1-1-2003

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Young K. Yun

Kamil Godula

Yeyu Cao
Marquette University

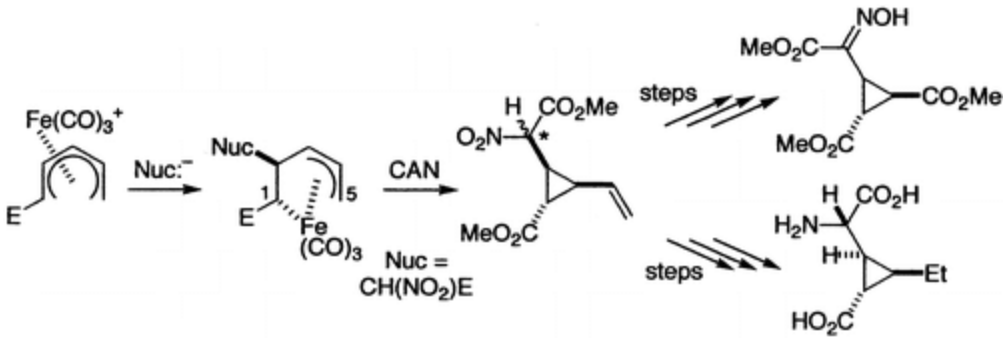
William A. Donaldson
Marquette University, william.donaldson@marquette.edu

Iron-Mediated Preparation of Vinylcyclopropanecarboxylates: Scope, Mechanism, and Applications

Young K. Yun
Department of Chemistry, Marquette University, Milwaukee, WI
Kamil Godula
Department of Chemistry, Marquette University, Milwaukee, WI
Yeyu Cao
Department of Chemistry, Marquette University, Milwaukee, WI
William A. Donaldson
Department of Chemistry, Marquette University, Milwaukee, WI

Journal of Organic Chemistry, Vol 68, No. 3 (2003): pg. 901-910. DOI.

Abstract



The addition of stabilized carbon nucleophiles to tricarbonyl(1-methoxycarbonylpentadienyl)iron(1+) cation (**1a**) proceeds via attack at C2 on the face of the ligand opposite the $Fe(CO)_3$ group to generate tricarbonyl(pentenediyl)iron complexes **2**. Oxidation of complexes **2** affords vinylcyclopropanecarboxylates in good yield. In general, the relative stereochemistry about the cyclopropane ring reflects reductive elimination with retention of configuration. In cases where the C2 substituent is bulky (i.e., **2b**) the major cyclopropane product **9b** represents ring closure with inversion at C3. A mechanism involving π−σ−π rearrangement of the initially oxidized (pentenediyl)iron species is proposed to account for these results. Experiments which probe the stereochemistry of deuterium labeling in the vinyl group of the vinylcyclopropanecarboxylate products were carried out, and these results are consistent with the proposed mechanism. This methodology for the preparation of vinylcyclopropanecarboxylates was applied to the synthesis of 2-(2′-carboxycyclopropyl)glycines (+)-**22** and (−)-**23** and the cyclopropane triester (−)-**26**.

Introduction

While the cyclopropane ring is a highly strained entity, it is nonetheless found in a wide variety of naturally occurring compounds including terpenes, pheromones, fatty acid metabolites, and unusual amino acids.[1] In addition, the rigidity of the three-membered ring renders this group an appealing structural unit for the preparation of molecules with defined orientation of pendant functional groups. There exist a variety of well-known methods for the preparation of cyclopropane rings.[2] Among these are (Scheme 1, counterclockwise from top left) addition of α-diazo carbonyls to olefins in the presence of a catalyst,[3] conjugate addition of oxosulfonium ylides to α,β-unsaturated olefins,[4] reactions of in situ generated metal−carbene complexes,[5] Simmons−Smith cyclopropanation with diiodomethane,[6] dialkylation of succinate esters with 1-bromo-1-chloroalkanes,[7]

