma and William A. Donaldson*

Department of Chemistry, Marquette University, P. O. Box 1881, Milwaukee, WI 53201-1881 USA
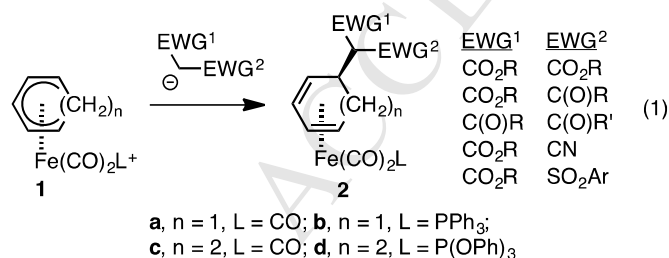*Phone: 414-288-7374; email: william.donaldson@marquette.edu*

ARTICLE INFO

ABSTRACT

The addition of phosphonate stabilized carbon nucleophiles to acyclic (pentadienyl)iron(1+) cations proceeds predominantly at an internal carbon to afford (pentenediyl)iron complexes. Those complexes bearing an electron withdrawing group at the σ-bound carbon (i.e. **13/14**) are stable and isolable, while complexes which do not contain an electron withdrawing group at the σ-bound carbon undergo CO insertion, reductive elimination and conjugation of the double bond to afford cyclohexenone products (**21/22**). Deprotonation of the phosphonate **13/14** or **21** and reaction with paraformaldehyde affords the olefinated products. This methodology was utilized to prepare oxygenated carvone metabolites (±)-**25** and (±)-**26**.

1. Introduction

Nucleophilic addition to cationic polyenyl-metal complexes is an exemplar of organometallic chemistry. Where these reactions proceed in good yield and with high regioselectivity, they have been utilized in organic synthesis.[1] There are numerous examples of the reaction of (cyclohexadienyl)- and (cycloheptadienyl)Fe(1+) cations (**1a-d**, eqn. 1) with stabilized carbon nucleophiles such as malonates,[2a-j] β-ketoesters,[2k-m] β-diketones,[2n-p] 2-cyano acetates,[2q-r] and arylsulfonyl acetates.[2s-t]

$$ (1) $$

EWG^1	EWG^2
CO$_2$R	CO$_2$R
CO$_2$R	C(O)R
C(O)R	C(O)R'
CO$_2$R	CN
CO$_2$R	SO$_2$Ar

a, n = 1, L = CO; **b**, n = 1, L = PPh$_3$;
c, n = 2, L = CO; **d**, n = 2, L = P(OPh)$_3$

In spite of their potential as synthons for Horner-Emmons olefination, there are few examples of the reaction of dienyl-iron cations[3] or other organometallic cations[4] with phosphonate stabilized carbon nucleophiles. Stephenson, *et al.*, reported the reaction of (cyclohexadienyl)Fe(CO)$_3^+$ cations **3a/b** with the potassium salt of α-phosphoramide acetates proceeded with good regioselectivity, but in only modest yields (eqn. 2).[3] Furthermore, the products **4** were not further processed into the corresponding alkenes via reduction of the ester and subsequent elimination.

$$ (2) $$

3a, R = H
3b, R = OMe

4a, R = H, R' = Me (46%)
4b, R = OMe, R' = CH$_2$CH$_2$CH=CMe$_2$ (50%)
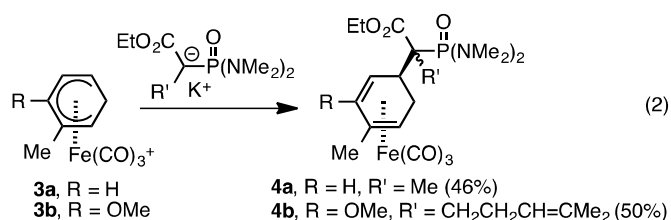
We and others have examined the reactivity of acyclic (pentadienyl)iron(1+) cations **5** with nucleophiles.[5] While certain nucleophiles attack at the pentadienyl terminus to generate *E,Z*-diene complexes **6**, other nucleophiles react via attack at an internal pentadienyl carbon to generate 2-substituted (3-pentene-1,5-diyl)Fe complexes **7**. This latter reactivity is relatively
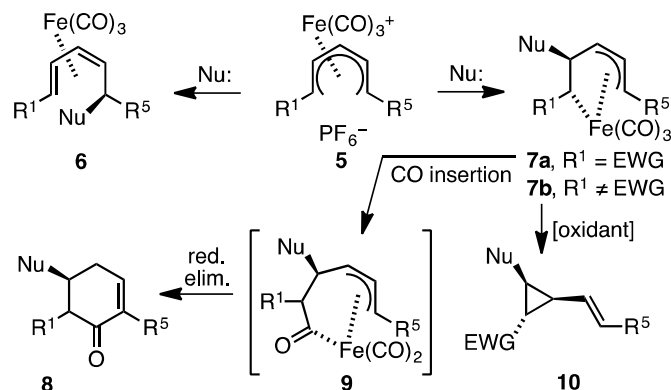
Scheme 1. Nucleophilic attack on acyclic pentadienyl-iron cations **5**.

unique to acyclic (pentadienyl)Fe^{+} cations compared to their cyclic counterparts **1**. Complexes **7a**, in which the R[1] substituent attached to the iron-bonded sp[3] carbon is not an electron-withdrawing group, are not stable and these eventually decompose to cyclohexenone products **8**, via CO insertion followed by reductive elimination and olefin isomerization.[6,7] In contrast, those complexes **7b** which possess an electron-withdrawing R[1] substituent are stable, isolable species which are resistant to CO insertion. Oxidatively induced-reductive elimination of complexes **7b** generate vinylcyclopropane-carboxylates **10**.[8]

We herein report on the reaction of acyclic (pentadienyl)iron cations with phosphonate stabilized carbon nucleophiles, culminating in an application to the synthesis of oxygenated metabolites of carvone.

2. Results and Discussion[9]

Addition of the anion generated from trimethyl phosphonoacetate or diethyl (2-oxopropyl)phosphonate to (1-methoxypentadienyl)iron cation (**11**)[10] proceeded at the C2 carbon to afford the 2-substituted (pentenediyl)iron complexes **13a** or **13b** (Scheme 2, Table 1). In a similar fashion, addition of the anions generated from trimethyl phosphonoacetate or [6-(*t*-butyldiphenylsilyl)oxy]-2-oxohexylphosphonic acid dimethyl ester[11] with cation (**12**)[8k] afforded the (pentenediyl)iron complexes **14a** or **14b**. Complexes **13a**, **13b**, **14a**, **14b** were obtained as inseparable mixtures of diastereomers at the indicated (*) carbon, as determined by ^{1}H NMR spectroscopy. Each exhibited two doublet signals in the range δ 0.01-0.80 ppm which were assigned to the hydrogen attached to the σ-bound carbon (H[1]) of each diastereomer.[8c,i,k] That **13a**, **14a**, and **13b** were diastereomeric at the indicted carbon was further corroborated by their conversion to a single enoate or enone (**15a**, **16a** or **15b**) upon Horner-Emmons olefination with paraformaldehyde.
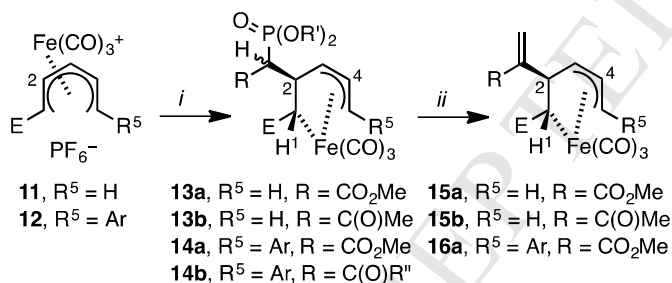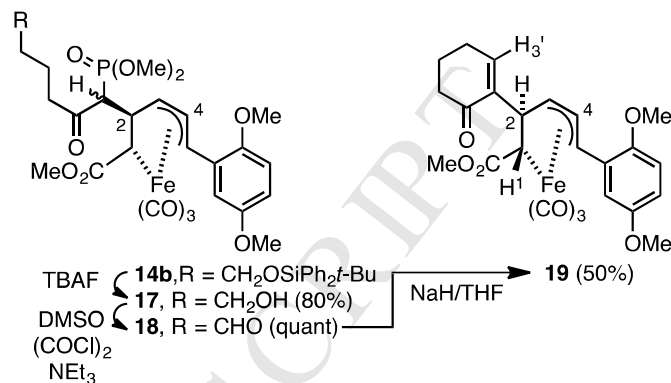

Scheme 2. Addition of phosphonate stabilized nucleophiles to (1-methoxycarbonylpentadienyl)iron(1+) cations, and subsequent HWE olefination. Ar = 2,5-dimethoxyphenyl; R" = $(CH_2)_4OSiPh_2t$-Bu. Reagents: *i*) Na^{+} [−]CH[P(O)(OR')$_2$R]; *ii*) base, paraformaldehyde.

