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Reactivity of (Bicyclo[5.1.0]octadienyl)iron(1+) Cations: Application to the Synthesis of cis-2-(2'-Carboxycyclopropyl)glycines

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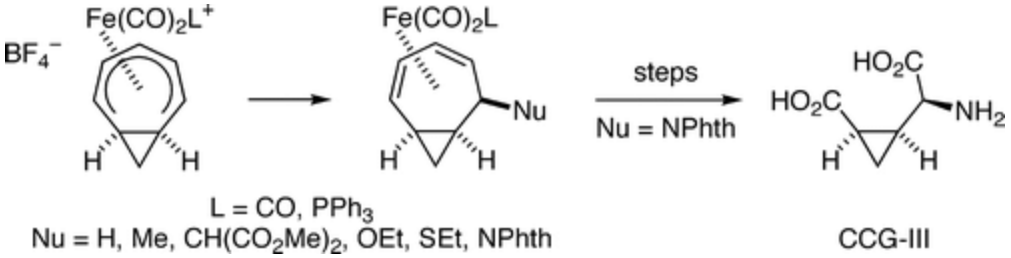
Abstract



The addition of carbon and heteroatom nucleophiles to (bicyclo[5.1.0]octadienyl)$Fe(CO)_2L^+$ cations **5** or **8** (L = CO, PPh_3) generally proceeds via attack at the dienyl terminus on the face of the ligand opposite to iron to generate 6-substituted (bicyclo[5.1.0]octa-2,4-diene)iron complexes (**11** or **13**). In certain cases, these products are unstable with respect to elimination of a proton and the nucleophilic substituent to afford (cyclooctatetraene)$Fe(CO)_2L$ (**4** or **7**). Decomplexation of **13f**, arising from addition of phthalimide to **8**, gave *N*-(bicyclo[5.1.0]octa-3,5-dien-2-yl)phthalimide (**19**). Oxidative cleavage of **19** ($RuCl_3/NaIO_4$) followed by esterification gave the cyclopropane diester **22**, which upon hydrolysis gave *cis*-2-(2`-carboxycyclopropyl)glycine (CCG-III, **18**) **(**eight steps from **4**, 43% overall yield). This methodology was also utilized for preparation of stereospecifically deuterated CCG-III (***d*-18**) and optically enriched (−)-**18**. Deprotonation of **22** resulted in cyclopropane ring opening to afford the benzoindolizidine (**23**).

Introduction

The 1,2-disubstituted cyclopropane ring appears as a key structural feature in a number of naturally occurring compounds [e.g., curacin A (**1**),[1] constanolactones (**2**),[2] and FR-900848 (**3**),[3] Chart 1). Of the number of routes to access this functionality,[4] the selective rearrangement of homoallyl cations to cyclopropylcarbinyl cations[5] has become of renewed interest.[6,7] This transformation is made possible by the presence of two alkyl groups (eq 1)[6] or an allylsilane substituent (eq 2)[7] in order to stabilize the cyclopropylcarbinyl cation. These reactions take place with inversion of configuration at the carbon that undergoes ionization. The lowest energy transition state is that in which the substituents are on opposite sides of the forming cyclopropane ring, thus giving rise to a *trans*-1,2-disubstituted cyclopropane.

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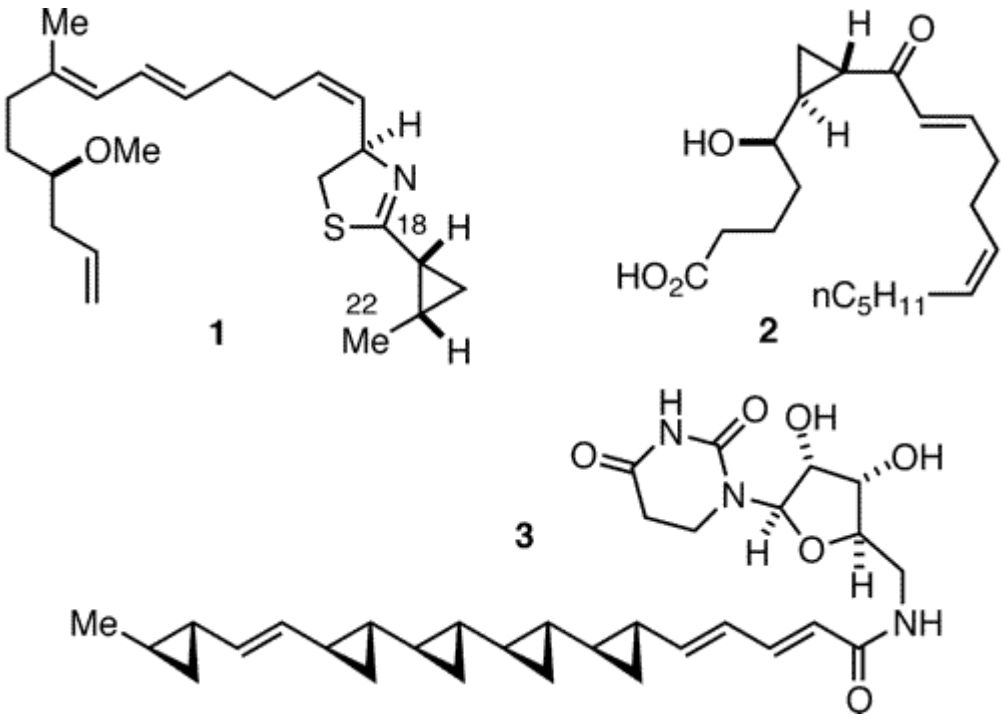
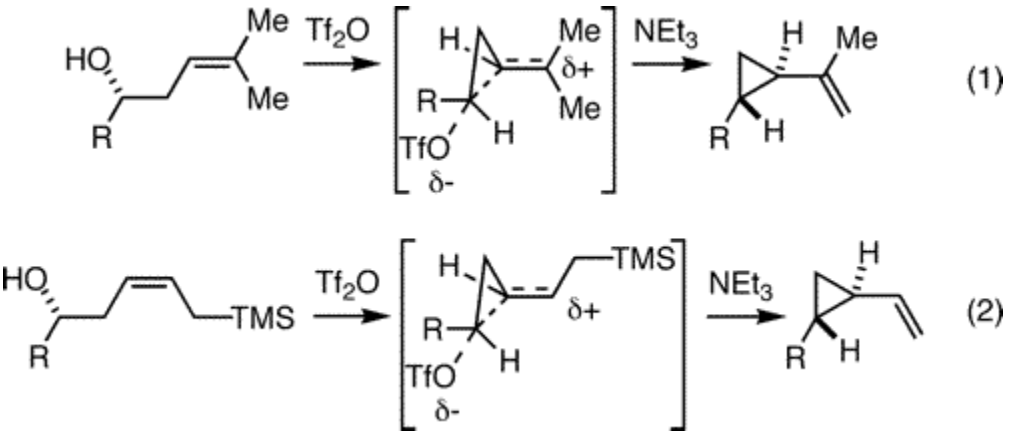


Chart 1



Protonation of (cyclooctatetraene)$Fe(CO)_3$ (**4**) by noncoordinating acids is known to afford the bicyclic cation **5** possessing a *cis*-disubstituted cyclopropane ring (Scheme 1).[8] Davison et al. originally proposed *exo*-protonation of **4** to give the intermediate η^5-octatrienyl complex **6**; homoallyl-to-cyclopropylcarbinyl rearrangement gives the bicyclic cation **5**.[8a] Low-temperature NMR spectroscopic monitoring of this reaction provided evidence for the homoallylic cation **6**.[8b] Notably, treatment of **5** with base (e.g., KOH)

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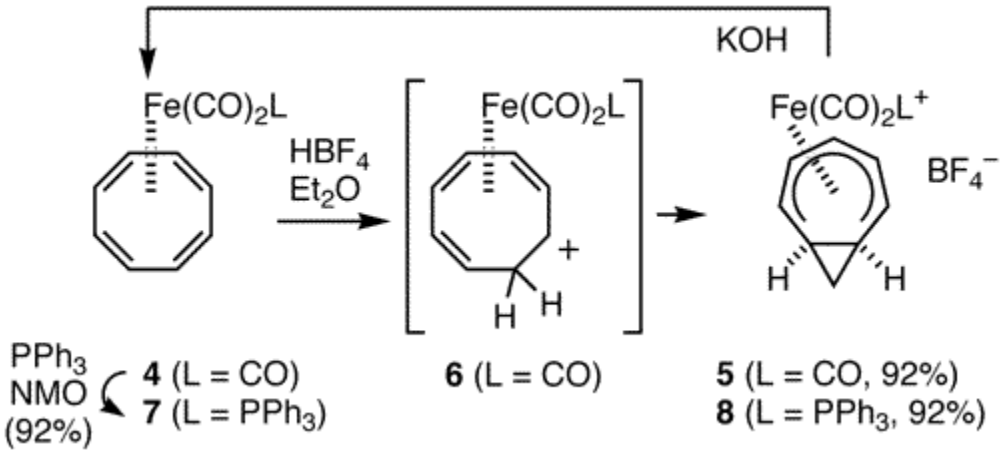
regenerates the neutral complex **4**. In comparison to the extensive examination of (cyclohexadienyl)- and (cycloheptadienyl)iron(1+) cations,[9,10] the reactivity of bicyclic cation **5** with nucleophilies has been considerably less studied.[11] As part of our interest in the preparation of cyclopropanes by organoiron methodology,[12] we here report on the reactivity of (bicyclo[5.1.0]octadienyl)iron(1+) cations and application of these reactions to organic synthesis.



Scheme 1

Results and Discussion

Preparation, Characterization, and Reactivity of Bicyclic Cations.

Protonation of **4**, according to the literature procedure,[8] gave the tricarbonyl ligated iron cation **5** in excellent isolated yield (Scheme 1). It is well-known that replacement of CO by a phosphine ligand can affect the regioselectivity of nucleophilic addition to dienyl iron complexes.[13] To this end, **4** readily underwent ligand substitution with triphenylphosphine in the presence of trimethylamine *N*-oxide to give **7** in excellent yield (Scheme 1). Like the parent complex **4**,[14] the phosphine-ligated complex **7** is fluxional at 20 °C. The ^{1}H NMR spectrum of **7** exhibits a single peak (8H) at δ 4.95 for the cyclooctatetraene protons due to relatively fast "ring-whizzing" of the $Fe(CO)_2PPh_3$ moiety about the polyene ligand.

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Protonation of **7** with HBF_4 gave the bicyclic cation **8** (Scheme 1). The ^1H NMR spectrum of **8** in CD_3OD at 30 °C exhibited only five of the six expected signals for the bicyclo[5.1.0]octadienyl ligand (see Figure 1 in the Supporting Information). The geminal protons of the cyclopropane ring were observed at δ 1.1−1.2 (1H) and 1.2−1.3 (1H), as well as two broad multiplets at δ 2.3−2.5 (2H) and 5.0−5.3 (2H) and a one downfield signal (δ 7.7, br t). Upon lowering the temperature, the two multiplets at δ 2.3−2.5 and 5.0−5.3 (2H each) separated to give four signals (δ 2.2−2.3, 2.3−2.5, 4.9−5.1, and 5.4−5.6; 1H each). Additionally, two multiplets arose from the baseline at δ 3.6−3.8 and 5.3−5.4 (1H each); these latter signals were not observed in the 30 °C spectrum. Due to the chemical shift difference of the latter two signals (Δδ = ca. 1.8), coalescence of these signals at 30 °C occurs with severe broadening such that the coalesced signal resides in the baseline of the spectrum at ambient temperature.