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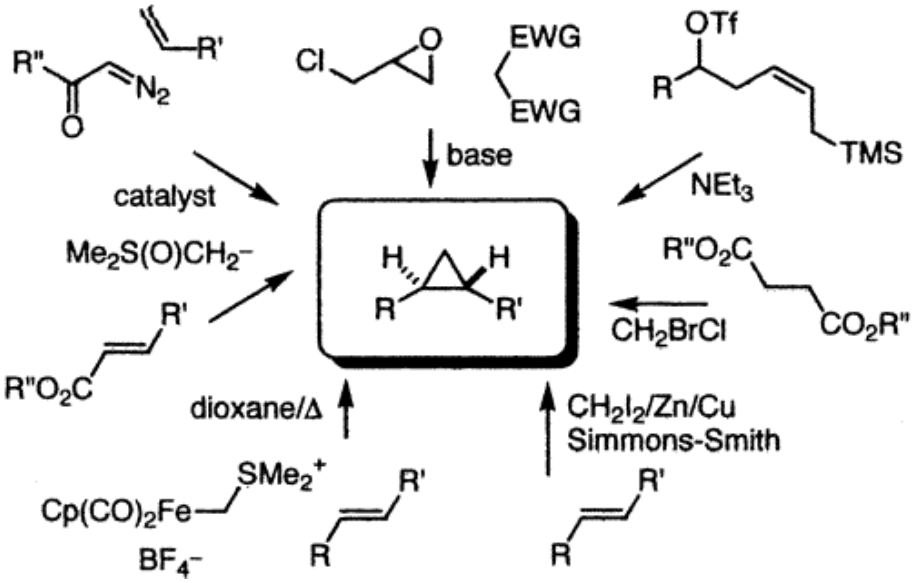
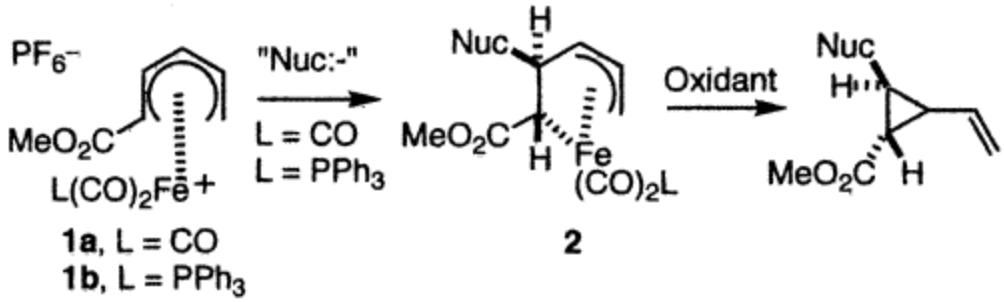
homoallyl to cyclopropylmethyl carbocation rearrangements,[8] and reaction of active methylene compounds with epichlorohydrin.[9]



Scheme 1

We herein report on the scope, mechanism, and applications of a novel, iron-mediated methodology for the preparation of 1,2,3-trisubstituted cyclopropanes. This methodology relies on nucleophilic addition to (pentadienyl)iron cations **1** to generate (pentenediyl)iron complexes **2** (Scheme 2).[10-12] The oxidatively induced reductive elimination of complexes **2** affords vinylcyclopropanes.[12a,b,13]



Scheme 2

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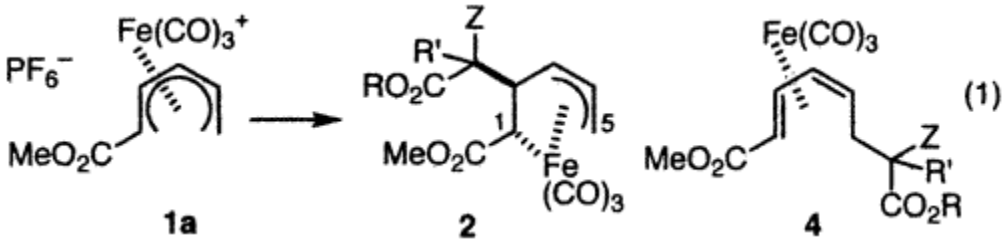
Results and Discussion

Nucleophilic Addition to (Pentadienyl)iron Cations.