Table 1. Addition of phosphonate stabilized nucleophiles to (1-methoxycarbonylpentadienyl)iron(1+) cations, and subsequent HWE olefination (E = CO_2Me)

R[5]	R	R'	Product (yield)	Base	Product (yield)
H	CO_2Me	Me	**13a** (69%)	NaH	**15a** (84%)
H	C(O)Me	Et	**13b** (66%)	NaH	**15b** (50%)
Ar	CO_2Me	Me	**14a** (85%)	*n*-BuLi	**16a** (90%)
Ar	C(O)R"	Me	**14b** (98%)		

Ar = 2,5-dimethoxyphenyl; R" = $(CH_2)_4OSiPh_2t$-Bu

Deprotection of the silyl ether of alkylated β-ketophosphonate **14b**, gave the alcohol **17** (Scheme 3), which upon Swern oxidation afforded aldehyde **18**; both **17** and **18** were obtained as a mixture of diastereomers. Subsequent intramolecular Horner-Emmons olefination of **18** gave the cyclohexenone **19** as a single diastereomer. Notably, a signal at δ 6.20 ppm in the ^{1}H NMR spectrum corresponds to H3' and signals at δ 198.4, 143.9, and 141.8 ppm in the ^{13}C NMR spectrum correspond to the carbonyl and olefinic carbons of the cyclohexenone fragment.


Scheme 3. Intramolecular Horner-Emmons olefination to generate cyclohexenone (pentenediyl)iron complex **19**.

The regioselectivity for addition of the phosphonate stabilized nucleophiles to cation **11** is similar to the addition of malonate, arylsulfonyl acetates and alkenyl Grignards to this same cation.[8a,c,e,f,i] In contrast, the regioselectivity for addition to **12** is considerably greater than that for addition of alkenyl Grignards to this cation.[8k] Additionally, the functionality introduced onto the (pentenediyl) ligand by the present sequence of nucleophilic addition/Horner-Emmons olefination would not be available within an alkenyl Grignard reagent.

In contrast to the above results, reaction of (pentadienyl)iron cation **20** with sodium trimethyl phosphonylacetate gave a mixture of regioisomeric cyclohexenones **21a/22a**, each of which consisted of a mixture of diastereomers at the indicated (*) carbon (Scheme 4, Table 2). The ratio of **21a**:**22a** was determined by integration of the ^{1}H NMR signals for H3 of **21a** compared to the integration of the H3 signal for **22a**. Olefination of the mixture of **21a/22a** with paraformaldehyde gave a mixture of **23a/24a**; a pure sample of **23a** could be obtained by column chromatography. In a similar fashion, reaction of **20** with sodium diethyl (2-oxopropyl)phosphonate or with sodium diethyl (phenylsulfonyl)-methanephosphonate gave a mixture of **21b/22b** or **21c** respectively; each of which consisted of a mixture of diastereomers. Olefination of the mixture of **21b/22b** with formaldehyde gave a mixture of **23b/24b**, while olefination of **21c** gave the vinylsulfonate **23c**. The structures of **21** and **23** were assigned as 5-substituted-2-methylcyclohexenones on the basis of their NMR spectral data. In particular, the signals for H-3 and the Me-2 appear at ca. δ 6.7-6.6 (m) and 1.75-1.80 (s) ppm respectively in their ^{1}H NMR spectra, while the signals for C1, C2, C3 and Me-2 appear at ca. δ 199, 135, 144, and 15.9 ppm respectively in their ^{13}C NMR spectra.

Formation of cyclohexenone product **21** is rationalized by nucleophilic attack at an internal pentadienyl carbon of **20** to afford the (pentenediyl)iron complex **9** (R[1] = H, R[5] = Me, Scheme 1). Carbonyl insertion followed by reductive elimination and subsequent conjugation of the double bond affords **21**.
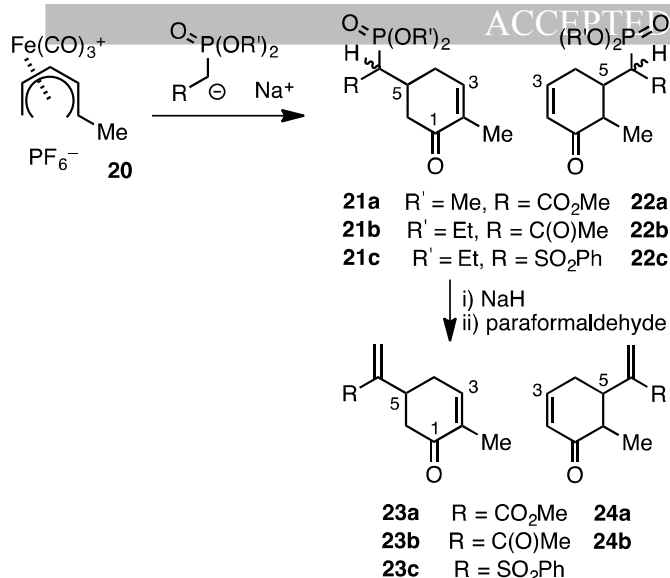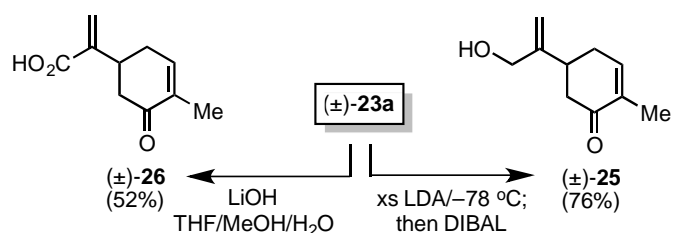
Scheme 4. Addition of phosphonate stabilized nucleophiles to (1-methylpentadienyl)Fe(CO)₃⁺ cation.

Table 2. Addition of phosphonate stabilized nucleophiles to (1-methylpentadienyl)iron(1+) cations, and subsequent HWE olefination[a]

R	OR'	Product (ratio,[a] yield)	Product (ratio,[a] yield)
CO₂Me	OMe	**21a+22a** (10:1, 87%)	**23a+24a** (10:1, 69%)
COMe	OEt	**21b+22b** (6:1, 74%)	**23b+24b** (6:1, 89%)
SO₂Ph	OEt	**21c** (47%)	**23c** (72%)

[a]Ratio of constitutional isomeric products determined by ¹H NMR integration of the β-hydrogen signals.

10-Hydroxycarvone (**25**, Scheme 5) has been isolated from *Hyssopus cuspidatus*, a plant used in Chinese folk medicine for the treatment of fever and broncusus asthma.[12a] This terpene has also been isolated as a minor carvone metabolite from cultured cells of the Madagascar periwinkle, *Catharanthus roseus*,[12b] and as an excreted metabolite of carvone in the urine of rabbits,[13a] and human volunteers,[13b,c] while carvonic acid (**26**) has also been isolated as a human metabolite of carvone.[13b,c] 10-Hydroxycarvone has been prepared from carvone by regioselective chlorination at C10 and subsequent solvolysis of the halide.[14,15] Saponification of **23a** afforded carvonic acid **26**. Attempted reduction of **26** with borane gave a complex mixture of products. Alternatively, α-deprotonation of the cyclohexenone **23a** with LDA, followed by addition of DIBAL gave **25** after workup. The spectral data obtained for **25** and **26** were consistent with their literature values.[13b,14a]

Scheme 5. Synthesis of oxygenated metabolites of carvone.