This fluxional behavior is characteristic of a tetragonal pyramidal iron complex, in which the phosphine ligand is rapidly exchanging between basal sites (**8B** and **8B'**, Scheme 2). At 30 °C, the "windshield-wiper" motion of the $Ph_3P(CO)_2Fe$ moiety is sufficiently fast that only time-averaged signals appear for the pairs H_1/ H_1', H_2/H_2', and H_3/H_3'. As the temperature is lowered, rotation about the Fe-dienyl ligand slows, and the phosphine occupies one of two equivalent basal sites. With the loss of symmetry, protons H_1, H_2, and H_3 become nonequivalent with H_1', H_2', and H_3', respectively. No additional resonances were observed in the ^1H NMR spectrum that might correspond to an apical isomer conformation (**8A**). This was further corroborated by a variable-temperature ^{31}P NMR study. In this case, only a single resonance (δ 58) was observed in the temperature range +16 to −100 °C. Exchange of the phosphine ligand between equivalent basal sites gives rise to a single ^{31}P NMR resonance signal; if basal−apical exchange of the phosphine ligand had occurred, an additional ^{31}P NMR resonance would be expected at low temperature due to the apical phosphine rotomer. The cyclopropane methine protons (H_1 and H_1') coalesce at 0 °C, corresponding to k_c = 119 s^{-1} and $\Delta G_c^{\ddagger}$ = 13.3 kcal mol^{-1}. This activation energy is comparable with that found for apical−basal phosphite exchange in (hexadienyl)$Fe(CO)_2(EPTB)^+$ (**9**) and (heptadienyl)$Fe(CO)_2(EPTB)^+$ (**10**) (9.8 and 11.4 kcal mol^{-1}, respectively).[15]

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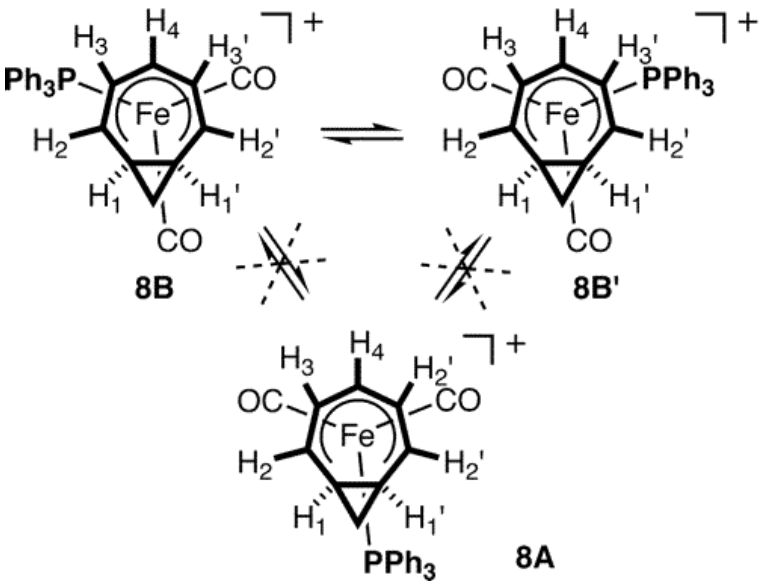

Scheme 2

Aumann has previously reported[11c,d] that the reaction of cation **5** with BH_4^- gave a mixture of bicyclo[5.1.0]octadiene complex **11a** and the σ-alkyl-π-allyl complex **12** (eq 3, Table 1). Similarly, the reaction of **5** with a variety of carbon and heteroatom nucleophiles gave predominantly the corresponding 6-substituted bicyclo[5.1.0]octa-2,4-diene complexes **11b**–**f**, along with varying amounts of $(COT)Fe(CO)_3$ (**4**). This latter product arises either from direct deprotonation of the cation **5** or from nucleophilic attack followed by elimination.[16] Notably, diene complexes **11d**–**f** are relatively unstable in solution and/or to exposure to typical chromatographic adsorbents (Al_2O_3, SiO_2) with respect to elimination. Judicious solvent selection is critical to obtaining a good yield of the addition product. Complexes **11b**–**f** were assigned as bicyclo[5.1.0]octa-2,4-diene structures by comparison of their ^1H NMR spectral data with that of the known[11c] compound **11a**. In particular, the ^1H NMR spectra for complexes **11** exhibit four high field resonances corresponding to the cyclopropane hydrogens, while the ^{13}C NMR spectra contain two signals at ca. δ 86–92 corresponding to the internal diene carbons.

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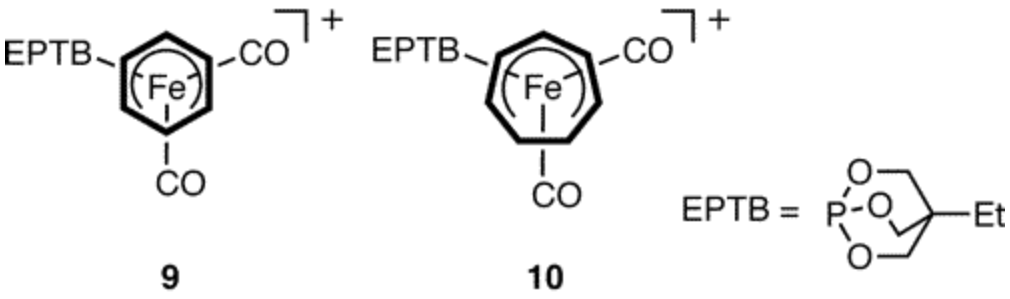
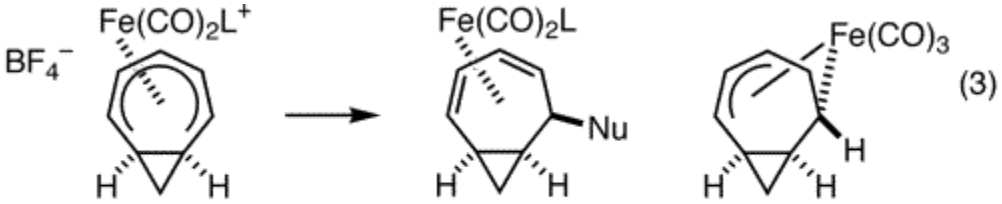


9 **10**

Table 1. Nucleophilic Addition to (Bicyclo[5.1.0]octadienyl)$Fe(CO)_2L^+$



5 (L = CO)
8 (L = PPh_3)

11 (L = CO)
13 (L = PPh_3)

12

cation	nucleophile	products (isolated yields, %)
5	$NaBH_4/Et_2O$/ice water	**11a/12** (5:1), Nu = H (90)[a]
5	MeLi/CuBr/SMe_2/Et_2O	**11b**, Nu = Me (62)
5	$LiCH(CO_2Me)_2/Et_2O$	**11c**, Nu = CHE_2 (62)
5	EtOH/NaOAc	**11d**, Nu = OEt (65)
5	EtSH/NaOAc/Et_2O	**11e**, Nu = SEt (85)
5	KNPhth/acetone	**11f**, Nu = NPhth (41), **4** (12)
8	$NaBH_3CN$/moist Et_2O	**13a**, Nu = H (50)
8	$LICH(CO_2Me)_2/Et_2O$	**13c**, Nu = CHE_2 (61)
8	H_2NCH/Me)Ph	**7** (80)
8	EtOH/MaOAc	**7** (86)
8	EtSH/NaOAc/Et_2O	**13e**, Nu = SEt (95)
8	KNPhth/ether	**13f**, Nu = NPhth (>99)

[a] Reference 11c,d.

In comparison, reaction of phosphine-ligated cation **8** with ethanol or α-methylbenzylamine gave only $(COT)Fe(CO)_2PPh_3$ (**7**), while reaction with hydride, malonate anion, thiolate anion, and phthalimide anion gave predominantly the diene complexes **13a**,**c**,**e**,**f** in good to excellent yields (eq 3, Table 1). In comparison to the tricarbonyl-ligated complexes **11**, the phosphine ligated complexes **13a**,**c**,**e**,**f** are isolated as air-stable solids. Complexes **13** were

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assigned as bicyclo[5.1.0]octa-2,4-diene structures on the basis of their NMR spectral data. In particular, the ^{1}H NMR spectra for complexes **13** exhibit four high-field resonances corresponding to the cyclopropane hydrogens, while the ^{13}C NMR spectra contain three upfield signals at ca. δ 16−21, two signals at ca. δ 60−67, and two signals at ca. δ 87−90 corresponding to the cyclopropane, terminal diene, and internal diene carbons, respectively. For both cations **5** and **8**, nucleophilic addition occurs in a stereoselective fashion; only one diastereomer is obtained. Attack on the face of the dienyl ligand opposite to the metal was tentatively assigned by analogy to the direction of attack on (cycloheptadienyl)Fe(CO)$_3^+$ cations.[10a] This tentative assignment was eventually corroborated for complex **13f** (vide infra).

In contrast, reaction of **8** with MeLi/CuBr gave an inseparable mixture of diene complex **13b** and (η^4-7-ethylcyclohepta-1,3,5-triene)Fe(CO)$_3$ **14b** (2:7 ratio, Scheme 3); the latter product results from nucleophilic attack at the cyclopropane ring. The structure of **14b** was assigned on the basis of its NMR spectral data. In particular, a triplet in the ^{1}H NMR spectrum at δ 0.78 (3H) was assigned to the CH_3 of the ethyl group, while signals at δ 128.5 and 130.0 in the ^{13}C NMR spectrum were assigned to the uncomplexed olefinic carbons. While the mixture of **13b** and **14b** was inseparable by chromatography, a chemical separation was affected by treatment of the mixture with a stoichiometric amount of OsO_4 to give a separable mixture of **13b** and the (cyclohepta-3,5-dienone)iron complex **15** (Scheme 3). On the basis of the initial ratio of **13b** and **14b**, the recovery of **13b** was ca. 66%, while the yield of converted **15** was ca. 49%. The structural assignment of **15** was based on its spectral data. In particular, an IR absorption at 1708 cm^{-1} along with a signal at δ 207.7 provided evidence for the ketone functionality, while the triplet in the ^{1}H NMR spectrum at δ 0.75 (3H) was assigned to the CH_3 of the ethyl group. (Cyclohepta-3,5-dienone)iron complex **15** presumably arises via dihydroxylation of the uncomplexed olefin of **14b** on the face opposite to iron to give **16**,[17] followed by a pinacol rearrangement (Scheme 3). Selective ionization of the hydroxyl adjacent to the complexed diene of **16** occurs since the resultant carbocation **17** is stabilized by electron donation from iron.

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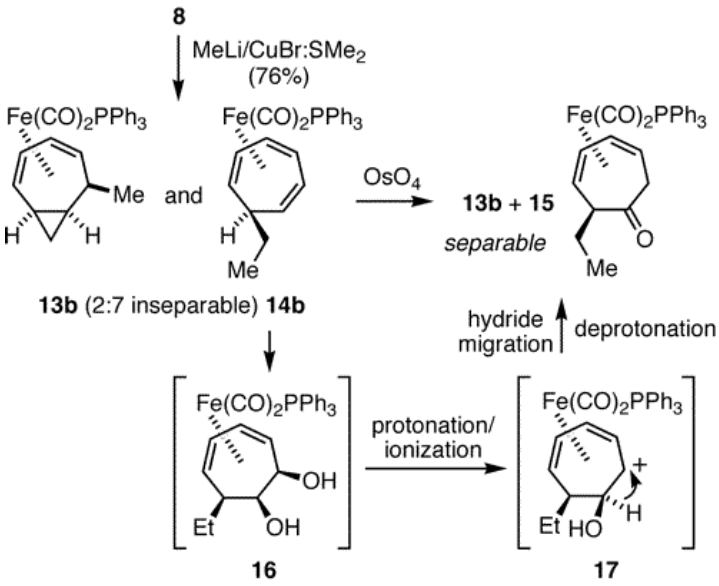

Scheme 3

Synthesis of (±)-cis-2-(2'-Carboxycyclopropyl)glycine.[18]

L-Glutamic acid (Chart 2) is the major excitatory neurotransmitter for a wide variety of receptors in mammalian systems.[19] The selective activation of different glutamate receptors may depend on recognition of a particular conformer of this flexible molecule. In particular, the folded conformation, as exemplified by *cis*-2-(2'-carboxycyclopropyl)glycine (CCG-III, **18**) and *trans*-pyrrolidine-2,4-dicarboxylate (TPDC), is believed to be a common feature for inhibitors of glutamate transport.[20] Stereoselective routes to **18** have been previously reported.[21]