We have previously reported the reaction of **1a** with lithium dimethyl malonate or lithium dimethyl methylmalonate (**3a** or **3b**) to give predominantly **2a** or **2b**, respectively (eq 1, Table 1), whose relative configurations were established by X-ray diffraction analysis.[10a] In a similar fashion the reaction of **1a** with the anions derived from methyl phenylsulfonylacetate **3c**, methyl nitroacetate **3d**, ethyl *N*-(diphenylmethylene)glycinate **3e**, or diethyl *N*-acetamidomalonate **3f** gave predominantly the (pentenediyl)iron complexes **2c–f** (eq 1, Table 1). In comparison, reaction of cation **1a** with the anions derived from (*R*)-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine (**5**)[14a] or benzyl (2*R*,3*S*)-6-oxo-2,3-diphenyl-4-morpholinecarboxylate (**6**)[14b] gave only minor amounts of (methyl 6-hydroxy-2,4-hexadienoate)$Fe(CO)_3$ (**7**) derived presumably from hydrolysis of the cation upon aqueous workup.

Table 1. Nucleophilic Addition to $(1\text{-}MeO_2CC_5H_6)Fe(CO)_3^+$ (**1a**)



nucleophile	products (isolated yields, %)		ref
3a	**2a** (61)	**4a** (5)	13a
3b	**2b** (66)	**4b** (0)	13a
3c	**2c/2c`** (82)	**4c** (0)	
3d	**2d/2d`** (72)	**4d** (7)	
3e	**2e/2e`** (18)	**4e** (0)	
3f	**2f** (95)	**4f** (0)	
5	(0)	(0)[a]	
6	(0)	(0)[a]	

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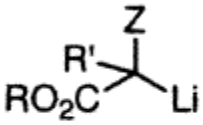
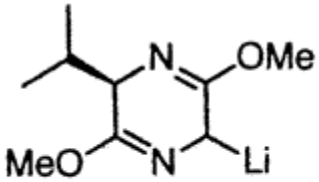
[a] (Methyl 6-hydroxy-2,4-hexadienoate)$Fe(CO)_3$ (**7**) is formed in this reaction.



3a, R = Me, R' = H, Z = CO_2Me
3b, R = Me, R' = Me, Z = CO_2Me
3c, R = Me, R' = H, Z = SO_2Ph
3d, R = Me, R' = H, Z = NO_2
3e, R = Et, R' = H, Z = $N{=}CPh_2$
3f, R = Et, R' = NHAc, Z = CO_2Et



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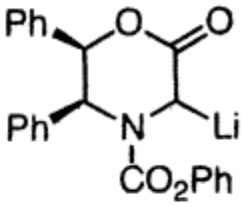

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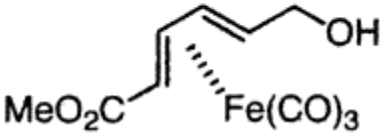

7

Notably, the strongly electron withdrawing methoxycarbonyl substituent lowers the relative energy of the pentadienyl LUMO, thus allowing for better energy match with the metal d orbitals.[15] This effects a greater transfer of electron density from the metal to the pentadienyl ligand at C1, C3, and C5. Thus, formation of the pentenediyl products **2a–f** from nucleophilic attack at C2 of **1a** is the result of charge control (i.e., greater δ+ charge at C2/C4).

Complexes **2c–f** were assigned (pentenediyl)iron structures by comparison of their ^{1}H NMR spectral data with those for known complexes **2a**,**b**. In particular, signals at ca. δ −0.1 to +0.5 ppm (d, *J* = ca. 9 Hz) and at ca. δ 2.5−2.0 ppm (dd, *J* = ca. 2.5, 12 Hz) are characteristic of the H1 and H5*endo* protons, respectively. Complexes **2c–e** were formed as 1:1 mixtures of diastereomers (**2c**/**2c'**, **2d**/**2d'**, **2e**/**2e'**) as evidenced by the presence of two sets of the above characteristic signals in each mixture. For complexes **2c**/**2c'** and **2d**/**2d'**, isolation of one of the diastereomers was possible by fractional crystallization. The structures of pentenediyl complexes **2c** and **2d'** were unambiguously established by single-crystal X-ray diffraction analysis (for **2d'** see Figure 1). In both cases, the new C−C bond is situated *trans* to the $Fe(CO)_3$ group (i.e., nucleophilic attack opposite the metal). The bond distances and angles for **2c** and **2d'** are