3. Conclusions

In contrast to the addition of α-phosphoramide acetate anions to (cyclohexadienyl)iron(1+) cations, the addition of phosphonate stabilized carbon nucleophiles to *acyclic* (pentadienyl)iron(1+) cations occurs primarily at an internal dienyl carbon to form (pentenediyl)iron complexes. The fate of the (pentenediyl)iron products depends on the presence or absence of an electron withdrawing ester substiuent at the σ-bound carbon. Horner Wadsworth Emmons olefination of the phosphonate addition products generates (2-alkenyl-3-pentene-1,5-yl)iron complexes or 5-alkenyl-2-methyl-2-cyclohexenones. The latter are suitable precursors for the preparation of 10-hydroxycarvone and carvonic acid.

4. Experimental

4.1. General Data.

All reactions involving moisture or air sensitive reagents were carried out under an nitrogen atomosphere in oven-dried glassware with anhydrous solvents. THF and ether were distilled from sodium/benzophenone. Purifications by chromatography were carried out using flash silica gel (32-63 μ). NMR spectra were recorded on either a Varian Mercury+ 300 MHz or a Varian UnityInova 400 MHz instrument. CDCl₃, CD₃OD, d₆-acetone were purchased from Cambridge Isotope Laboratories. ¹H NMR spectra were calibrated to 7.27 ppm for residual CHCl₃, 3.31 ppm for CD₂HOD, or 2.05 ppm for d₅-acetone. ¹³C NMR spectra were calibrated from the central peak at 77.23 ppm for CDCl₃, 49.15 ppm for CD₃OD, or 29.92 ppm for d₆-acetone. Coupling constants are reported in Hz. Elemental analyses were obtained from Midwest Microlabs, Ltd., Indianapolis, IN, and high-resolution mass spectra were obtained from the University of Nebraska Center for Mass Spectrometry and the COSMIC lab at Old Dominion University.

4.2. Tricarbonyl(5-(methoxycarbonyl)-4-(1-methoxycarbonyldimethylphosphonomethyl)-2-penten-1,5-diyl)iron. (±)-**13a**.

To a stirring suspension of sodium hydride (175 mg, 7.2 mmol) in dry THF (120 mL) at 0 °C under N₂, was added trimethyl phosphonoacetate (885 mg, 4.86 mmol). The reaction mixture was stirred for 30 min, and then a solution/suspension of (±)-**11** (2.00 g, 4.86 mmol) in dry THF (60 mL) was added. The reaction mixture was stirred overnight, and then quenched with water. The mixture was diluted with CH₂Cl₂ and the layers were separated. The aqueous layer was extracted once with CH₂Cl₂ and the combined organic extracts were washed once with saturated aqueous NaCl, and dried (MgSO₄), and concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂, ethyl acetate) to afford the product (±)-**13a** (372 mg, 69%) as a yellow oil; δ_H (400 MHz, CDCl₃) 4.69-4.39 (2H, m, H-3 and H-4), 3.81-3.55 (14H, m, 4 x OCH₃ and H-2 and H-6), 2.67-2.39 (2H, m, H-5exo and H-5endo), 0.33 and 0.01 (1H total, 2 x d, J 8.7 Hz each, H-1). δ_C (partial, 100 MHz, CDCl₃) 210.2, 209.9, 209.7, 209.6, 203.5, 203.3, 179.7, 179.6, 167.3 (d, J_{CP} 5.3 Hz), 166.7 (d, J_{CP} 4.7 Hz), 97.9, 97.4, 62.7, 62.6, 60.8, 60.6, 37.4 (J_{CP} 3.8 Hz), 37.0 (J_{CP} 4.0 Hz), 13.3 (J_{CP} 1.9 Hz), 12.1 (J_{CP} 14.1 Hz). HRMS (FAB): MNa⁺–3CO, found 385.0110. C₁₂H₁₉O₇PFeNa requires 385.0114.

4.3. Tricarbonyl(5-(methoxycarbonyl)-4-(1-diethylphosphono-2-oxopropyl)-2-penten-1,5-diyl)iron. (±)-**13b**.

The reaction of the anion generated from diethyl (2-oxopropyl) phosphonate (240 mg, 1.21 mmol) and sodium hydride in dry THF with cation **11** (500 mg, 1.21 mmol) was carried out in a

fashion similar to the preparation of **13a**. The residue was purified by column chromatography (SiO$_2$, ethyl acetate) to afford (±)-**13b** (365 mg, 66%) as a yellow oil; δ_H (400 MHz, CDCl$_3$) 4.79-4.50 (2H, m, H-3 and H-4), 4.29-4.05 (4H, m, –OC$\underline{H_2}$CH$_3$), 4.01-3.87 and 3.72-3.63 (2H total, H-2 and H-6), 3.76 and 3.74 (3H total, 2 x s, OCH$_3$), 2.98-2.51 (2H, m, H-5exo and H-5endo), 2.37 and 2.18 (3H total, 2 x s, COC$\underline{H_3}$), 1.48-1.31 (6H, m, –OCH$_2$C$\underline{H_3}$), 0.44 and 0.01 (1H total, 2 x d, J 8.4 Hz each, H-1). δ_C (partial, 100 MHz, CDCl$_3$) 210.0 [209.7] ($\underline{C}$OMe), 203.3 [203.2], 201.9 [201.8], 201.21 [201.20] (Fe-CO), 179.6 [179.5] (-$\underline{C}$O$_2$CH$_3$), 97.0 [96.8] (C-4), 64.2, 61.7, 61.5, 54.4, 51.3 [51.2] (-CO$_2$$\underline{C}H_3$), 36.5, 36.1, 32.3, 29.8, 12.5, 11.9 [11.8] (C-1). HRMS (FAB): MNa$^+$, found 397.0476. C$_{14}$H$_{23}$O$_6$PFeNa requires 397.0474.

4.4. Tricarbonyl(5-(methoxycarbonyl)-4-(1-methoxycarbonyldimethylphosphonomethyl)-1-(2,5-dimethoxyphenyl)-2-penten-1,5-diyl)iron. (±)-**14a**

The anion generated from trimethyl phosphonoacetate (0.40 g, 2.2 mmol) and NaH (58 mg, 2.4 mmol) in dry THF (10 mL) at 0 °C was added by cannula to a solution of (±)-**12** (1.1 g, 2.0 mmol) in dry CH$_2$Cl$_2$ (50 mL) at –78 °C. After stirring for 1h at –78 °C, the reaction mixture was slowly warmed to room temperature, and then quenched with saturated aqueous NH$_4$Cl. Workup of the reaction mixture was similar to that for **13a**. The residue was purified by column chromatography (SiO$_2$, gradient ethyl acetate → ethyl acetate-methanol = 4:1) to afford (±)-**14a** as a yellow solid (0.99 g, 85%). An analytically pure mixture of diastereomers (ca. 2:1 ratio) was obtained by recrystallization from CH$_2$Cl$_2$/hexanes; mp 150-151 °C; [Found: C, 47.37; H, 4.92. C$_{23}$H$_{30}$O$_{12}$PFe requires C, 47.20; H, 5.17%]; δ_H (400 MHz, CDCl$_3$) major diastereomer 6.70-6.85 (3H, m, Ar$\underline{H}$), 5.27 (1H, dd, J 7.2, 12.7 Hz, H-4), 4.66 (1H, d, J 12.8 Hz, H-5), 4.32 (1H, t, J 7.2 Hz, H-3), 3.87, 3.72, 3.69, 3.67 (19H total, 4 x s & m, OC$\underline{H_3}$ and H-2), 2.71 (1H, dd, $^3J_{HH}$ 11.3, $^2J_{PH}$ 20.6 Hz, C$\underline{H}$(CO$_2$Me)P(O)(OMe)$_2$), 0.77 (1H, d, J 8.5 Hz, H-1); minor diastereomer: 6.85-6.70 (3H, m, Ar$\underline{H}$), 5.33 (1H, dd, J 7.2, 12.7 Hz, H-4), 4.61 (1H, d, J 12.8 Hz, H-5), 4.52 (1H, t, J 7.2 Hz, H-3), 3.76, 3.74, 3.69, 3.67, 3.64, 3.59 (19H, 6 x s & m, OC$\underline{H_3}$ and H-2), 2.69 (1H, dd, $^3J_{HH}$ 11.3, $^2J_{PH}$ 20.6 Hz, C$\underline{H}$(CO$_2$Me)P(O)(OMe)$_2$), 0.44 (1H, d, J 8.5 Hz, H-1); δ_C (100 MHz, CDCl$_3$) major diastereomer: 210.2, 209.4, 203.7, 179.8, 167.4 (J_{CP} 5.2 Hz), 153.6, 151.3, 128.3, 113.4, 111.5, 109.4, 93.5, 70.2, 55.9, 55.8, 54.7, 54.0, 53.4, 53.3, 52.8, 52.5, 51.4, 37.0 (J_{CP} 7.5 Hz), 12.8 (J_{CP} 8.5 Hz); minor diastereomer: 210.0, 209.4, 203.8, 179.7, 166.8 (J_{CP} 4.9 Hz), 153.6, 151.3, 128.3, 113.4, 111.5, 109.4, 93.0, 56.2, 55.9, 54.8, 54.5, 53.6, 53.5, 52.7, 51.4, 37.5 (J_{CP} 4.2 Hz), 11.6 (J_{CP} 13.9 Hz); δ_P (CDCl$_3$, 162 MHz) 21.4 (major), 21.6 (minor).