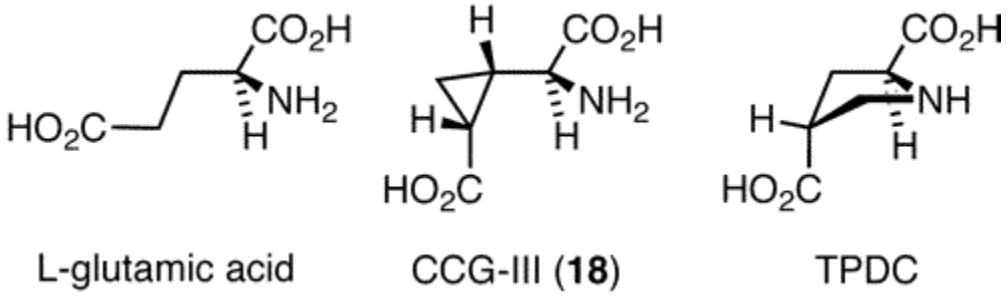

Chart 2

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Complex *rac*-**13f** readily underwent oxidative decomplexation with ceric ammonium nitrate (CAN) to liberate the ligand *rac*-**19** (Scheme 4). The tentative structural assignment for *rac*-**19** was based on its NMR spectral data. In particular, the ^{1}H NMR spectrum of **19** contains four upfield signals which are coupled to each other (δ 0.99, 1.28, 1.90, 2.25) which correspond to the cyclopropane hydrogens, while the ^{13}C NMR spectrum exhibits seven downfield signals corresponding to the four olefinic and three aryl carbons. This tentative assignment was eventually corroborated by single-crystal X-ray diffraction analysis, which demonstrated that the phthalimide substituent is *endo* with respect to the bicyclic ring system.[22] Initial attempts at oxidative cleavage of the diene of **19** proved frustratingly difficult. Ozonolysis of **19** gave uncharacterizable mixtures, regardless of the nature of the workup (oxidative or reductive) of the intermediate ozonide. Similarly, osmylation under Lemieux−Johnson conditions[23] (OsO_4−IO_4^-) also failed to give the expected dialdehyde. Cleavage of the cycloheptadiene ring was eventually accomplished by exhaustive hydroxylation of **19** with catalytic OsO_4/NMO to give a mixture of partially separable diastereomeric tetrols **20a** and **20b** (2:1 ratio by ^{1}H NMR integration). Glycol cleavage of the mixture of tetrols **20a**/**b** in aqueous THF gave a dialdehyde which was unstable to chromatography on silica. Oxidation of the crude dialdehyde with Jones reagent cleanly gave the diacid **21**. Since purification of **21** by column chromatography proved difficult, direct esterification gave the diester **22**. Alternatively, Sharpless oxidation[24] ($RuCl_3$/IO_4^-) of **19** gave the diacid **21**, which was subsequently protected by esterification to give **22** in excellent overall yield. Acidic hydrolysis of **22**, followed by treatment of the hydrochloride salt with propylene oxide, gave *rac*-CCG-III (*rac*-**18**, Scheme 5). The ^{1}H and ^{13}C NMR spectral data of *rac*-**18** were consistent with published spectral data.[21c] In summary, *rac*-CCG-III was prepared from **4** in eight steps (via the $RuCl_3$/IO_4^- route) in 43% overall yield.

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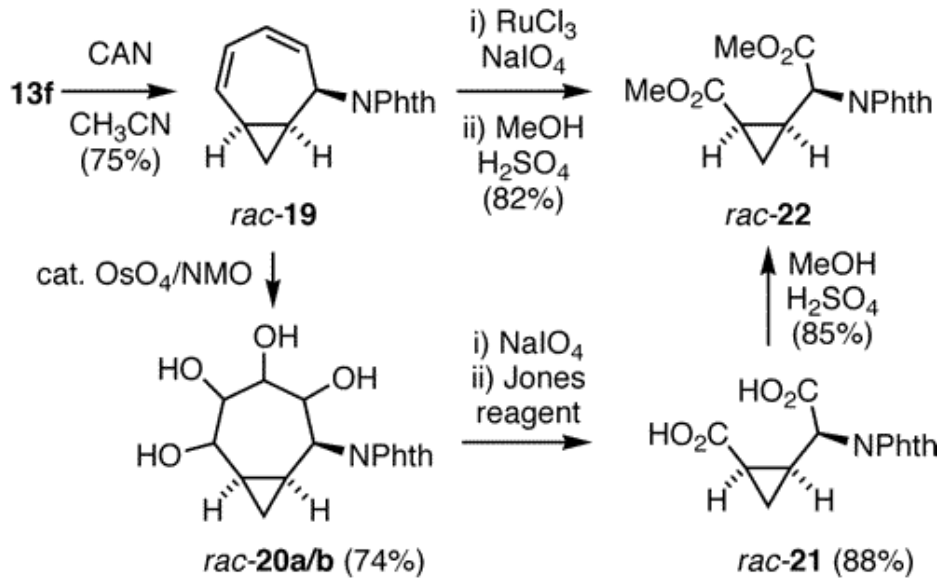
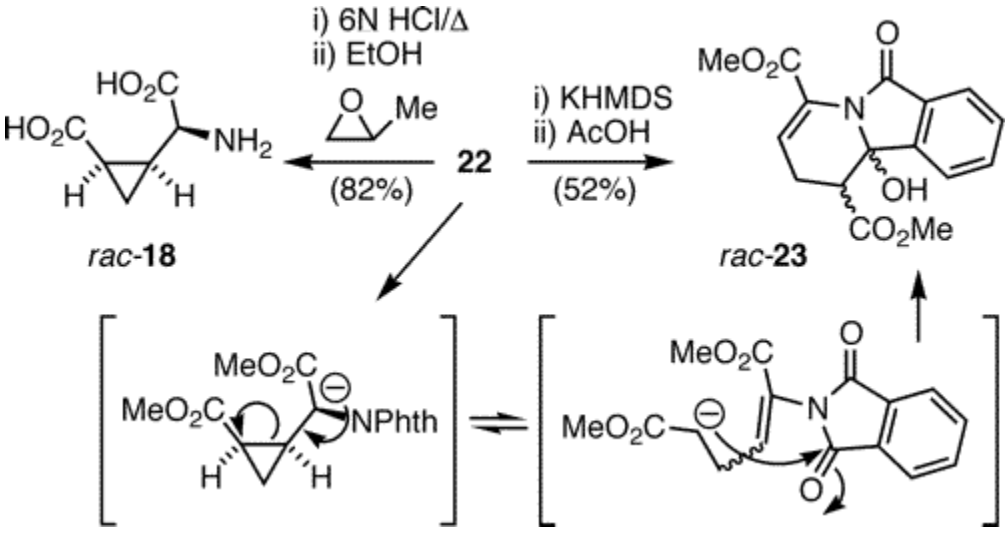


Scheme 4



Scheme 5

With the preparation of the *rac*-CCG-III completed, it was envisioned that the *trans*-2-(2`-carboxycyclopropyl) glycine (CCG-I) might be prepared by epimerization of **22**, followed by hydrolysis.[25] In an attempt to effect this isomerization, the diester *rac*-**22** was treated with KHMDS in THF at −78 °C, followed by quench with acetic acid. The *trans*-diester was not formed, but rather benzoindolizidine *rac*-**23** was afforded in moderate yield (Scheme 5). The structural assignment of *rac*-**23** was based on its NMR spectral data. In particular, the expected highfield cyclopropane signals were absent from the ^{1}H NMR

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spectrum of **23**, while the aromatic region contained four distinct signals, whose splitting pattern did not resemble the AA`BB` multiplet typically observed for phthalimide adducts. Additionally, a single olefinic proton resonance was observed at δ 6.29 in the ^{1}H NMR spectrum, typical of the β-proton of an unsaturated carbonyl compound, and a quarternary carbon signal was observed at δ 84 in the ^{13}C NMR spectrum corresponding to the aminal carbon.[26] The relative stereochemistry of the tricyclic ring system could not be determined by spectral analysis. Presumably, benzoindolizidine *rac*-**23** arises from the deprotonation of **22** at the glycinyl C1-center (Scheme 5). Subsequent ring opening of this anion gives the ester enolate anion and intramolecular addition to the phthalimide carbonyl gives **23** upon acidic workup.

It has been established that deuteration of **4** occurs via direct attack on the ligand on the face opposite to the metal, resulting in the stereospecifically *exo*-deuterated product **5**.[8b,c] Similarly, reaction of the phosphine-ligated complex **7** with D_2SO_4, followed by anion metathesis gave the deuterated cation ***d*-8** (Scheme 6). Integration of the ^{1}H NMR spectrum of ***d*-8** prepared in this fashion indicated >80% D incorporation at the 8-*exo* position. Beginning with ***d*-8**, the deuterated CCG-III (***d*-18**) was prepared in 31% yield. The ^{1}H NMR spectra of the deuterated intermediates ***d*-19** and ***d*-22** were similar to those of the nondeuterated intermediates, with the exception of simplification of the cyclopropyl resonances. The percentage deuteration remained ca. 80% throughout the synthesis within limits of error of ^{1}H NMR and MS spectral analysis.

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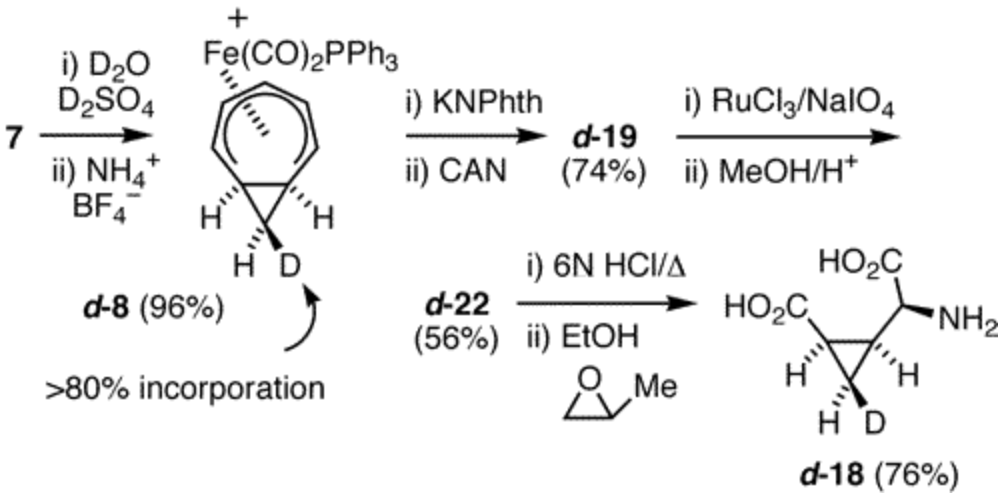

Scheme 6

Synthesis of Optically Enriched cis-2-(2'-Carboxycyclopropyl)glycine.

Because cation **8** possesses a plane of symmetry, the above syntheses necessarily produce *rac*-**18**. Pearson et al. have reported the diastereoselective addition of chiral enolate nucleophiles to (cycloheptadienyl)- and (cyclohexadienyl)$Fe(CO)_2L^+$ cations (20−50% de).[27] Unfortunately, attempts to desymmetrize cation **8** by addition of a chiral amine, α-methylbenzylamine, were nonproductive resulting in the formation of (COT)$Fe(CO)_2PPh_3$ (see Table 1). Alternatively, Howell has reported diastereoselective addition of cyanide anion to a (cyclohexadienyl)iron(1+) cation bearing a chiral phosphine ligand (ca. 2:1 dr).[28] To this end, **4** readily underwent ligand substitution with (*S*)-neomenthyldiphenylphosphine [NMDPP] in the presence of trimethylamine *N*-oxide [TMANO] to give phosphine-ligated (−)-**24** in high yield (Scheme 7). The structural assignment of (−)-**24** was aided by comparison of its ^{13}C NMR spectral data with that for the known[28] (cyclohexadiene)$Fe(CO)_2$(NMDPP). In particular, the spectrum of (−)-**24** contained two M−CO resonances at δ 218.8 and 217.0, with both signals appearing as doublets due to C−P coupling (J_{CP} = 15.6 and 10.9 Hz, respectively). Additionally, eight signals were observed in the aromatic region (δ 127−138) which were assigned to the diastereotopic phenyl groups. Finally a singlet at δ 99.2 was assigned to the octatetraene ligand (averaged due to "ring-whizzing").