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in good agreement with those for other (pentenediyl)iron complexes reported in the literature.[11a-d,12a,b]

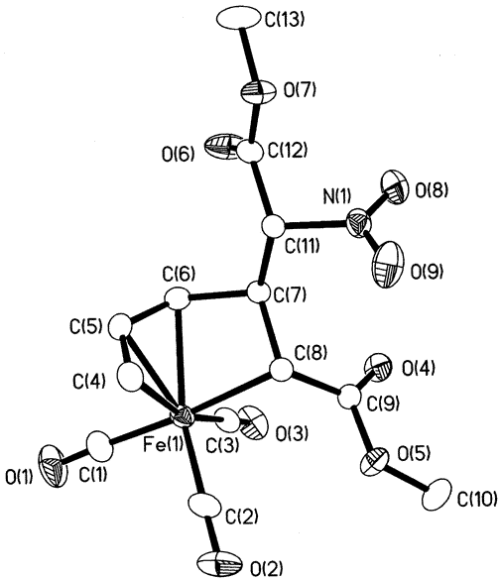

Figure 1 ORTEP representation of the X-ray crystal structure of **2d'**. Selected bond lengths (A): Fe(1)−C(4), 2.143(3); Fe(1)−C(5), 2.087(3); Fe(1)−C(6), 2.146(3); Fe(1)−C(8), 2.106(2); C(4)−C(5), 1.396(4); C(5)−C(6), 1.394(4); C(6)−C(7), 1.515(3); C(7)−C(8), 1.514(3).

Oxidatively Induced Reductive Elimination.

Oxidatively induced reductive elimination is an important reaction step in numerous stoichiometric and catalytic transition-metal-mediated carbon−carbon bond formations. This process is well-known to occur with retention of stereochemistry.[16] Oxidation of **2a** with cerium ammonium nitrate (CAN; 10 equiv) gave vinylcyclopropane **8a** as the major product (Scheme 3). The relative configuration of **8a** is based on its ^{1}H NMR spectral data. In particular, the signals at δ 2.57 (ddd), 2.33 (dd), and 1.76 (dd) ppm are assigned to the H2', H3', and H1' cyclopropane hydrogens. These assignments were aided by coupling of the H2' signal at δ 2.57 ppm with the malonate methine proton at δ 3.04 ppm (11 Hz), and coupling of the H3' signal at δ 2.33 ppm with the vinylic proton at δ 5.26 ppm (8 Hz). The large coupling between H2' and H3' (9 Hz) indicates a *cis* relationship, while smaller couplings between H1' and H2' and between H1' and H3' (4.9 Hz each) indicate a *trans* relationship.[17] Cyclopropane **9a**, which is epimeric with **8a** at the C3' stereocenter, was detected as

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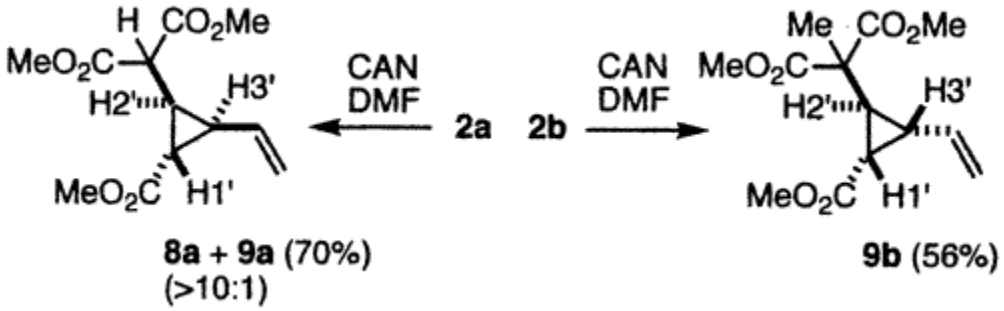
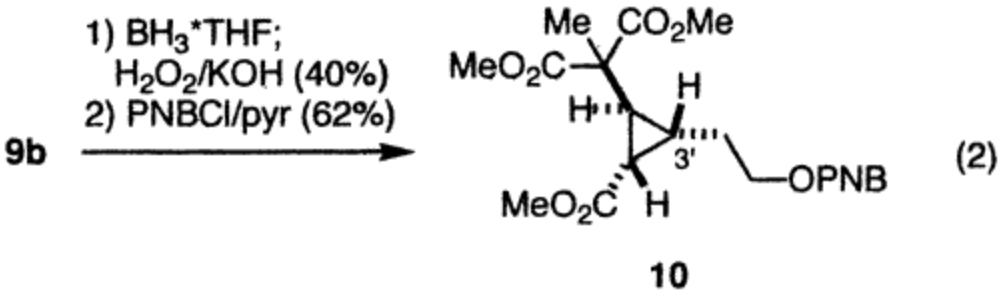
a very minor product in the crude reaction mixture (**8a**:**9a** > 10:1). The cyclopropane stereochemistry in **8a** is consistent with an oxidatively induced reductive elimination occurring with retention of configuration.