4.5. Tricarbonyl[4-(6-t-butyldiphenylsilyloxy-1-(dimethylphosphonyl)-2-oxohexyl]-5-methoxycarbonyl-1-(2,5-dimethoxyphenyl)-2-penten-1,5-diyl]iron. (±)-**14b**

A solution of the anion prepared from [6-(*t*-butyldiphenyl-silyl)oxy]-2-oxohexylphosphonic acid dimethyl ester (0.46 g, 1.0 mmol) and NaH (48 mg, 1.2 mmol) in dry THF (30 mL) at 0 °C, was subsequently cooled to –78 °C and a solution of (±)-**12** (0.82 g, 1.5 mmol) in dry CH$_2$Cl$_2$ (50 mL) was added with stirring. Workup of the reaction mixture was similar to that for **14a**. The residue was purified by column chromatography (SiO$_2$, hexanes-ethyl acetate = 4:1 → 2:1 gradient) to afford an equimolar mixture of diastereomers (±)-**14b** (0.85 g, 98%) as a yellow solid; mp 44-46 °C; [Found: C, 58.37; H, 5.99. C$_{42}$H$_{54}$O$_{12}$PSiFe requires C, 58.27; H, 6.29%]; δ_H (400 MHz, CDCl$_3$) 7.68-7.62 (4H, m, SiP$\underline{h_2}$), 7.43-7.33 (6H, m, SiP$\underline{h_2}$), 6.88-6.79 (3H, m, Ar$\underline{H}$), 5.35 and 5.15 (1H total, 2 x dd, J 7.2, 12.8 Hz each, H-4), 4.70 and 4.64 (1H total, 2 x d, J 12.8 Hz each, H-5), 4.57 and 4.30 (1H total, 2 x t, J 7.2 Hz each, H-3), 3.92, 3.86, 3.79, 3.76, 3.74, 3.73, 3.72, 3.71, 3.67 and 3.65 (17 H total, 10 x s and m, OC$\underline{H_3}$ and C$\underline{H_2}$OSi), 3.00 (0.5H, dd, $^3J_{HH}$ 11.7, $^2J_{PH}$ 22.0 Hz, C$\underline{H}$(COR)P(O)(OMe)$_2$), 2.92 (0.5H, dd, $^3J_{HH}$ 11.8, $^2J_{PH}$ 21.3 Hz, C$\underline{H}$(COR)P(O)(OMe)$_2$), 2.73-2.64 (1H, m), 2.40-2.30 (1H, m), 1.75-1.45 (4H, m), 1.022 and 1.018 (9H, 2 x s, SiC(C$\underline{H_3}$)$_3$), 0.80 and 0.33 (1H total, 2 x d, J 8.4 Hz each, H-1); δ_P (162 MHz, CDCl$_3$) 21.0, 22.0. Due to the presence of two diastereomers, as well as ^{31}P coupling, interpretation of the ^{13}C NMR spectrum was not attempted.

4.6. Tricarbonyl(4-(1-methoxycarbonylethenyl)-5-(methoxycarbonyl)-2-penten-1,5-diyl)iron. (±)-**15a**

To a solution of (±)-**13a** (40 mg, 0.088 mmol) in dry THF (3 mL) at 0 °C was added NaH (2.6 mg). The mixture was stirred for 15 min, and then paraformaldehyde (2.6 mg, 0.11 mmol) was added at 0 °C. The reaction mixture was warmed to room temperature over a 3 h period and then quenched with H$_2$O. The mixture was diluted with CH$_2$Cl$_2$ and the layers were separated. The aqueous layer was extracted once with CH$_2$Cl$_2$ and the combined organic extracts were washed once with saturated aqueous NaCl, and dried (MgSO$_4$), and concentrated under reduced pressure. The residue was purified by column chromatography (SiO$_2$, hexanes–ethyl acetate = 17:3) to afford (±)-**15a** (25 mg, 84%) as a yellow oil which solidified in the refrigerator. δ_H (400 MHz, CDCl$_3$) 6.08 (1H, d, J 1.2 Hz, C=CH$_2$), 5.36 (1H, d, J 1.6 Hz, C=CH$_2$), 4.70 (1H, td, J 7.4, 12.0 Hz, H-4), 4.60 (1H, t, J 7.2 Hz, H-3), 4.11 (1H, br t, J 8.2 Hz, H-2), 3.72 (3H, s, OC$\underline{H_3}$), 3.69 (3H, s, OC$\underline{H_3}$), 3.48 (1H, td, J 1.8, 7.6 Hz, H-5exo), 2.21 (1H, dd, J 2.0, 12.4 Hz, H-5endo), 0.34 (1H, d, J 8.8 Hz, H-1). δ_C (100 MHz, CDCl$_3$) 211.0, 210.4, 204.1, 180.1, 166.3, 142.7, 123.5, 97.8, 62.1, 53.9, 51.7, 51.3, 40.0, 11.0. HRMS (FAB): M$_2$Na$^+$–6CO, found 555.0386. (C$_{11}$H$_{14}$O$_4$Fe)$_2$Na requires 555.0386.

4.7. Tricarbonyl(4-(1-methenyl-2-oxopropyl)-5-(methoxycarbonyl)-2-penten-1,5-diyl)iron. (±)-**15b**

The Horner-Emmons olefination of (±)-**13b** (360 mg, 0.789 mmol) with sodium hydride (1.13 mmol) in dry THF (30 mL), followed by the addition of paraformaldehyde (24 mg, 0.80 mmol) was carried out in a fashion similar to the preparation of **15a**. Purification of the residue by column chromatography (SiO$_2$, hexanes-ethyl acetate = 17:3) gave (±)-**15b** (131 mg, 50%) as a yellow oil. δ_H (400 MHz, CDCl$_3$) 5.91 (1H, d, J 1.8 Hz, C=CH$_Z$), 5.51 (1H, d, J 1.8 Hz, C=CH$_E$), 4.69 (1H, t, J 7.0 Hz, H-3), 4.61 (1H, td, J 7.5, 11.6 Hz, H-4), 4.15 (1H, t, J 9.0 Hz, H-2), 3.72 (3H, s, OC$\underline{H_3}$), 3.45 (1H, d, J 8.4 Hz, H-5exo), 2.25 (3H, s, COC$\underline{H_3}$), 2.18 (1H, d, J 11.2 Hz, H-5endo), 0.36 (1H, d, J 8.8 Hz, H-1); δ_C (100 MHz, CDCl$_3$) 210.8, 210.1, 204.0, 180.4, 142.9, 124.0, 97.8, 62.4, 54.1, 52.0, 51.6, 40.3, 11.5. HRMS (FAB): M$_2$Na$^+$, found 523.0483. (C$_{11}$H$_{14}$O$_3$Fe)$_2$Na requires 523.0477.