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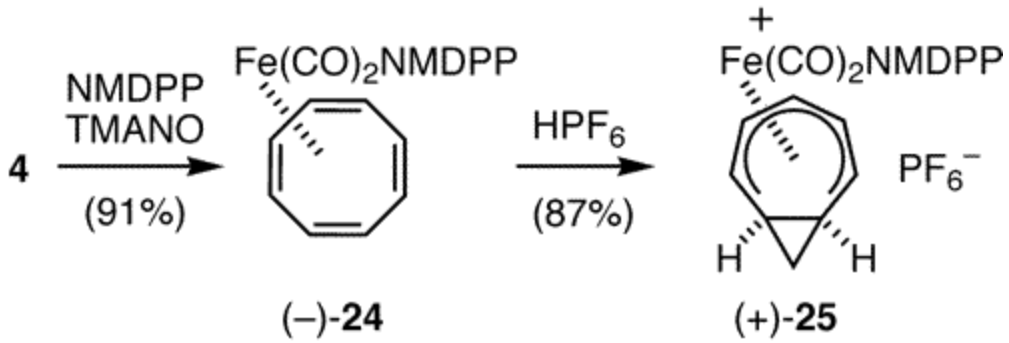
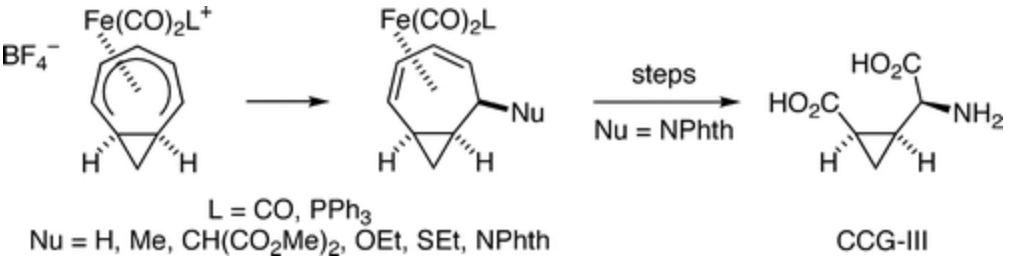


Scheme 7

Protonation of (−)-**24** with HPF_6 gave the bicyclic cation (+)-**25** (Scheme 7). Attempts to characterize (+)-**25** by either ^{1}H or ^{13}C NMR spectroscopy proved fruitless, due to the fluxional nature of the cation and signal overlap. The room-temperature ^{31}P NMR spectrum of (+)-**25** consisted of a broad singlet (δ 61.4) for the phosphine ligand as well as a septet for the hexafluorophosphate anion (δ −141.8). Upon cooling (5 °C), the singlet separated into two signals (δ 65.3 and 57.5) of unequal intensity, while at −65 °C the spectrum exhibited a total of four signals (δ 67.2, 64.2, 57.5, and 53.8) of unequal intensity. It should be noted that the basal-phosphine conformers **25B** and **25B`** (Scheme 8) are *diastereomeric*, and therefore, a unique ^{31}P NMR shift should be observed for each rotamer. The observation of four signals at lower temperature may be due to rotamers about the Fe−P bond for each of the individual conformers.[29] It was not possible to assign which diastereomeric rotomer was the major species.



Scheme 8

The reaction of (+)-**25** with potassium phthalimide at 0 °C gave a mixture of diastereomeric phthalimide adducts **26** and **27** (ca. 3:1 ratio), along with the deprotonation product (−)-**24** (Scheme 9). Unfortunately, attempted separation of the diastereomers **26** and **27** was complicated by partial decomplexation. Therefore, the mixture of

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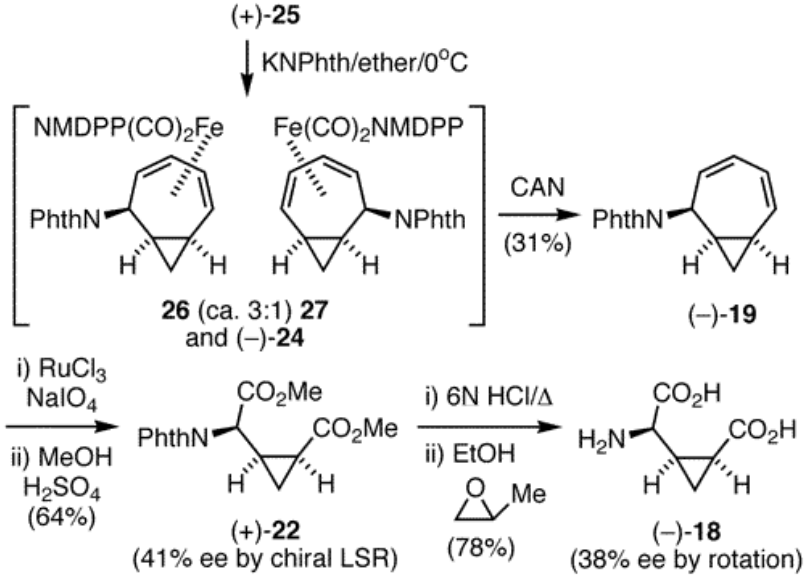
diastereomers **26**/**27** was decomplexed to give optically enriched (−)-**19**. The absolute configurations of diastereomers **26** and **27** were ultimately assigned by preparation of optically enriched target CCG-III. This level of diastereoselectivity is comparable with that observed by Pearson for the addition of chiral enolate nucleophiles to (cycloheptadienyl)- and (cyclohexadienyl)$Fe(CO)_2L^+$ cations (20−50% de, L = CO, PPh_3)[27] and to the diastereoselectivity observed by Howell for nucleophilic addition to (cyclohexadienyl)$Fe(CO)_2(NMDPP)^+$ cation.[28] Finally, and perhaps most interestingly, there exists an unusual temperature dependence on the product ratio of **26**/**27**. Performing the reaction (in Et_2O) either at ambient temperature or at 0 °C gave similar diastereomeric ratios (ca. 3:1). When the nucleophilic addition was carried out at −60 °C, *a reversal* in the asymmetric induction was observed favoring the other diastereomer (i.e., **26**/**27** ca. 1:2). No change in the ratio of **26**/**27** was observed upon allowing this mixture to stand in ether in the presence of potassium phthalimide at 23 °C for 15 h. Thus, in this case nucleophilic addition does not appear to be reversible. This unusual temperature-dependent diastereoselectivity suggests a complex mechanism for which a rationale is not apparent at this time. In the absence of this rationale, we deferred an exploration of other chiral phosphine ligands.



Scheme 9

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Oxidative cleavage of (−)-**19** by $RuCl_3/NaIO_4$ followed by esterification of the intermediate diacid gave (+)-**22** (Scheme 9). Examination of *rac*-**22** by ^1H NMR spectroscopy in the presence of $Eu(hfc)_3$ ($CDCl_3$) indicated separation of one of the methoxycarbonyl signals. By this method, (+)-**22** was determined to be 41% ee. Hydrolysis of (+)-**22**, followed by treatment of the hydrochloride salt with propylene oxide, afforded the optically enriched target (−)-**18**. Comparison of the optical rotation ($[\alpha]^{20}_D = -7.9$) for this product with literature values indicated that the product was ca. 38% ee, in favor of the non-natural configuration.

In summary, nucleophilic attack on (bicyclo[5.1.0]octadienyl)iron(1+) cations **4** or **7** generally occurs on the face opposite to the iron to give 6-substituted (bicyclo[5.1.0]octa-1,4-diene)iron complexes **11** or **13**. In certain cases, the products **11**/**13** were unstable with respect to elimination of a proton and the nucleophile to afford a (cyclooctatetraene)iron product. This methodology was applied to the synthesis of racemic *cis*-2-(2`-carboxycyclopropyl)glycine **18**. Nucleophilic addition of phthalimide to a chiral phosphine-ligated (bicyclo[5.1.0]octadienyl)iron cation proceeded with modest diastereoselectivity; the product was utilized in the preparation of optically enriched (−)-**18**. Our planned studies on the reactivity of bicyclo[5.1.0]octadienes produced from cation **5**, particularly with respect to [4 + 2] cycloaddition and intramolecular olefin metathesis, will be reported in due course.

Experimental Section[30]

Dicarbonyl(cyclooctatetraene)(triphenylphosphine)iron (7).

To a solution of tricarbonyl(cyclooctatetraene)iron (2.50 g, 10.0 mmol) and triphenylphosphine (4.00 g, 15.1 mmol) in acetone (90 mL) was added anhydrous trimethylamine *N*-oxide (1.34 g, 17.5 mmol) in one portion. Effervescence was observed upon the addition. The reaction was stirred at rt under a blanket of N_2 and was monitored by TLC. After 60 min, additional triphenylphosphine (1.00 g, 3.77 mmol) and TMANO (0.36 g, 4.7 mmol) were added. After another 30 min, a final portion of TMANO (0.36 g, 4.7 mmol) was added. After

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being stirred for a total of 2.25 h, the reaction mixture was passed through a short bed of silica and the filter bed was washed with reagent acetone until the washings were colorless. The filtrates were concentrated, and the resulting red solid was adsorbed to silica using acetone. The material was purified by column chromatography (SiO_2, hexanes−ethyl acetate = 20:1 → 10:1 → 4:1 gradient) to give **7** as a red solid (4.46 g, 93%): mp 169−171 °C; IR (KBr) 3053, 1969, 1913, 1481, 1433 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.95 (d, J_{HP} = 1.5 Hz, 8H), 7.37−7.43 (m, 9H), 7.47−7.57 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 99.4, 128.4 (d, J_{CP} = 9.5 Hz), 130.0 (d, J_{CP} = 1.7 Hz), 133.3 (d, J_{CP} = 10.4 Hz), 135.9 (d, J_{CP} = 39.2 Hz), 217.6 (d, J_{CP} = 14.1 Hz). Anal. Calcd for $C_{28}H_{23}FeO_2P$: C, 70.31; H, 4.85. Found: C, 70.30; H, 4.99.

Dicarbonyl(bicyclo[5.1.0]octadienyl)(triphenylphosphine)iron(1+) Tetrafluoroborate (8).

To an ice-cold solution of iron complex **7** (4.00 g, 8.36 mmol) in Ac_2O (37 mL) was carefully added a cold solution of aqueous tetrafluoroboric acid (60 wt %, 7.8 mL) in Ac_2O (19 mL). After several minutes of stirring, the orange solution was added dropwise to a large excess of ether (1300 mL). The resulting precipitate was collected by vacuum filtration, washed with ether, and dried in vacuo to give **8** as an orange powder (4.34 g, 92%): mp >133 °C dec; IR (KBr) 3075, 2025, 1984, 1481, 1437 cm^{-1}; ^1H NMR (CD_3OD, −20 °C) δ 1.09−1.19 (m, 1H), 1.24−1.34 (m, 1H), 2.20−2.34 (br m, 1H), 2.34−2.48 (br m, 1H), 3.63−3.79 (br m, 1H), 4.91−5.06 (br m, 1H), 5.30−5.43 (br m, 1H), 5.43−5.55 (br m, 1H), 7.45−7.68 (m, 15H), 7.71 (br t, $J \approx 5.9$ Hz, 1H); ^{31}P NMR (121 MHz, CD_3OD, 16 °C) δ 58.1. Anal. Calcd for $C_{28}H_{24}O_2BF_4FeP$: C, 59.41; H, 4.27. Found: C, 58.99; H, 4.18.

Dicarbonyl(bicyclo[5.1.0]octa-2,4-diene)(triphenylphosphine)iron (13a).

To a stirring suspension of cation **8** (0.1332 g, 0.2353 mmol) in water-saturated ether (5 mL) under nitrogen was added $NaBH_3CN$ (0.062 g, 0.9373 mmol) in portions over a period of 20 min. One hour after the first addition, the mixture was diluted with ether, washed with water followed by brine, dried, and concentrated. The residue was

purified by rapid column chromatography (SiO_2, hexanes−ethyl acetate= 30:1) to give **13a** as an unstable yellow solid (0.0560 g, 50%): mp 126−130 °C; IR (KBr) 3061, 1960, 1900, 1479, 1434, 1090, 696 cm^{-1}; ^1H NMR ($CDCl_3$) δ −0.42 to −0.50 (m, 1H), 0.49−0.60 (m, 1H), 0.77−0.93 (m, 1H), 1.19−1.34 (m, 1H), 2.03−2.17 (m, 1H), 2.23−2.39 (m, 1H), 2.50−2.69 (m, 1H), 2.88−3.02 (m, 1H), 4.27−4.37 (m, 1H), 4.50−4.60 (m, 1H), 7.31−7.41 (m, 9H), 7.41−7.51 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 14.9, 15.6, 17.5, 25.0, 60.0, 61.5, 85.7, 88.0, 127.9 (d, J_{CP} = 9.2 Hz), 129.2 (d, J_{CP} = 1.7 Hz), 132.8 (d, J_{CP} = 10.4 Hz), 135.6 (d, J_{CP} = 36.9 Hz). A satisfactory elemental analysis was not obtained for this compound.