Scheme 3

In contrast, oxidative decomplexation of **2b** with CAN gave **9b** (Scheme 3). The ^{1}H NMR signal at δ 2.00 ppm (dt) could be assigned to the H3‘ proton of **9b** on the basis of its coupling to the vinylic proton at δ 6.14 ppm (ca. 9 Hz); however, the *unambiguous* assignment of the remaining cyclopropane signals (δ 2.61 and 2.18 ppm) to H1‘ and H2‘ was not possible since each appeared as a doublet of doublets. While the signal for H3‘ is coupled to one *cis* and one *trans* cyclopropane proton, it is not clear whether H1‘ is *cis* and H2‘ is *trans* (as is the case for **8a**) or vice versa. To assign the relative stereochemistry of **9b**, a crystalline derivative was sought. Hydroboration of **9b** gave a primary alcohol, which was esterified with *p*-nitrobenzoyl chloride to give **10** (eq 2). The crystal structure of **10** established that the 3‘-substituent is *cis* with respect to the methoxycarbonyl substituent.[18] On this basis, cyclopropane **9b** is assigned with the vinyl and ester substituents *cis*. *The stereochemistry of* **9b** *represents an oxidatively induced reductive elimination of* **2b** *with apparent inversion of configuration at C3.*



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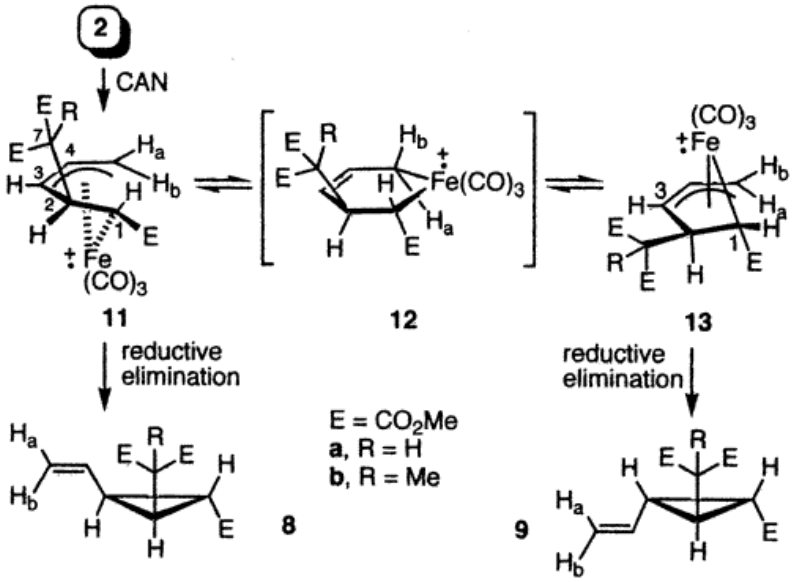
The following mechanism is proposed to rationalize these results (Scheme 4). Oxidation of pentenediyl complex **2a** leads directly to the species **11a**. Reductive elimination of **11a**, with retention of configuration, leads to vinylcyclopropane **8a**. For vinylcyclopropane **9b**, the apparent inversion of configuration results from π−σ−π rearrangement of **11b**, via the metallocyclohexene intermediate **12b** to generate **13b** (inversion of configuration at C3 with respect to the configuration at C1) followed by reductive elimination. For **11a** (R = H), the π−σ−π rearrangement is slow with respect to reductive elimination. In comparison, the rate of reductive elimination from **11b** is slow in comparison to rearrangement to **13b** (R = Me). This may be due (i) to a decrease in the rate of formation of **8b** due to increased steric repulsion in the product and/or (ii) to destabilization of **11b** with respect to **13b** due to steric strain in **11b**. As a measure of this latter steric strain, the C4−C3−C2−C7 torsional angle for **2b** in the crystal state (81.3°) is considerably larger than that for **2a** (65.3°).[10a]