4.8. Tricarbonyl(5-(methoxycarbonyl)- 4-(1-methoxycarbonylethenyl)-1-(2,5-dimethoxyphenyl)-2-penten-1,5-diyl)iron (±)-**16a**

To a solution of (±)-**14a** (0.40 g, 0.68 mmol) in dry THF (20 mL) at –78 °C was added a solution of *n*-butyl lithium in hexanes (0.47 mL, 1.6 M, 0.75 mmol). The mixture was stirred for 1 h, and then paraformaldehyde (41 mg, 1.36 mmol) was added. The reaction mixture was warmed to room temperature over a 3 h period and then quenched with saturated aqueous NH$_4$Cl. The mixture was extracted several times with ether and the combined organic extracts were dried (Na$_2$SO$_4$), and concentrated under reduced pressure. The residue was purified by column chromatography (SiO$_2$, hexanes–ethyl acetate = 4:1) to afford

(±)-**16a** (0.30 g, 90%) as a yellow solid. mp 163-166 $^{\circ}$C (dec). [Found: C, 54.37; H, 4.66. $C_{22}H_{22}O_9Fe$ requires C, 54.34; H, 4.56%]; δ_H (400 MHz, CDCl$_3$) 6.87 (1H, d, *J* 2.4 Hz, ArH), 6.86-6.77 (2H, m, ArH), 6.11 (1H, d, *J* 2.0 Hz, C=CH$_Z$), 5.45 (1H, d, *J* 2.0 Hz, C=CH$_E$), 5.41 (1H, dd, *J* 7.2, 12.4 Hz, H-4), 4.52 (1H, t, *J* 7.2 Hz, H-3), 4.42 (1H, d, *J* 12.4 Hz, H-5), 4.23 (1H, br t, *J* 8.4 Hz, H-2), 3.89, 3.76, 3.75 and 3.72 (12H total, 4 x s, OC$\underline{H}_3$), 0.85 (1H, d, *J* 8.8 Hz, H-1); δ_C (100 MHz, CDCl$_3$) 210.3, 209.9, 204.3, 180.4, 166.5, 153.7, 151.4, 142.6, 128.7, 124.3, 113.2, 111.6, 109.4, 93.4, 69.8, 56.1, 56.0, 55.9, 51.9, 51.6, 40.5, 10.6.

*4.9. Tricarbonyl[4-(1-(dimethylphosphonyl)-6-hydroxy-2-oxohexyl]-5-methoxycarbonyl-1-(2,5-dimethoxyphenyl)-2-penten-1,5-diyl]iron. (±)-**17***

To a solution of (±)-**14b** (1.00 g, 1.15 mmol) in dry THF (50 mL) under N$_2$, was added a solution of TBAF in THF (2.3 mL, 1$\underline{M}$, 2.3 mmol). The reaction mixture was stirred at room temperature for 18 h, concentrated under reduced pressure, and the residue purified by column chromatography (SiO$_2$, ethyl acetate → ethyl acetate-methanol = 4:1) to afford an equimolar mixture of diastereomers (±)-**17** as a yellow solid (0.58 g, 80%). mp 45-47 $^{\circ}$C; δ_H (400 MHz, CDCl$_3$) 6.88-6.77 (3H, m, ArH), 5.33 and 5.20 (1H total, 2 x dd, *J* 7.2, 12.8 Hz each, H-4), 4.68 and 4.64 (1H total, 2 x d, *J* 12.8 Hz each, H-5), 4.32 and 4.13 (1H total, t, *J* 7.1 Hz each, H-3), 3.96-3.92 (1H, m), 3.91, 3.90, 3.76, 3.74, 3.73, 3.72, 3.69, 3.68, 3.66 (15H, 9 x s, OCH$_3$), 3.60-3.56 (2H, m), 3.03 (0.5H, dd, $^3J_{HH}$ 11.7, $^2J_{PH}$ 22.0 Hz, C$\underline{H}$(COR)P(O)(OMe)$_2$), 2.92 (0.5H, dd, $^3J_{HH}$ 11.7, $^2J_{PH}$ 21.1 Hz, C$\underline{H}$(COR)P(O)(OMe)$_2$), 2.86-2.56 (1H, m), 2.40-2.30 (1H, m), 2.20 (1H, br s), 1.75-1.45 (4H, m), 0.74 and 0.33 (1H total, 2 x d, *J* 8.4 Hz each, H-1); δ_C (100 MHz, CDCl$_3$) 210.0 [209.9], 209.4 [209.1], 204.1 (d, J_{PC} 4.7), 203.7 [203.5], 203.1 (d, J_{PC} 3.7), 179.9 [179.7], 153.6, 151.2, 128.2, 113.2, 111.5, 109.2 [109.1], 92.7 [92.6], 70.0, 61.9, 60.9, 60.6, 59.7, 56.0, 55.81, 55.77, 55.7, 55.4, 55.2, 53.3, 53.2, 53.1, 52.9, 51.4, 51.3, 45.3, 42.9, 36.9, 36.5, 31.6 [31.5], 19.5 [19.4], 12.4, 11.7 [11.6]; δ_P (162 MHz, CDCl$_3$) 21.9, 21.0. HRMS (ESI): MNa$^+$, found 647.0958. $C_{26}H_{33}O_{12}PFeNa$ requires 647.0957.

*4.10. Aldehyde (±)-**18***

To a solution of oxalyl chloride (0.13 g, 1.0 mmol) in dry CH$_2$Cl$_2$ (10 mL) at –78 $^{\circ}$C under N$_2$ was added dropwise a solution of DMSO (0.14 mL, 2.0 mmol) in dry CH$_2$Cl$_2$ (10 mL). The reaction mixture was stirred for 2 min, and then a solution of (±)-**17** (0.30 g, 0.48 mmol) in dry CH$_2$Cl$_2$ (10 mL) was added dropwise over a period of 5 min. After stirring for 15 min, triethylamine (0.5 g, 5.0 mmol) was added and the reaction mixture was stirred for 5 min. The reaction mixture was warmed to room temperature over a period of 1 h, and quenched with water (50 mL). The mixture was extracted several times with CH$_2$Cl$_2$, and the combined extracts were concentrated under reduced pressure. The residue purified by column chromatography (SiO$_2$, ethyl acetate–methanol = 10:1) to afford an equimolar mixture of diastereomers (±)-**18** (0.30 g, quant.) as a yellow solid. mp 40-42 $^{\circ}$C; δ_H (400 MHz, CDCl$_3$) 9.76 and 9.70 (1H total, 2 x t, *J* 1.0 Hz each, C$\underline{H}$O), 6.90-6.70 (m, 3H, ArH), 5.35 and 5.22 (1H total, 2 x dd, *J* 7.2, 12.8 Hz each, H-4), 4.71 and 4.65 (1H total, 2 x d, *J* 12.8 Hz each, H-5), 4.54 and 4.32 (1H total, 2 x t, *J* 7.2 Hz each, H-3), 3.92, 3.91, 3.80, 3.78, 3.77, 3.75, 3.74, 3.715, 3.71, 3.70, 3.68, 3.67 (16H, 12 x s and m, OCH$_3$ and H-2), 2.99 (0.5H, dd, $^3J_{HH}$ 11.6, $^2J_{PH}$ 22.0 Hz, C$\underline{H}$(COR)P(O)(OMe)$_2$), 2.90 (0.5H, dd, $^3J_{HH}$ 11.6, $^2J_{PH}$ 21.2 Hz, C$\underline{H}$(COR)P(O)(OMe)$_2$), 2.82 (0.5H, t, *J* 7.0 Hz), 2.77 (0.5H, t, *J* 7.2 Hz), 2.52-2.34 (3H, m), 1.95-1.75 (2H, m), 0.77 and 0.32 (1H total, 2 x d, *J* 8.4 Hz, H-1); δ_P (162 MHz, CDCl$_3$) 21.7, 20.8. HRMS (ESI): MNa$^+$, found 645.0811. $C_{26}H_{31}O_{12}PFeNa$ requires

645.0801. Due to the presence of two diastereomers, as well as ^{31}P coupling, interpretation of the ^{13}C NMR spectrum was not attempted.