Tricarbonyl(6-methylbicyclo[5.1.0]octa-2,4-diene)iron (11b).

To a stirring mixture of $CuBr{-}SMe_2$ (0.3331 g, 1.604 mmol) in freshly distilled THF (20 mL) at −65 °C was added a solution of methyllithium (2.0 mL, 1.6 M in ether, 3.2 mmol). The solution was stirred for 1 h, and then solid cation **5** (0.1779 g, 0.5361 mmol) was added in a single portion. The mixture was stirred for 2 h, after which time it was allowed to warm to rt for 30 min. The cold mixture was poured onto saturated aqueous NH_4Cl and extracted with Et_2O. The combined extracts were washed with brine, dried, and filtered through a short column of alumina. The filtrate was concentrated to give **11b** as a low-melting, volatile yellow solid (0.1085 g, 78%): mp < 35 °C; IR (neat) 2962, 2041, 1971, 1452 cm^{-1}; ^1H NMR ($CDCl_3$) δ −0.38 (dddd, *J* = 0.6, 4.1, 4.7, 6.9 Hz, 1H), 0.55 (ddd, *J* = 3.8, 8.2, 9.4 Hz, 1H), 0.77−0.90 (m, 1H), 1.13 (d, *J* = 6.7 Hz, 3H), 1.31−1.42 (m, 1H), 2.43−2.56 (m, 1H), 2.97 (tdd, *J* = 1.1, 4.1, 8.2 Hz, 1H), 3.66 (ddd, *J* = 1.5, 7.0, 8.3 Hz, 1H), 4.97 (dddd, *J* = 0.6, 1.2, 4.7, 7.9 Hz, 1H), 5.10 (ddd, *J* = 1.6, 4.9, 8.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 15.58, 15.62, 21.2, 26.7, 28.7, 64.2, 69.1, 86.1, 87.5, 211.6. Anal. Calcd for $C_{12}H_{12}O_3Fe$: C, 55.42; H, 4.65. Found: C, 55.62; H, 4.69.

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Dicarbonyl(η⁴-7-ethylcyclohepta-1,3,5-triene)(triphenylphosphine)iron (13b) and Dicarbonyl(6-methylbicyclo[5.1.0]octa-2,4-diene)(triphenylphosphine)iron (14b).

The reaction of **8** (0.315 g, 0.556 mmol) with CH_3Li/CuBr was carried out in the same fashion as for the reaction of **5** with CH_3Li/CuBr. Purification of the residue by column chromatography (Al_2O_3, hexanes−ethyl acetate = 20:1) gave an inseparable mixture of triene **14b** and diene **13b** (0.209 g, 76%) in a ratio of ~7:2 as determined by integration of the ^1H NMR spectrum. Data for **14b** as a mixture with **13b**: ^1H NMR ($CDCl_3$) δ 0.78 (t, J = 7.5 Hz, 3H), 1.26−1.42 (m, 2H), 2.32−2.49 (m, 3H), 4.71−4.84 (m, 2H), 5.01−5.09 (m, 1H), 5.73−5.83 (m, 1H), 7.34−7.41 (m, 9H), 7.42−7.51 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 11.8, 31.8, 44.0, 53.5, 64.2, 88.2, 94.7, 128.3 (d, J_{CP} = 9.2 Hz), 128.5, 129.7 (d, J_{CP} = 2.3 Hz), 130.0, 133.2 (d, J_{CP} = 11.0 Hz), 135.7 (d, J_{CP} = 38.0 Hz), 217.9 (d, J_{CP} = 15.0 Hz), 218.3 (d, J_{CP} = 12.7 Hz). This mixture was used in the next reaction without further characterization.

Chemical Derivatization/Separation of 13b and 14b.

To a stirring mixture of **13b** and **14b** (0.209 g, 0.423 mmol, 7:2, respectively) in pyridine (1.5 mL) and THF (2.8 mL) was added a solution of OsO_4 in toluene (3.2 mL, 0.20 M, 0.64 mmol). After 24 h, saturated sodium bisulfite was added, and the black mixture was stirred for an additional 16 h and then filtered through a bed of filter-aid. The filter bed was washed with ethyl acetate, the filtrate and washings were combined, and the biphasic solution was transferred to a separatory funnel. The aqueous layer was removed, and the organic phase was washed with water followed by brine and concentrated. The residue was purified by column chromatography (SiO_2, hexanes−ethyl acetate = 20:1 → 8:1 → 1:1 gradient) to give the unreacted diene **13b** (R_f = 0.42, hexanes−ethyl acetate = 8:1) as a viscous yellow oil (0.0303 g, ~66% recovery based upon theoretical quantity) followed by dienone **15** (R_f = 0.20, hexanes−ethyl acetate = 8:1) as a light yellow foam (0.0829 g, 49% based upon theoretical quantity). Complex **15** was recrystallized from pentane−ethyl acetate.

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13b: IR (neat): 3058, 3001, 2955, 2919, 2866, 1965, 1907, 1480, 1434, 1091 cm^{-1}; ^1H NMR ($CDCl_3$) δ −0.45 to −0.57 (m, 1H), 0.34−0.46 (m, 1H), 0.75−0.92 (m, 1H), 1.03 (d, *J* = 6.5 Hz, 3H), 1.23−1.37 (m, 1H), 2.40−2.60 (m, 2H), 2.85−2.97 (m, 1H), 4.27−4.37 (m, 1H), 4.51−4.61 (m, 1H), 7.29−7.41 (m, 9H), 7.41−7.53 (6H).

15: mp >122 °C dec; IR (KBr) 3062, 2950, 2923, 1967, 1916, 1708, 1480, 1434, 1091 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.75 (t, *J* = 7.5 Hz, 3H), 1.17−1.32 (m, 1H), 1.49−1.64 (m, 1H), 2.21−2.31 (m, 1H), 2.31−2.42 (m, 1H), 2.61 (ddd, *J* = 1.9, 5.4, 15.7 Hz, 1H), 2.79−2.88 (m, 1H), 2.86−2.96 (m, 1H), 4.67−4.78 (m, 1H), 4.78−4.88 (m, 1H), 7.37−7.50 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 12.0, 27.1, 45.0, 50.6, 55.32, 55.33, 58.0, 89.3, 89.8, 128.5 (d, J_{CP} = 9.2 Hz), 130.0 (d, J_{CP} = 1.7 Hz), 133.2 (d, J_{CP} = 10.4 Hz), 134.9 (d, J_{CP} = 38.6 Hz), 207.7. Anal. Calcd for $C_{29}H_{27}O_3PFe$: C, 68.25; H, 5.33. Found: C, 68.45; H, 5.39.

Tricarbonyl[dimethyl 2-(Bicyclo[5.1.0]octa-3',5'-dien-2'-yl)propanedioate]iron (11c).

To a cold stirring solution of dimethyl malonate (0.160 mL, 1.36 mmol) in dry ether (4.5 mL) was added a solution of *n*-BuLi (0.54 mL, 2.5 M in hexanes, 1.4 mmol). The mixture was stirred for 10 min at rt, at which time cation **5** (0.400 g, 1.21 mmol) was added in one portion. After 2 h, the orange reaction mixture was quenched with water and the biphasic solution was extracted with ether until the extractions were colorless. The combined organic layers were dried and concentrated. Purification of the residue by column chromatography (Al_2O_3, hexanes−ethyl acetate = 10:1) gave **11c** as a yellow crystalline solid (0.283 g, 62%): mp 95−96 °C; IR (KBr) 3005, 2044, 1986, 1952, 1754, 1727, 613 cm^{-1}; ^1H NMR ($CDCl_3$) δ −0.26 to −0.35 (m, 1H), 0.60−0.70 (m, 1H), 0.90−1.04 (m, 1H), 1.41−1.53 (m, 1H), 2.83−2.90 (m, 1H), 3.20−3.26 (m, 2H), 3.66 (br t, *J* ≈ 7.6 Hz, 1H), 3.72 (s, 3H), 3.79 (s, 3H), 4.94−5.02 (m, 1H), 5.14−5.21 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 16.6, 17.0, 18.1, 34.9, 52.9, 53.0, 61.0, 61.8, 63.7, 87.3, 87.7, 167.4, 168.2, 209.6. A satisfactory elemental analysis was not obtained for this compound.

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Dicarbonyl[dimethyl 2-(bicyclo[5.1.0]octa-3',5'-dien-2'-yl)propanedioate](triphenylphosphine)iron (13c):

The reaction of **8** (0.302 g, 0.533 mmol) with lithium dimethyl malonate was carried out in a fashion similar to the reaction of **5** with lithium dimethyl malonate. Purification of the residue by column chromatography (Al_2O_3, hexanes−ethyl acetate = 8:1 → 4:1 gradient) gave **13c** as a yellow foam (0.200 g, 61%): mp >49 °C dec; IR (KBr) 2951, 1971, 1913, 1735, 1434, 697 cm^{-1}; ^1H NMR ($CDCl_3$) δ −0.38 to -0.49 (m, 1H), 0.46−0.57 (m, 1H), 0.88−1.07 (m, 1H), 1.37−1.51 (m, 1H), 2.23−2.38 (m, 1H), 2.94−3.06 (m, 1H), 3.09 (br d, *J* = 10.0 Hz, 1H), 3.22−3.33 (m, 1H), 3.58 (s, 3H), 3.68 (s, 3H), 4.36−4.56 (m, 2H), 7.32−7.46 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 15.9, 17.2, 18.6, 35.5, 52.67, 52.73, 59.1, 60.6, 62.4, 87.3, 87.7, 128.0 (d, J_{CP} = 9.2 Hz), 129.4 (d, J_{CP} = 1.7 Hz), 132.8 (d, J_{CP} = 10.4 Hz), 135.1 (d, J_{CP} = 37.4 Hz), 167.7, 168.3. Anal. Calcd for $C_{33}H_{31}O_6PFe$: C, 64.93; H, 5.12. Found: C, 65.40; H, 5.21.

Reaction of 8 with (S)-α-Methylbenzylamine.

To a stirring mixture of **8** (0.567 g, 1.00 mmol) in dry Et_2O (10 mL) under N_2 was added (*S*)-α-methylbenzylamine (0.19 g, 0.16 mmol). After 45 min, additional (*S*)-α-methylbenzylamine (0.19 g, 0.16 mmol) was added to the reaction mixture. After being stirred for an additional 30 min, the red mixture was transferred to a separatory funnel and washed with water. The organic phase was dried and filtered through a short bed of silica gel using Et_2O to wash the pad. The filtrate and washings were combined and concentrated. Purification of the residue by column chromatography (SiO_2, hexanes−ethyl acetate = 10:1) gave **7** as a red solid (0.381 g, 80%).

Tricarbonyl(6-ethoxybicyclo[5.1.0]octa-2,4-diene)iron (11d).

A solution of cation **5** (0.402 g, 1.21 mmol) and powdered anhydrous sodium acetate (0.41 g, 4.9 mmol) in absolute ethanol (10 mL) was stirred for 45 min, during which time the reaction mixture became orange. The mixture was filtered, and the filtrate was

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concentrated. Purification of the residue by column chromatography (Al_2O_3, hexanes−ethyl acetate = 40:1) gave **11d** (0.228 g, 65%) as an unstable orange oil: IR (Neat) 2977, 2866, 2043, 1964, 1381, 1071 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.03−0.12 (m, 1H), 0.76 (ddd, *J* = 4.1, 8.5, 9.1 Hz, 1H), 1.00−1.12 (m, 1H), 1.22 (t, *J* = 7.0 Hz, 3H), 1.52−1.64 (m, 1H), 3.02 (dd, *J* = 4.5, 8.1 Hz, 1H), 3.44−3.72 (m, 3H), 4.31 (dd, *J* = 4.5, 7.5 Hz, 1H), 5.09 (ddd, *J* = 0.8, 5.0, 7.9 Hz, 1H), 5.36 (ddd, *J* = 1.5, 5.0, 7.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 16.6, 18.5, 18.6, 19.9, 61.4, 63.6, 63.8, 75.8, 87.5, 89.3, 209.7. A satisfactory elemental analysis was not obtained for this compound.

Reaction of 8 with Ethanol.