*4.11. Tricarbonyl(5-(methoxycarbonyl)- 4-(6-oxo-1-cyclohexenyl)-1-(2,5-dimethoxyphenyl)-2-penten-1,5-diyl)iron. (±)-**19***

To a suspension of NaH (8 mg, 0.3 mmol) in dry THF (10 mL) at 0 $^{\circ}$C under N$_2$ was added dropwise a solution of (±)-**18** (0.10 g, 0.16 mmol) in dry THF (10 mL). The reaction mixture was stirred for 5 h, warmed to room temperature, and then heated at reflux for 4 h. After cooling to room temperature, the reaction mixture was quenched with saturated NH$_4$Cl (20 mL) and the resulting mixture was extracted several times with CH$_2$Cl$_2$. The combined extracts were concentrated under reduced pressure, and the residue purified by column chromatography (SiO$_2$, hexanes–ethyl acetate = 1:1) to afford (±)-**19** (40 mg, 50%) as a bright yellow solid. mp 160-162 $^{\circ}$C; δ_H (400 MHz, CDCl$_3$) 6.85-6.75 (3H, m, ArH), 6.49 (1H, br s, H-3'), 5.29 (1H, dd, *J* 7.0, 12.2 Hz, H-4), 4.63 (1H, t, *J* 7.6 Hz, H-3), 4.36 (1H, d, *J* 12.8 Hz, H-5), 4.20 (1H, br t, *J* 8.4 Hz, H-2), 3.90, 3.74, 3.73 (9H, 3 x s, OCH$_3$), 2.36-2.25 (4H, m), 1.89-1.84 (2H, m), 0.86 (1H, d, *J* 8.8 Hz, H-1); δ_C (100 MHz, CDCl$_3$) 210.6, 210.1, 204.4, 198.4, 180.6, 153.7, 151.4, 143.9, 141.8, 129.1, 113.0, 111.6, 109.3, 93.1, 69.4, 58.3, 56.0, 55.9, 51.6, 39.3, 38.9, 25.9, 22.7, 9.7. HRMS (ESI): MNa$^+$, found 519.0712. $C_{24}H_{24}O_8FeNa$ requires 519.0718.

*4.12. Carvonic acid methyl ester (±)-**23a***

To a solution of the anion generated from trimethyl phosphonoacetate (0.533 g, 2.73 mmol) and NaH (262.3 mg, 5.460 mmol) in dry THF (50 mL) at 0 $^{\circ}$C, was added solid cation **20** (1.0 g, 2.7 mmol) in one portion. The reaction mixture warmed to room temperature and stirred for 2 h, during this time a yellow-brown turbidity began to appear. The reaction mixture was diluted CH$_2$Cl$_2$ (50 mL), saturated solution of methanolic NaHCO$_3$ (80 mL) was added, and the mixture stirred overnight. Water (30 mL) was added, and the mixture extracted several times with CH$_2$Cl$_2$. The combined extracts were dried (MgSO$_4$) and concentrated. The residue was purified by flash column chromatography (SiO$_2$, ethyl acetate–hexanes = 50% → 70% gradient) to afford a mixture of diastereomeric cyclohexenones **21a/22a** as a light yellow oil (458 mg, 87%). Due to the complex nature of the ^{1}H and ^{13}C NMR spectra, this mixture was not further characterized. The mixture of diastereomeric phosphonate esters (210 mg, 0.721 mmol) was added to a suspension of sodium hydride (43 mg, 1.1 mmol) in dry THF (20 mL) at 0 ºC. The mixture was stirred at 0 ºC for 30 min. Paraformaldehyde (43.4 mg, 1.48 mmol) was added slowly at a rate such that the temperature remained below 30 ºC, and the mixture was stirred for 1 h. The mixture was diluted with H$_2$O and extracted several times with CH$_2$Cl$_2$. The combined extracts were dried (MgSO$_4$) and concentrated. The residue was purified by flash chromatography (SiO$_2$, ether–hexanes = 0% → 75% gradient) to afford a mixture of (±)-**23a** and (±)-**24a** (10:1 ratio by ^{1}H NMR integration) as a pale oil (136 mg, 97%). Careful column chromatography gave a pure sample of **23a**. v_{max} (CH$_2$Cl$_2$) 3470, 2924, 2853, 1717, 1675 1457, 1375 cm^{-1}; δ_H (400 MHz, CDCl$_3$) 6.76-6.72 (1H, m, H-3), 6.27 (1H, s, C=CH$_2$), 5.58 (1H, s, C=CH$_2$), 3.74 (3H, s, OC$\underline{H}_3$), 3.29-3.20 (1H, m), 2.62 (1H, ddd, *J* 2.4, 4.0, 16.2 Hz, H-6), 2.62-2.53 (1H, m), 2.44 (1H, dd, *J* 12.8, 16.0 Hz, H-6), 2.35-2.25 (1H, m), 1.79 (3H, s, 2-Me); δ_C (100 MHz, CDCl$_3$) 199.2, 167.0, 144.4, 142.4, 135.7, 124.8, 52.2, 43.1, 37.0, 31.9, 15.9. HRMS (ESI): MNa$^+$, found 411.1786. $(C_{11}H_{14}O_3)_2Na$ requires 411.1778.

4.13. Diethyl (1-(4-methyl-3-oxocyclohex-4-en-1-yl)-2-oxopropyl)phosphonate (±)-21b and diethyl (1-(2-methyl-3-oxocyclohex-4-en-1-yl)-2-oxopropyl)phosphonate (±)-22b

To an ice cold stirring suspension of NaH (25 mg, 0.62 mmol) in freshly distilled THF (10 mL) was added dropwise diethyl 2-oxopropylphosphonate (79 mg, 0.41 mmol) in drops. The resultant mixture was stirred at 0 °C for 45 min. The solid cation **20** (150 mg, 0.409 mmol) was added slowly. The reaction mixture was stirred at room temperature for 2 h. The reaction mixture was diluted with CH_2Cl_2 (10 mL) and saturated $NaHCO_3$/MeOH (10 mL). The reaction was stirred for 24 h. The reaction was quenched with water (10 mL). The organic portions were extracted several times with CH_2Cl_2, washed with brine, dried (Na_2SO_4) and concentrated. Purification of the residue by flash column chromatography (SiO_2, ethyl acetate-hexane = 0-60% gradient) afforded an inseparable mixture of regioisomeric cyclohexenones (±)-**21b** and (±)-**22b** (~ 7:1 ratio by ^1H NMR integration) as a colorless oil (89.7 mg, 74%). ^1H NMR (CDCl$_3$, major isomer, 300 MHz) δ 6.75-6.62 (1H, m, H-3), 4.18-4.07 (4H, m, P(O)(OCH$_2$CH$_3$)$_2$), 3.22 and 3.15 (1H total, 2 x dd, J 8.7, 9.3 Hz each, CH(COMe)P(O)(OEt)$_2$), 2.89-2.66 (2H, m), 2.43-2.21 (3H, m), 2.33 and 2.29 (3H total, 2 x s, C(O)Me), 1.75 (3H, s, Me-2), 1.32 (6H total, t, J 7.2 Hz, OCH$_2$CH$_3$); ESI-HRMS m/z 325.1175 (calcd. for $C_{14}H_{23}O_5PNa$ (M+Na) m/z 325.1175). Due to the presence of two diastereomers, as well as ^{31}P coupling, interpretation of the ^{13}C NMR spectrum was not attempted.

4.14. 2-Methyl-5-(1-methylene-2-oxopropyl)-2-cyclohexenone (±)-23b and 6-Methyl-5-(1-methylene-2-oxopropyl)-2-cyclohexenone (±)-24b

The Horner-Wadsworth-Emmons olefination of **21b**/**22b** (74 mg, 0.25 mmol) with paraformaldehyde (14 mg, 0.47 mmol) was carried out in a fashion similar to the preparation of **23a**/**24a**. The residue was purified by flash column chromatography (SiO$_2$, ethyl acetate-hexane: 0-60% gradient) to afford an inseparable mixture of regioisomers (±)-**23b** and (±)-**24b** (~5:1 by ^1H NMR integration) as a pale oil (39 mg, 89%). **23b**: δ$_H$ (300 MHz, CDCl$_3$) 6.75-6.69 (1H, m, H-3), 6.14 (1H, C=CH$_2$), 6.01 (1H, s, C=CH$_2$), 3.42-3.28 (1H, H-5), 2.58-2.42 (2H, m, H-6 & H-6'), 2.41-2.30 (4H, m & s, MeCO & H-4), 2.26-2.12 (1H, m, H-4'), 1.78 (3H, s, Me-2); δ$_C$ (75 MHz, CDCl$_3$) 199.5, 199.3, 150.7, 144.6, 135.6, 125.2, 43.1, 35.4, 32.1, 26.6, 15.9. **24b**: δ$_H$ (300 MHz, CDCl$_3$, partial) 6.93-6.84 (m), 6.20 (s), 6.05-5.98 (m), 6.87 (s), 3.13-2.99 (m), 2.72-2.60 (m). HRMS (ESI): MNa$^+$, found 201.0886. $C_{11}H_{14}O_2Na$ requires 201.0887.