Reaction of **8** (0.401 g, 0.708 mmol) with ethanol and powdered anhydrous sodium acetate was carried out in a fashion similar to the reaction of **5**. During the 90 min of reaction time, the mixture became red in color. The reaction mixture was concentrated, and the residue was purified by column chromatography (SiO_2, hexanes−ethyl acetate = 4:1) to give **7** as a red solid (0.29 g, 86%), as indicated by ^1H NMR spectral analysis.

Tricarbonyl(6-ethanesulfanylbicyclo[5.1.0]octa-2,4-diene)iron (11e).

To a mixture of **5** (0.3334 g, 1.005 mmol) and anhydrous sodium acetate (0.3321 g, 4.008 mmol) in ether (10 mL) was added ethanethiol (1.2 mL, 16 mmol). After 90 min, the mixture was filtered through a short bed of Al_2O_3, and the filter pad was washed with ether. The filtrate and washings were combined and concentrated to give **11e** as an unstable red-brown oil (0.2602 g, 85%): IR (neat) 2972, 2042, 1966, 1455 cm^{-1}; ^1H NMR ($CDCl_3$) δ −0.05−0.04 (m, 1H), 0.75−0.85 (m, 1H), 1.05−1.19 (m, 1H), 1.29 (t, *J* = 7.5 Hz, 3H), 1.51−1.63 (m, 1H), 2.63−2.79 (m, 2H), 3.22−3.31 (m, 1H), 3.65−3.76 (m, 2H), 4.99−5.08 (m, 1H), 5.17−5.27 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 15.7, 18.6, 18.9, 20.6, 26.4, 43.5, 63.5, 63.8, 87.1, 87.3, 209.8. Anal. Calcd for $C_{13}H_{14}FeO_3S$: C, 51.00; H, 4.61. Found: C, 51.25; H, 4.60.

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Dicarbonyl(6-ethanesulfanylbicyclo[5.1.0]octa-2,4-diene)(triphenylphosphine)iron (13e).

The reaction of **8** (0.4247 g, 0.7502 mmol) with ethanethiol and NaOAc was carried out in a fashion similar to the reaction of **5**. After being stirred for 4.5 h, the green solution was concentrated using a stream of N_2. The viscous material was dissolved in fresh ether and washed with water followed by brine. The organic solution was dried, filtered through a short bed of alumina, and concentrated to give **13e** as a yellow foam (0.3855 g, 95%), which was unstable toward extended exposure to common chromatographic adsorbents: mp >34 °C dec; IR (KBr) 3057, 2969, 1968, 1909, 1480, 1434, 1090, 696 cm^{-1}; ^1H NMR (C_6D_6) δ 0.12−0.20 (m, 1H), 0.59−0.69 (m, 1H), 1.10−1.23 (m, 1H), 1.14 (t, *J* = 7.3 Hz, 3H), 1.43−1.55 (m, 1H), 2.39 (q, *J* = 7.3 Hz, 2H), 2.91−3.01 (m, 1H), 3.13−3.23 (m, 1H), 4.01 (dd, *J* = 4.6, 7.5 Hz, 1H), 4.34−4.43 (m, 1H), 4.51−4.60 (m, 1H), 6.93−7.04 (m, 9H), 7.47−7.56 (m, 6H); ^{13}C NMR (C_6D_6) δ 16.8, 18.7, 20.4, 22.3, 26.8, 45.2, 61.9, 64.1, 87.7, 88.2, 128.9 (d, J_{CP} = 9.2 Hz), 130.2 (d, J_{CP} = 2.3 Hz), 133.7 (d, J_{CP} = 10.4 Hz), 136.4 (d, J_{CP} = 36.9 Hz). Anal. Calcd for $C_{30}H_{29}FeO_2PS$: C, 66.67; H, 5.41. Found: C, 66.33; H, 5.49.

Tricarbonyl[N-(bicyclo[5.1.0]octa-3',5'-dien-2'-yl)phthalimide]iron (11f).

A solution of cation **5** (0.509 g, 1.53 mmol) and potassium phthalimide (0.58 g, 3.1 mmol) in reagent acetone (35 mL) was stirred for 1 h, during which time the reaction mixture turned brown. The mixture was filtered though filter-aid, and the filtrate was concentrated to give a red residue. The residue was purified by column chromatography (Al_2O_3, hexanes−ethyl acetate = 100% hexanes → 40:1 → 20:1 → 10:1 gradient) to give **4** (0.044 g, 12%) identified by ^1H NMR spectroscopy, followed by **11f** (0.245 g, 41%) as a sticky yellow foam: IR (KBr) 3007, 2044, 1964, 1767, 1708 cm^{-1}; ^1H NMR (C_6D_6) δ 0.38 (ddd, *J* = 3.8, 8.5, 8.8 Hz, 1H), 0.66−0.74 (m, 1H), 0.78−0.92 (m, 1H), 1.03−1.16 (m, 1H), 2.33 (dd, *J* = 3.8, 7.6 Hz, 1H), 3.19 (t, *J* = 7.3 Hz, 1H), 4.45−4.55 (m, 1H), 4.98−5.08 (m, 1H), 5.38 (dd, *J* = 3.8, 7.6 Hz, 1H), 6.87−6.96 (AA'BB', 2H), 7.42−7.52

(AA'BB', 2H); ^{13}C NMR (C_6D_6) δ 18.7, 19.9, 20.0, 50.9, 58.8, 64.1, 87.2, 92.3, 123.3, 132.9, 133.9, 167.9, 210.7. Anal. Calcd for $C_{19}H_{13}FeNO_5 \cdot 0.1\ H_2O$: C, 58.07; H, 3.39; N, 3.56. Found: C, 57.74; H, 3.73; N, 3.48.

Dicarbonyl[N-(bicyclo[5.1.0]octa-3',5'-dien-2'-yl)phthalimide](triphenylphosphine)iron (rac-13f).

To a rapidly stirring suspension of cation **8** (4.33 g, 7.65 mmol) in dry ether (175 mL) under N_2 was added potassium phthalimide (10.11 g, 53.49 mmol) in portions over a 24 h period. Periodically during this time, the orange ethereal mother liquors were decanted from any solid and the reaction flask was charged with additional ether (150 mL). This was repeated until the mother liquors were colorless. The resulting ethereal layers were combined and concentrated to give *rac*-**13f** as an orange solid (4.81 g, >99%), which was used in the next reaction without further purification. An analytically pure sample could be prepared by chromatography (SiO_2, hexanes−ethyl acetate = 4:1) to give *rac*-**13f** as a yellow foam, at the expense of reduced yields due to elimination of potassium phthalimide. The reaction time could be dramatically reduced from ca. 24−36 h to ca. 1.5 h by using water-saturated ether, with no change in the yield of **13f**: mp >82 °C dec; IR (KBr) 3055, 2954, 1972, 1914, 1764, 1708 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.52−0.61 (m, 2H), 1.00−1.13 (m, 1H), 1.45−1.56 (m, 1H), 2.27−2.37 (m, 1H), 2.83−2.96 (m, 1H), 4.53−4.64 (m, 1H), 4.83−4.96 (m, 1H), 5.44 (ddd, *J* = 0.9, 3.8, 7.6 Hz, 1H), 7.34−7.40 (m, 9H), 7.41−7.50 m, 6H), 7.63−7.70 (AA'BB', 2H), 7.74−7.81 (AA'BB', 2H); ^{13}C NMR (C_6D_6) δ 18.10, 18.12, 19.1, 51.4, 57.0, 60.2, 87.0, 92.2, 122.7, 128.5 (d, J_{CP} = 9.2 Hz), 129.8 (d, J_{CP} = 2.0 Hz), 132.8, 133.1, 133.4 (d, J_{CP} = 10.4 Hz), 136.0 (d, J_{CP} = 38.0 Hz), 168.1. Anal. Calcd for $C_{36}H_{28}FeNO_4P$: C, 69.13; H, 4.51; N, 2.24. Found: C, 69.28; H, 4.38; N, 2.16.

N-(Bicyclo[5.1.0]octa-3,5-dien-2-yl)phthalimide (rac-19).

To a stirring solution of the unpurified complex *rac*-**13f** (6.35 g, 9.96 mmol) in acetonitrile (230 mL) was added, in one portion,

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ammonium cerium nitrate [CAN] (5.93 g, 10.7 mmol). After 1 h, TLC monitoring indicated the presence of unreacted complex *rac*-**13f**. Additional CAN (2.82 g, 5.07 mmol) was added and the mixture was stirred for another 1 h. The reaction mixture was filtered through a small bed of silica gel and the filter bed washed with reagent acetone. The filtrates were concentrated, and the resultant orange solid was taken up in CH_2Cl_2 and washed with water. The organic phase was separated, and the aqueous phase was back-extracted with additional CH_2Cl_2. The organic solutions were combined and concentrated, and the resulting solid was purified by column chromatography (SiO_2, hexanes−ethyl acetate = 10:1 → 4:1 gradient) to give *rac*-**19** as a colorless solid (1.87 g, 75%): mp 162−163 °C; IR (KBr) 3023, 1765, 1711, 1607, 1381 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.99 (dddd, *J* = 0.9, 4.7, 8.5, 8.8 Hz, 1H), 1.22−1.34 (m, 1H), 1.85−1.95 (m, 1H), 2.25 (ddd, *J* = 5.6, 5.6, 5.6 Hz, 1H), 5.43−5.62 (m, 3H), 5.83 (ddd, *J* = 2.8, 6.0, 11.5 Hz, 1H), 6.23 (dd, *J* = 7.5, 11.5 Hz, 1H), 7.69−7.76 (AA'BB', 2H), 7.82−7.89 (AA'BB', 2H); ^{13}C NMR ($CDCl_3$) δ 9.0, 15.2, 43.8, 49.8, 122.6, 123.4, 126.2, 126.9, 132.1, 134.1, 135.2, 167.9; GC/MS *m*/*z* 251. Anal. Calcd for $C_{16}H_{13}NO_2$: C, 76.48; H, 5.21; N, 5.57. Found: C, 76.20; H, 5.28; N, 5.48.

Dicarbonyl(7-deuteriobicyclo[5.1.0]octadienyl)(triphenylphosphine)iron(1+) Tetrafluoroborate (d-8).

To an ice-cold stirring solution of ***7*** (1.2814 g, 2.6790 mmol) in dry ether (13.5 mL) was added a solution of D_2SO_4 in D_2O (3.3 g, 98 wt %, 33 mmol of D_2SO_4) over a period of 5 min. The mixture was stirred for 20 min during which time the starting material dissolved and a yellow precipitate formed. A solution of NH_4BF_4 (0.595 g, 5.68 mmol) in water (15.4 mL) was then added and the mixture stirred for an additional 30 min. The solid was collected by filtration, washed with water followed by ether, and dried in vacuo for an extended period of time to give ***d*-8** as a yellow-orange powder (1.4516 g, 96%): mp >136 °C dec; IR (KBr) 3076, 2025, 1984, 1481, 1436 cm^{-1}; ^1H NMR (CD_3OD, 17 °C) δ 1.10−1.18 (m, 1H), 2.34 (br s, 2H), 5.14 (br s, 2H), 7.45−7.68 (m, 15H), 7.71 (br t, *J* ≈ 6.4 Hz, 1H). A residual multiplet was also present at 1.26−1.33 due to incomplete deuteration (>80% by ^1H NMR) of the exo position. At ambient temperature, 2 H's have

coalesced into the baseline. Anal. Calcd for $C_{28}H_{23}DBF_4FeO_2P \cdot 0.1H_2O$: C, 59.11; H, 4.46. Found: C, 58.80; H, 4.76.

N-(7-Deuteriobicyclo[5.1.0]octa-3,5-dien-2-yl)phthalimide (d-19).

The reaction of cation ***d*-8** (1.2960 g, 2.2852 mmol) with potassium phthalimide in water-saturated ether was carried out in a fashion similar to the reaction of **8** with potassium phthalimide. The crude ***d*-13f** was dissolved in acetonitrile and treated with CAN in a fashion similar to the decomplexation of **13f**. After workup, the residue was purified by column chromatography (SiO_2, hexanes−ethyl acetate = 10:1 → 4:1 gradient) to give ***d*-19** as a colorless solid (0.4248 g, 74%): mp 163−164 °C; IR (KBr) 3024, 1765, 1712, 1606, 1382 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 (ddd, *J* = 0.9, 8.2, 9.1 Hz, 1H), 1.22−1.34 (m, 1H), 1.85−1.95 (m, 1H), 5.43−5.62 (m, 3H), 5.84 (ddd, *J* = 2.6, 5.9, 11.5 Hz, 1H), 6.23 (dd, *J* = 7.5, 11.5 Hz, 1H), 7.69−7.76 (AA'BB', 2H), 7.82−7.90 (AA'BB', 2H); ^{13}C NMR ($CDCl_3$) δ 9.3 (t, J_{CD} = 24.7 Hz), 15.5, 44.0, 50.0, 122.2, 123.0, 125.8, 126.6, 131.7, 133.7, 134.8, 167.3; GC/MS *m*/*z* 252. Compound ***d*-19** was found to have 80% *d*-incorporation by ^1H NMR spectral analysis and 79% *d*-incorporation by GC/MS analysis (M^+). Anal. Calcd for $C_{16}H_{12}DNO_2$: C, 76.17; H, 5.59; N; 5.55. Found: C, 76.26; H, 5.37; N, 5.64.

Dicarbonyl(cyclooctatetraene)((S)-neomenthyldiphenylphosphine)iron ((−)-24).

The ligand substitution of tricarbonyl(cyclooctatetraene)iron (0.8899 g, 3.647 mmol) with (*S*)-neomenthyldiphenylphosphine (1.0019 g, 3.0899 mmol) was carried out in a fashion similar to the preparation of **7**. The reaction mixture was filtered through a small bed of alumina using ether to wash the filter pad until the filtrates were colorless. The combined organic material was concentrated and purified by column chromatography (Al_2O_3, basic-Brockmann I, hexanes−ether = 100% → 60:1 → 40:1 gradient followed by hexanes−ethyl acetate = 20:1) to yield (−)-**24** as a rust-colored foam (1.5209 g, 91%): mp >59 °C dec; IR (KBr) 2955, 1974, 1912, 1432, 1090, 695 cm^{-1}; $[\alpha]^{20}_D = -1.1 \times 10^3$ (*c* 0.0588, $CHCl_3$); ^1H NMR

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($CDCl_3$) δ 0.18 (d, *J* = 7.0 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H), 1.10 (d, *J* = 7.0 Hz, 3H), 1.21−1.33 (m, 1H), 1.60−1.82 (m, 4H), 1.86−2.11 (m, 3H), 2.36−2.45 (m, 1H), 2.94−3.07 (m, 1H), 4.80 (d, J_{HP} = 1.2 Hz, 8H), 7.27−7.35 (m, 5H), 7.42−7.51 (m, 3H), 7.88−7.97 (m, 2H); ^{13}C NMR (DEPT, $CDCl_3$) δ 18.4 (s, CH_3), 20.7 (s, CH_3), 21.6 (d, J_{CP} = 12.1 Hz, CH_2), 24.5 (s, CH_3), 28.6 (d, J_{CP} = 6.3 Hz, CH), 29.3 (s, CH_2), 31.1 (d, J_{CP} = 4.0 Hz, CH), 31.5 (d, J_{CP} = 5.8 Hz, CH_2), 38.4 (d, J_{CP} = 21.9 Hz, CH), 40.2 (s, CH), 99.2 (s, CH), 127.4 (d, J_{CP} = 9.2 Hz, CH), 128.0 (d, J_{CP} = 8.1 Hz, CH), 128.3 (s, CH), 129.3 (d, J_{CP} = 7.5 Hz, CH), 130.1 (s, CH), 131.3 (d, J_{CP} = 29.4 Hz, C), 136.2 (d, J_{CP} = 9.8 Hz, CH), 137.5 (d, J_{CP} = 33.4 Hz, C), 217.0 (d, J_{CP} = 10.9 Hz, C), 218.8 (d, J_{CP} = 15.6 Hz, C). The product was contaminated with traces of NMDPP, and thus a satisfactory combustion analysis was not obtained. This product was used in the next reaction without further purification.

Dicarbonyl(bicyclo[5.1.0]octadienyl)((S)-neomenthyldiphenylphosphine)iron(1+) Hexafluorophosphate ((+)-25).

To an ice-cold stirring mixture of chiral complex (−)-**24** (1.1086 g, 2.0512 mmol) in Ac_2O (7.6 mL) was added an ice-cold solution of aqueous HPF_6 (60 wt %, 4.0 mL, 27 mmol) in Ac_2O (4.0 mL). The solution was allowed to warm to rt and stir for 10 min, at which time it was added dropwise to a beaker containing distilled water (100 mL). The resulting precipitate was harvested by vacuum filtration on a sintered glass funnel. The solid was washed with distilled water followed by pentane. The damp material was dried in vacuo for several days to afford (+)-**25** as a light yellow amorphous solid (1.2243 g, 87%): mp >100 °C dec; IR (KBr) 2957, 2036, 1993, 1436, 1092, 699 cm^{-1}; $[\alpha]^{20}_D$ = +91 (*c* 0.0672, CH_3CN). Anal. Calcd for $C_{32}H_{38}F_6FeO_2P_2$: C, 55.99; H, 5.58. Found: C, 56.26; H, 5.38. This compound was used in the subsequent reaction without further characterization.

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Optically Enriched N-(Bicyclo[5.1.0]octa-3,5-dien-2-yl)phthalimide ((−)-19).

To a cold (1−3 °C) rapidly stirring suspension of cation (+)-**25** (1.5040 g, 2.1910 mmol) in ether (100 mL) was added excess potassium phthalimide (2.50 g, 13.2 mmol) in one portion. After 30 h, the red-orange mixture was filtered, and ether was used to wash the residual solid until the washings were colorless. The organic filtrates were combined and concentrated to give a red foam (~1.57 g). The ^{1}H NMR spectrum revealed this to be a mixture of two diastereomeric iron complexes **26** and **27** (**26**/**27** = 3:1) along with (−)-**24** produced by via elimination of phthalimide. Decomplexation of the mixture of **26** and **27** (1.57 g) with CAN was carried out in a fashion similar to the decomplexation of **13f**. The reaction mixture was concentrated to ~1/2 volume, poured onto water, and extracted with ether followed by ethyl acetate. The extractions were combined, dried and concentrated to give a solid. Purification of the solid by column chromatography (SiO_2, hexanes−ethyl acetate = 10:1 → 4:1 gradient) gave diene (−)-**19** as a white solid (0.1682 g, 31%). The ^{1}H NMR spectral data for (−)-**19** was identical with that obtained for *rac*-**19**: mp 152−156 °C; $[\alpha]^{20}_D$ = −62.4 (*c* 0.314, $CHCl_3$).

N-(3,4,5,6-Tetrahydroxybicyclo[5.1.0]oct-2-yl)phthalimide (rac-20a/b).

To a stirring solution of the diene *rac*-**19** (1.05 g, 4.18 mmol) in acetone (8.40 mL) was added a solution of *N*-methylmorpholine *N*-oxide (1.54 g, 12.8 mmol) in water (1.00 g) followed by a solution of OsO_4 in toluene (0.20 M, 3.00 mL, 0.60 mmol, 14 mol %). After being stirred at rt for 24 h, the reaction was quenched by the addition of $Na_2S_2O_5$ (1.10 g). The black mixture was stirred for an additional 45 min, concentrated, and adsorbed to silica using methanol. Purification by column chromatography (SiO_2, CH_2Cl_2−methanol = 10:1) gave partially separated diastereomers *rac*-**20a** and *rac*-**20b** (**a/b** ≈ 2:1 by ^{1}H NMR spectral integration) contaminated with *N*-methylmorpholine. The impurity could be removed by washing with ether followed by CH_2Cl_2 to give the products as whites solids (total **20a** + **20b**: 0.99 g, 74%).

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***rac*-20a:** mp 229−230 °C; IR (KBr) 3404, 3011, 2916, 1759, 1702, 1387 cm^{-1}; ^1H NMR (CD_3OD) δ 0.74−0.89 (m, 2H), 1.19 (dddd, *J* = 2.6, 6.6, 9.2, 9.2 Hz, 1H), 1.39 (dddd, *J* = 4.8, 7.0, 9.2, 9.2 Hz, 1H), 3.54 (dd, *J* = 2.2, 2.2 Hz, 1H), 4.10−4.14 (m, 1H), 4.27 (dd, *J* = 1.8, 11.0 Hz, 1H), 4.44−4.50 (m, 1H), 5.16 (dd, *J* = 2.6, 10.6 Hz, 1H), 7.76−7.89 (m, 4H); ^{13}C NMR (CD_3OD, "doublets" due to slowed rotation of the phthalimide substituent shown in parentheses) δ 6.7, 18.6, 20.7, 50.7, 68.7, 69.6, 76.0, 80.9, 123.7 (124.1), 133.2 (133.6), 135.1 (135.2), 169.8 (170.2). Anal. Calcd for $C_{16}H_{17}NO_6 \cdot 0.2H_2O$: C, 59.51; H, 5.43; N, 4.34. Found: C, 59.56; H, 5.49; N, 4.35.

***rac*-20b:** mp 241−244 °C; IR (KBr) 3494, 3460, 3347, 3277, 3008, 2942, 1755, 1697, 1381 cm^{-1}; ^1H NMR (CD_3OD) δ 0.63 (ddd, *J* = 5.3, 9.0, 9.0 Hz, 1H), 1.02−1.23 (m, 2H), 1.53−1.63 (m, 1H), 4.00 (s, 2H), 4.34 (d, *J* = 3.5 Hz, 1H), 4.59 (d, *J* = 10.6 Hz, 1H), 5.05 (dd, *J* = 2.9, 11.2 Hz, 1H), 7.75−7.87 (m, 4H); ^{13}C NMR (CD_3OD) δ 7.2, 18.0, 19.7, 51.6, 66.2, 68.6, 75.8, 76.3, 123.9 (br), 133.2 (br), 135.1 (br), 170.1 (br).

1,3-Dihydro-α-[2-(carboxy)cyclopropyl]-1,3-dioxo-2H-isoindole-2-acetic Acid (rac-21).

To a stirring solution of tetrols *rac*-**20a**/**b** (0.55 g, 1.7 mmol) in THF (7.3 mL) was added water (7.3 mL) followed by sodium periodate (1.14 g, 5.22 mmol). After 10 min of stirring at rt, the mixture had thickened due to the formation of sodium iodate, and additional 50% aqueous THF (6 mL) was added. After 3 h, ethyl acetate and water were added to the reaction mixture. The biphasic solution was transferred to a separatory funnel, the organic layer removed, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were dried and concentrated to give a light yellow tacky foam (0.43 g, 97%): IR (KBr) 3108, 2855, 2743, 1774, 1718, 1378 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.59−1.74 (m, 2H), 2.15 (dddd, *J* = 3.5, 5.3, 7.9, 8.4 Hz, 1H), 2.52 (dddd, *J* = 7.0, 8.4, 8.4, 11.0 Hz, 1H), 4.74 (d, *J* = 11.0 Hz, 1H), 7.72−7.79 (AA'BB', 2H), 7.83−7.90 (AA'BB', 2H), 9.64 (d, *J* = 3.5 Hz, 1H), 9.76 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 14.7, 22.1, 25.0, 57.7, 123.9, 131.7, 134.6, 167.4, 194.7, 199.6. This compound was

unstable to column chromatography on silica gel and was used in the next step without further purification or characterization. To a vigorously stirring ice-cold solution of the above crude dialdehyde (0.53 g, 2.1 mmol) in acetone (5.2 mL) was added dropwise Jones reagent (2.8 mL). After the addition, the reaction mixture was warmed to rt and stirred for 75 min. The reaction was quenched with methanol (0.80 mL) and stirred for an additional 15 min, at which time it was partitioned between brine and CH_2Cl_2. Additional water was added to dissolve the remaining blue precipitate. The organic layer was removed, and the aqueous layer extracted with CH_2Cl_2 followed by ethyl acetate. The combined organic layers were dried and concentrated to give *rac*-**21** as a white solid (0.54 g, 91%). An analytically pure sample was prepared by recrystallization from water: mp 224−227 °C; IR (KBr) 3107, 2933, 1770, 1701, 1394 cm^{-1}; ^1H NMR (CD_3OD) δ 1.36−1.46 (m, 2H), 1.78 (ddd, *J* = 5.7, 7.5, 8.8 Hz, 1H), 2.50 (dddd, *J* = 7.0, 8.8, 8.8, 10.6 Hz, 1H), 4.87 (d, *J* = 11.0 Hz, 1H), 7.80−7.89 (m, 4H); ^{13}C NMR (CD_3OD) δ 15.5, 18.4, 22.1, 53.4, 124.2, 132.9, 135.5, 168.7, 172.1, 175.2. Anal. Calcd for $C_{14}H_{11}NO_6$: C, 58.13; H, 3.83; N, 4.84. Found: C, 57.90; H, 3.91; N, 4.77.