4.15. 2-Methyl-5-(1-phenylsulfonylethenyl)-2-cyclohexenone (±)-23c

To an ice cold stirring suspension of NaH (25 mg, 0.62 mmol) in freshly distilled THF (10 mL) was added dropwise diethyl (phenylsulfonyl)methylphosphonate (116 mg, 0.409 mmol). The resultant mixture was stirred at 0 °C for 45 min. The solid cation **20** (150 mg, 0.409 mmol) was added slowly. The reaction mixture was stirred at room temperature for 2 h. The reaction mixture was diluted with CH_2Cl_2 (10 mL) and saturated $NaHCO_3$/MeOH (10 mL). The reaction was stirred for 24 h. The reaction was quenched with water (10 mL). The organic portions were extracted several times with CH_2Cl_2, washed with brine, dried (Na_2SO_4) and concentrated. Purification of the residue by flash column chromatography (SiO$_2$, ethyl acetate-hexane = 0-80% gradient) afforded **21c** as a pale oil (76 mg, 47%). HRMS (ESI): MNa$^+$, found 423.1002. $C_{18}H_{25}O_6SPNa$ requires 423.1002. This compound was used in the olefination reaction without further characterization. To an ice-cold stirring suspension of NaH (6 mg, 0.2 mmol) in dry THF (3 mL) was added **21c** (50 mg, 0.13 mmol). The mixture was stirred at 0 °C for 30 min, paraformaldehyde (14 mg, 0.47 mmol) was added slowly at such a rate that the temperature remained below 30 °C and the reaction mixture stirred for 1 h at room temperature. The reaction mixture was diluted H_2O (10 mL) and the mixture extracted several times with CH_2Cl_2. The combined extracts were dried (MgSO$_4$) and concentrated. The residue was purified by flash column chromatography (SiO$_2$, ethyl acetate-hexane = 0-45% gradient) to afford (±)-**23c** (25 mg, 72%) as a pale oil. δ$_H$ (300 MHz, CDCl$_3$) 7.85 (2H, d, J 7.7 Hz, ArH), 7.65 (1H, t, J 8.3 Hz, ArH), 7.55 (2H, t, J 7.7 Hz, ArH), 6.66 (1H, d, J 5.8 Hz, H-3), 6.53 (1H, s, C=CH$_2$), 5.89 (1H, s, C=CH$_2$), 3.08-2.95 (1H, m), 2.67-2.55 (1H, m), 2.43-2.23 (3H, s & m), 1.74 (3H, s, Me-2); δ$_C$ (75 MHz, CDCl$_3$) 197.8, 153.1, 143.8, 138.9, 135.8, 134.1, 129.7, 128.3, 124.5, 43.6, 35.6, 33.0, 15.9. HRMS (ESI): MNa$^+$, found 299.0712. $C_{15}H_{16}O_3SNa$ requires 299.0709.

4.16. 10-Hydroxycarvone (±)-25

To a stirring solution of LDA in heptanes (0.91 mL, 2.0 M, 1.8 mmol) in THF (5 mL) at –78 °C was added dropwise a solution of **23a** (91 mg, 0.61 mmol) in THF (1 mL). The reaction mixture was stirred at this temperature for 30 min after which a solution of DIBAL–H in hexanes (2.8 mL, 1.0 M, 2.8 mmol) was slowly added. The reaction mixture was stirred at –78 °C for 3 h, after which the mixture was warmed to room temperature and stirred for 1 h. The reaction was quenched with water, extracted several times with CH_2Cl_2, and the combined extracts were washed with brine and concentrated. The residue was purified by flash column chromatography (SiO$_2$, acetone–hexanes = 0% → 35% gradient) to afford (±)-**25** (56 mg, 76%) as a yellow oil. δ$_H$ (300 MHz, CD$_3$OD) 6.92-6.85 (1H, m, H-3), 5.14 (1H, s, C=CH$_2$), 4.96 (1H, s, C=CH$_2$), 4.08 (2H, s, CH$_2$OH), 2.88-2.76 (1H, m), 2.62-2.35 (4H, m), 1.76 (3H, br s, Me-2); δ$_H$ (75 MHz, CDCl$_3$) 199.7, 150.4, 144.6, 135.8, 110.6, 65.1, 43.5, 38.5, 31.8, 15.9. The NMR spectral data for this product was consistent with the literature values.[14a]

4.17. Carvonic acid (±)-26

To a solution of (±)-**23a** (69 mg, 0.46 mmol) in THF/methanol/H$_2$O (2:2:1, 4 mL) was added in small portions lithium hydroxide (116 mg, 2.77 mmol). The mixture was stirred at room temperature for 1 h and then the mixture was acidified with dilute aqueous HCl and the resulting mixture was extracted several times with ethyl acetate. The combined extracts were washed with brine, dried (NaSO$_4$) and concentrated. The residue was purified by flash chromatography (SiO$_2$, acetone–hexanes = 0% → 50 % gradient) to afford carvonic acid (±)-**26** (43 mg, 52%) as a yellowish oil. δ$_H$ (300 MHz, CDCl$_3$) 6.80-6.72 (1H, m, H-2), 6.44 (1H, s, C=CH$_2$), 5.72 (1H, s, C=CH$_2$), 3.32-3.20 (1H, m, H-5), 2.66 (1H, dd, J 2.8, 11.8 Hz, H-6), 2.62-2.57 (1H, m), 2.48 (1H, dd, J 9.6, 12.3 Hz, H-6'), 2.40-2.29 (1H, m), 1.80 (3H, s, Me-2); δ$_C$ (CDCl$_3$, 75 MHz) 199.2, 144.4, 141.8, 135.8, 127.2, 43.1, 36.8, 31.8, 15.9, signal for COOH not observed. The NMR spectral data for this product was consistent with the literature values.[13b]

Acknowledgments

References and notes

1. (a) Harrington, P. J. *Transition Metals in Total Synthesis*, John Wiley & Sons: New York, 1990. (b) Pearson, A. J. *Science* **1984**, *223*, 895-901; Birch, A. J.; Kelly, L. F.; Weerasuria, D. V. *J. Org. Chem.* **1988**, *53*, 278-281; (c) Roe, C.; Stephenson, G. R. *Org. Lett.* **2008**, *10*, 189-192; Bauer, I.; Knolker, H. J. In *Chemistry of Organoiron Compounds*; Marek, I.; Rappoport, Z., Ed.; John Wiley & Sons Ltd: Chichester, UK, 2014; pp 155–232;

2. (a) Birch, A. J.; Kelly, L. F.; Thompson, D. J. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1006-1012. (b) Pearson, A. J.; Kole, S. L.; Ray, T. *J. Am. Chem. Soc.* **1984**, *106*, 6060-6074. (c) Paquette, L. A.; Daniels, R. G.; Gleiter, R. *Organometallics* **1984**, *3*, 560-567. (d) Pearson, A. J.; Burello, M. P. *Organometallics* **1992**, *11*, 448-456. (e) Millot, N.; Guillou, C.; Thal, C. *Tetrahedron* **1997**, *53*, 12553-12564. (f) Knoelker, H.-J.; Baum, E.; Heininger, M. *Tetrahedron Lett.* **1997**, *38*, 8021-8024. (g) Ong, C. W.; Wang, J. N.; Chien, T.-L. *Organometallics* **1998**, *17*, 1442-1445. (h) Anson, C. E.; Hudson, R. D. A.; Osborne, S. A.; Smyth, D. G.; Stephenson, G. R. *Tetrahedron Lett.* **1998**, *39*, 7603-7606. (i) Chou, S.-S. P.; Liu, S.-H. *J. Organomet. Chem.* **1998**, *555*, 227-236. (j) Graden, H.; Hallberg, J.; Kann, N.; Olsson, T. *J. Comb. Chem.* **2004**, *6*, 783-788. (k) Pearson, A. J.; Richards, I. C.; Gardner, D. V. *J. Org. Chem.* **1984**, *49*, 3887-3891. (l) Pearson, A. J.; Kole, S. L.; Yoon, J. *Organometallics* **1986**, *5*, 2075-2081. (m) Mincione, E.; Bovicelli, P.; Cerrini, S.; Lambda, D. *Heterocycles* **1985**, *23*, 1607-1610. (n) Birch, A. J.; Chamberlain, K. B.; Thompson, D. J. *J. Chem. Soc., Perkin Trans. 1* **1973**, 1900-1903. (o) Birch, A. J.; Bogsanyi, D.; Kelly, L. F. *J. Organomet. Chem.* **1981**, *214*, C39-C42. (p) Yeh, M. C. P.; Tsao, W. C.; Wang, Y. J.; Pai, H. F. *Organometallics* **2007**, *26*, 4271-4277. (q) Stephenson, G. R.; Finch, H.; Owen, D. A.; Swanson, S. *Tetrahedron* **1993**, *49*, 5649-5662. (r) Sandoe, E. J.; Stephenson, G. R.; Swanson, S. *Tetrahedron Lett.* **1996**, *37*, 6283-6286. (s) Pearson, A. J.; Roden, B. A. *J. Chem. Soc., Perkin Trans. 1* **1990**, 723-725. (t) Stephenson, G. R.; Voyle, M.; Williams, S. *Tetrahedron Lett.* **1990**, *31*, 3979-3982.