1,3-Dihydro-α-[2-(methoxycarbonyl)cyclopropyl]-1,3-dioxo-2H-isoindole-2-acetic Acid Methyl Ester (rac-22).

To a solution of diacid *rac*-**21** (0.15 g, 0.52 mmol) in methanol (30 mL) was added concentrated H_2SO_4 (10 drops). The reaction mixture was heated at reflux for 3.75 h, cooled to rt, concentrated to ~5 mL, and transferred to a separatory funnel using ethyl acetate (25 mL). The organic solution was washed sequentially with saturated sodium bicarbonate solution, water, and brine. The organic solution was dried and concentrated. The resultant colorless oil was purified by column chromatography (SiO_2, hexanes−ethyl acetate = 2:1) to give *rac*-**22** as a colorless oil, which upon agitation gave a colorless amorphous solid (0.14 g, 85%): mp 98−101 °C; IR (KBr) 3062, 2952, 1716, 1386, 1178 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.45 (ddd, *J* = 5.3, 7.9, 8.8 Hz, 1H), 1.53 (ddd, *J* = 5.5, 5.8, 7.0 Hz, 1H), 1.82 (ddd, *J* = 5.9, 7.9, 8.5 Hz, 1H), 2.45 (dddd, *J* = 6.9, 8.7, 8.7, 10.6 Hz, 1H), 3.61 (s, 3H), 3.78 (s, 3H), 4.95 (d, *J* = 10.6 Hz, 1H), 7.70−7.77 (AA'BB', 2H), 7.82−7.89 (AA'BB', 2H); ^{13}C NMR ($CDCl_3$) δ 14.5, 17.8, 21.1, 51.7, 52.5, 53.3, 123.7, 131.9, 134.3, 167.4, 169.3, 172.0; GC/MS *m/z*

317. Anal. Calcd for $C_{16}H_{15}NO_6$: C, 60.56; H, 4.76; N, 4.41. Found: C, 60.45; H, 4.83; N, 4.39.

Alternative Preparation of rac-22 by Sharpless Oxidation and Esterification.

To a biphasic mixture of diene *rac*-**19** (0.1250 g, 0.4975 mmol) and sodium periodate (0.89 g, 4.1 mmol) in carbon tetrachloride (1.00 mL), acetonitrile (1.00 mL), and distilled water (1.50 mL) was added $RuCl_3 \cdot 3H_2O$ (3.4 mg, 0.013 mmol, 2.6 mol %) (CAUTION: the reaction becomes exothermic!). After the mixture was stirred at rt for 2.5 h, CH_2Cl_2 and brine were added to the dark solution, followed by additional water to dissolve the remaining $NaIO_3$. The pink organic phase was removed, and the aqueous phase was extracted with CH_2Cl_2 followed by ethyl acetate. The organic extracts were combined, dried, and concentrated in vacuo to give a white foam (0.1378 g) whose crude ^{1}H NMR spectrum was consistent with that of the previously prepared diacid *rac*-**21**. The crude diacid was esterified with methanol/H_2SO_4 in a fashion similar to that described above. The residue was purified by column chromatography (SiO_2, hexanes−ethyl acetate = 2:1) to give *rac*-**22** as a faint yellow oil (0.1300 g, 82%) that gelatinized on standing. The ^{1}H NMR spectrum of this product was identical with that previously obtained.

Deuterated Diester (d-22).

The Sharpless oxidation/esterification of diene ***d*-19** (0.3781 g, 1.4987 mmol) was carried out in a fashion similar to that described above for **19**. Purification of the residue by column chromatography (SiO_2, hexanes−ethyl acetate = 2:1) gave ***d*-22** as a colorless oil which solidified upon agitation (0.2649 g, 56%): mp 90−96 °C; IR (KBr) 3056, 2951, 1717, 1386, 1173 cm^{-1};^{1}H NMR ($CDCl_3$) δ 1.44 (dd, *J* = 7.8, 8.8 Hz, 1H), 1.82 (dd, *J* = 7.8, 8.5 Hz, 1H), 2.45 (ddd, *J* = 8.5, 8.8, 10.9 Hz, 1H), 3.61 (s, 3H), 3.78 (s, 3H), 4.95 (d, *J* = 10.9 Hz, 1H), 7.70−7.77 (AA'BB', 2H), 7.82−7.89 (AA'BB', 2H); ^{13}C NMR ($CDCl_3$) δ 14.6 (t, J_{CD} = 24.8 Hz), 18.2, 21.5, 51.9, 52.6, 53.4, 123.3, 131.5, 133.8, 166.6, 168.6, 171.3; GC/MS *m*/*z* 318. The product ***d*-22** was found to contain 80% *d*-incorporation by ^{1}H NMR spectral analysis and 77% *d*-incorporation by GC/MS analysis (M^+). Anal. Calcd for

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$C_{16}H_{14}DNO_6$: C, 60.38; H, 5.06; N, 4.40. Found: C, 60.15; H, 4.75; N, 4.30.

Optically Enriched diester (+)-22.

The Sharpless oxidation/esterification of diene (−)-**19** (0.168 g, 0.669 mmol) was carried out in a fashion similar to that described above. Purification of the residue by column chromatography (SiO_2, hexanes−ethyl acetate = 4:1 → 2:1 gradient) gave (+)-**22** as a light yellow gel (0.1359 g, 64%): $[\alpha]^{20}_D$ = +4.0 (*c* 0.366, $CHCl_3$). The ^{1}H NMR spectrum of the diester obtained in this fashion was identical to that of *rac*-**22**. Analysis by ^{1}H NMR spectroscopy in the presence of a chiral shift reagent ($Eu(hfc)_3$, $CDCl_3$) indicated that the product was 41% ee.

rac-2-(2`-Carboxycyclopropyl)glycine [rac-CCG-III] (rac-18).

A mixture of *rac*-**22** (0.1506 g, 0.4746 mmol) in 6 N HCl (30 mL) containing PTFE boiling chips was heated at reflux for 90 min, during which time the solid dissolved. The reaction mixture was cooled, concentrated to ~1/2 volume, and washed repeatedly with ether to remove phthalic acid. The aqueous solution was concentrated, and the resulting solid was dried in vacuo. The solid was then dissolved in absolute ethanol (3.5 mL) to give a tan solution. Propylene oxide (1.00 mL, 14.1 mmol) was added and the mixture swirled for 45 min, during which time the free base precipitated as a white powder. The mixture was cooled to 0 °C and the solid collected by vacuum filtration. The solid was washed with cold ethanol and was combined with several aqueous washings obtained from rinsing the funnel and reaction vessel. Water was removed from the product using a gentle stream of N_2 gas. The resulting damp solid was dried in vacuo to afford *rac*-**18** as a colorless powder (0.0675 g, 82% based upon 0.8 waters of hydration), which could be further purified by recrystallization from water. The ^{1}H NMR and ^{13}C NMR spectra obtained for *rac*-CCG-III were consistent with literature[21c] spectral data: mp 178−179 °C (lit.[21c] mp 190−193 °C for (+)-**18**); IR (KBr) 3387, 1686, 1601, 1508, 1230 cm^{-1}; ^{1}H NMR (D_2O) δ 1.30 (ddd, *J* = 5.0, 5.9, 6.8 Hz, 1H), 1.44 (ddd, *J* = 5.0, 8.5, 8.8 Hz, 1H), 1.65 (dddd, *J* = 6.8,

7.9, 8.8, 10.8 Hz, 1H), 1.89 (ddd, *J* = 5.9, 7.9, 8.5 Hz, 1H), 3.90 (d, *J* = 10.8 Hz, 1H); ^{13}C NMR (D_2O) δ 16.8, 20.2, 24.5, 56.0, 175.3, 178.5. Anal. Calcd for $C_6H_9NO_4 \cdot 0.8H_2O$: C, 41.52; H, 6.15; N, 8.07. Found: C, 41.47; H, 6.33; N, 8.00.

Deuterated CCG-III (d-18).

Acidic hydrolysis of ***d*-22** (0.120 g, 0.377 mmol) followed by generation of the free-base by treatment with propylene oxide was carried out in a fashion similar to the preparation of *rac*-**18** to give ***d*-18** (0.0472 g, 76%, based upon 0.25 waters of hydration) as an off-white powder: mp 168−169 °C; IR (KBr) 3423, 1701, 1514, 1230 cm^{-1}; ^{1}H NMR (D_2O) δ 1.42 (br t, *J* = 8.7 Hz, 1H), 1.58−1.69 (m, 1H), 1.88 (br t, *J* = 8.0 Hz, 1H), 3.90 (d, *J* = 10.6 Hz, 1H); ^{13}C NMR (D_2O) δ 16.5 (t, J_{CD} = 23.5 Hz), 20.3, 24.3, 56.1, 175.3, 178.7. Compound ***d*-18** was found to contain 80% *d*-incorporation by ^{1}H NMR spectral integration. Anal. Calcd for $C_6H_8DNO_4 \cdot {}^1/_4H_2O$: C, 43.77; H, 5.20; N, 8.51. Found: C, 43.67; H, 5.47; N, 8.25.

(−)-2-(2'-Carboxycyclopropyl)glycine (−)-18.

Acidic hydrolysis of (+)-**22** (0.126 g, 0.397 mmol) followed by generation the free-base by treatment with propylene oxide was carried out in a fashion similar to the preparation of *rac*-**18** to give (−)-**18** as a tan solid (0.049 g, 78%): mp >145 °C dec; $[\alpha]^{20}_D$ = −7.9 (*c* 0.328, H_2O) (lit.[21c] $[\alpha]^{20}_D$ = +20.4 (*c* 0.5, H_2O). The ^{1}H NMR spectrum of (−)-**18** was identical to that of *rac*-**18**.

Benzoindolizidine (23).

A flame-dried vial was charged with the diester *rac*-**22** (0.0578 g, 0.182 mmol), KHMDS (40 mg, 0.19 mmol), and a stirbar. The vial was stoppered and cooled to −78 °C, and freshly distilled dry THF (0.40 mL) was added via a syringe. The solution was stirred for 30 min and then warmed to 0 °C over a period of 1 h. The vial was then recooled to −78 °C, and the reaction was quenched by the addition of a solution of acetic acid (30 μL) in THF (1 mL). The solution was diluted with ethyl acetate and washed with water. The organic phase was dried and filtered through silica gel, the filter bed was washed with

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ethyl acetate, and the combined organic phases were concentrated. The residue was purified by preparative TLC (SiO_2, hexanes−ethyl acetate = 2:1) to afford *rac*-**23** as an off-white foam (0.0299 g, 52%). This was identified as an 8:1 mixture of diastereomers by ^{1}H spectroscopy:. mp > 70 °C dec; IR (KBr) 3422, 2953, 1721, 1438, 1401, 1151 cm^{-1}; ^{1}H NMR ($CDCl_3$, major diastereomer) δ 2.59−2.71 (m, 2H), 2.84 (ddd, *J* = 2.9, 13.1, 19.8 Hz, 1H), 3.80 (s, 3H), 3.84 (s, 3H), 6.29 (dd, *J* = 2.9, 4.7 Hz, 1H), 7.47−7.61 (m, 3H), 7.78−7.82 (m, 1H), signal for OH not observed; ^{13}C NMR (DEPT, $CDCl_3$, major diastereomer) δ 25.9 (CH_2), 47.4 (CH), 52.95 (CH_3), 52.98 (CH_3), 84.4 (C), 120.6 (CH), 122.7 (CH), 124.0 (CH), 126.9 (C), 129.8 (C), 130.0 (CH), 132.8 (CH), 145.2 (C), 163.3 (C), 163.4 (C), 172.7 (C). Anal. Calcd for $C_{16}H_{15}NO_6 \cdot 0.5H_2O$: C, 58.89; H, 4.94; N, 4.29. Found: C, 58.81; H, 4.63; N, 4.21.

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Supporting Information Available

Copies of the ^{1}H and/or ^{13}C NMR spectra of **11c**,**d**, **13a**,**b**, **20b**, and (−)-**24**. This material is available free of charge via the Internet at http://pubs.acs.org.

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