3. Stephenson, G. R.; Milne, K. *Aust. J. Chem.* **1994**, *47*, 1605-1612. Paoltai, I. M.; Stephenson, G. R.; Kane-Maguire, L. A. P. *J. Organometal. Chem.* **1987**, *319*, C5-C10.

4. For an intramolecular addition of phosphonate-stabilized nucleophiles on cationic Ru-arenes see: Pigge, F. C.; Coniglio, J. J.; Dalvi, R. *J. Am. Chem. Soc.* **2006**, *128*, 3498-3499. For intermolecular substitution of haloarene-iron cations see: Artamkina, G. A.; Pazonov, P. K.; Beletskaya, I. P. *Tetrahedron Lett.* **2001**, *42*, 4385-4387.

5. For reviews see: (a) Gree, R. *Synthesis* **1989**, 341-355. (b) Gree, R.; Lellouche, J. P. In *Advances in Metal-Organic Chemistry*, Liebeskind, L. S., Ed.; JAI Press Inc.: Greenwich, CT, 1995; Vol. 4, pp 129-273. (c) Iwata, C.; Takemonto, Y. *Chem. Commun.* **1996**, 2497-2504. (d) Donaldson, W. A. *Aldrichimica Acta* **1997**, *30*, 17-24. (e) Cox, L. R.; Ley, S. V. *Chem. Soc., Rev.* **1998**, *27*, 301-314. (f) Donaldson, W. A. *Curr. Org. Chem.* **2000**, *4*, 837-868. (c) Donaldson, W. A.; Chaudhury, S. *Eur. J. Org. Chem.* **2009**, 3831-3843. (d) Knoelker, H.-J. In *Organometallics in Synthesis, Third Manual*, Schlosser, M. Ed.; John Wiley & Sons: New Jersey, 2013; pp 545-776.

6. (a) McDaniel, K. F.; Kracker, L. R., II *Tetrahedron Lett.* **1990**, *31*, 2373-2376. (b) Donaldson, W. A.; Shang, L.; Tao, C.; Yun, Y. K.; Ramaswamy, M.; Young, V. G., Jr. *J. Organomet. Chem.* **1997**, *539*, 87-98. (c) Chaudhury, S.; Donaldson, W. A. *J. Am. Chem. Soc.* **2006**, *128*, 5984-5985. (d) Chaudhury, S.; Li, S.; Bennett, D. W.; Siddiquee, T.; Haworth, D. T.; Donaldson, W. A. *Organometallics* **2007**, *26*, 5295-5303. (e) Manful, C. F.; Donaldson, W. A. *Eur. J. Org. Chem.* **2014**, 6787-6795.

7. For other organoiron routes to cyclohexenones see: (a) Aumann, R. *J. Am. Chem. Soc.* **1974**, *96*, 2361-2362. (b) Schulze, M. M.; Gockel, U. *J. Organomet. Chem.* **1996**, *525*, 155-158. (c) Taber, D. F.; Kanai, K.; Jiang, Q.; Bui, G. *J. Am. Chem. Soc.* **2000**, *122*, 6807-6808. (d) Taber, D. F.; Bui, G.; Chen, B. *J. Org. Chem.* **2001**, *66*, 3423-3426. (e) Taber, D. F.; Joshi, P. V.; Kanai, K. *J. Org. Chem.* **2004**, *69*, 2268-2271. (f) Taber, D. F.; Sheth, R. B. *J. Org. Chem.* **2008**, *73*, 8030-8032.

8. (a) Yun, Y.K.; W. A. Donaldson, W. A. *J. Am. Chem. Soc.*, **1997**, *119*, 4084-5. (b) Godula, K.; Donaldson, W. A. *Tetrahedron Lett.* **2001**, *42*, 153-154. (c) Yun, Y. K.; Godula, K.; Cao, Y.; Donaldson, W. A. *J. Org. Chem.* **2003**, *68*, 901-910. (d) Lukesh, J. M.; Donaldson, W. A. *Chem. Comm.* **2005**, 110-112. (e) Wallock, N. J.; Donaldson, W. A. *Org. Lett.* **2005**, *7*, 2047-2049. (f) Wallock, N. J.; Bennett, D. W.; Siddiquee, T. A.; Haworth, D. T. Donaldson, W. A. *Synthesis,* **2006**, 3639-3646. (g) Pandey, R. K.; Lindeman S.; Donaldson, W. A. *Eur. J. Org. Chem.* **2007**, 3829-3831. (h) Siddiquee, T. A.; Lukesh, J. M.; S. Lindeman, S.; Donaldson, W. A. *J. Org. Chem.*, **2007**, *72*, 9802-9803. (i) Pandey, R. K.; Wang, L.; Wallock, N. J.; Lindeman, S.; Donaldson, W. A. *J. Org. Chem.* **2008**, *73*, 7236-7245. (j) Gone, J. R.; Wallock, N. J.; Lindeman, S.; Donaldson, W. A. *Tetrahedron Lett.* **2009**, *50*, 1023-1025. (k) Lee, D. W.; Pandey, R. K.; Lindeman, S.; Donaldson, W. A. *Org. Biomol. Chem.* **2011**, *9*, 7742-7747.

9. All compounds are racemic mixtures of enantiomers. Only one enantiomer has been pictured for clarity.

10. Tao, C.; Donaldson, W. A. *J. Org. Chem.* **1993**, *58*, 2134-2143.

11. Toshima, H.; Aramaki, H.; Ichihara, A. *Tetrahedron Lett.* **1999**, *40*, 3587-3590.

12. (a) Furukawa, M.; Makino, M.; Ohkoshi, E.; Uchiyama, T.; Fujimoto, Y. *Phytochem.* **2011**, *72*, 2244-2252. (b) Hamada, H.; Yasumune, H.; Fuchikami, Y.; Hirata, T.; Sattler, I.; Williams, H. J.; Scott, A. I. *Phytochem.* **1997**, *44*, 615-621.

13. (a) Ishida, T.; Toyota, M.; Asakawa, Y.; *Xenobiotica* **1989**, *19*, 843-855. (b) Engel, W. *J. Agri. Food Chem.* **2001**, *49*, 4069-4075. (c) Engel, W. *J. Agri. Food Chem.* **2002**, *50*, 1686.

14. (a) Xuan, M.; Paterson, I.; Dalby, S. M. *Org. Lett.* **2012**, *14*, 5492-5495. (b) Weinges, K.; Schwarz, G. *Liebigs Ann. Chem.* **1993**, 811-814.

15. Parenthetically, (±)-carvone has been prepared from *racemic* tricarbonyl(2-methoxy-1-methylcyclohexadiene)iron in 3 steps, 14% overall yield: G. R. Stephenson, *J. Chem. Soc., Perkin Trans. 1* **1982**, 2449-2456.

Supplementary Material

The supplementary data associated with this article include ^{1}H and ^{13}C NMR spectra of compounds **13a**, **13b**, **14a**, **14b**, **15a**, **15b**, **16a**, **17**, **18**, **19**, **23a**, **21b/22b**, **23b/24b**, **23c**, **25**, and **26**, and can be found in the online version at