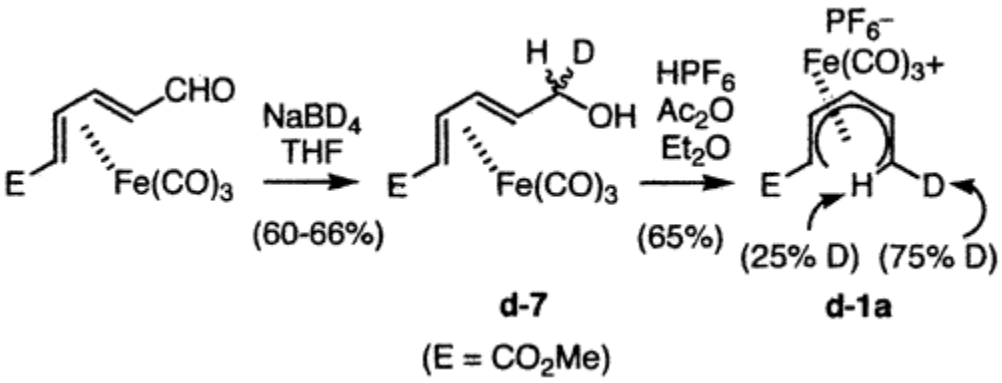


Scheme 4

It is proposed that the π−σ−π rearrangement of the pentenediyl complexes occurs readily only for the oxidized species **11**/**13**.[19] (Pentenediyl)iron complexes **2a** and **2b** are recovered unchanged upon stirring at room temperature in DMF for 18 h, in the absence of CAN. Furthermore, when the oxidation of **2a** was carried to less than

completion, unreacted **2a** was recovered *unchanged*, in addition to the vinylcyclopropane products.

It may be noted that the π−σ−π rearrangement of **11** to **13** occurs with inversion of the *exo*−*endo* stereochemistry at the σ-bound end of the allylic portion of **11**. If the proposed mechanism is valid, this inversion of stereochemistry should be reflected in the products. Toward this end, deuterium-labeling studies were carried out. Reduction of (methyl 6-oxo,2,4-hexadienoate)$Fe(CO)_3$ with $NaBD_4$ gave the deuterated dienol complex **d-7** (Scheme 5). Dehydration of **d-7** with HPF_6/Ac_2O gave the stereoselectively deuterium labeled cation **d-1a**. Integration of the ^1H NMR signals at δ 4.09 ppm (H5*exo*) and δ 2.62 ppm (H5*endo* and H1) indicates that the deuterium label is ca. 75% in the *exo*-position and 25% in the *endo*-position.



Scheme 5

The reaction of **d-1a** with **3a** gave **d-2a** along with the diene complex **d-4a** (6:1), while reaction of **d-1a** with **3b** gave **d-2b** and **d-4b** (8:1) (Scheme 6). This increase in the ratio of attack at C5 vs C2 is attributed to an inverse α-secondary isotope effect. The signals for H5*exo* and H5*endo* of **2a**/**2b** appear at ca. δ 2.7 and 1.9 ppm, respectively. Integration of these signals for **d-2a** and **d-2b** indicates that deuterium label in each pentenediyl complex is located ca. 75% in the H5*exo* position. The oxidative decomplexation of **d-2a** gave **d-8a**. Examination of the ^1H NMR spectrum of **d-8a** indicated that 72% of the terminal vinylic hydrogen is *trans* (δ 4.93, d, J = 16.8 Hz) with respect to the internal vinylic hydrogen, while 28% of the product has the terminal vinylic hydrogen *cis* (δ 4.88 ppm, d, J = 10.5 Hz) with respect to the internal vinylic hydrogen. Thus, **d-8a** is 72% *E*. In

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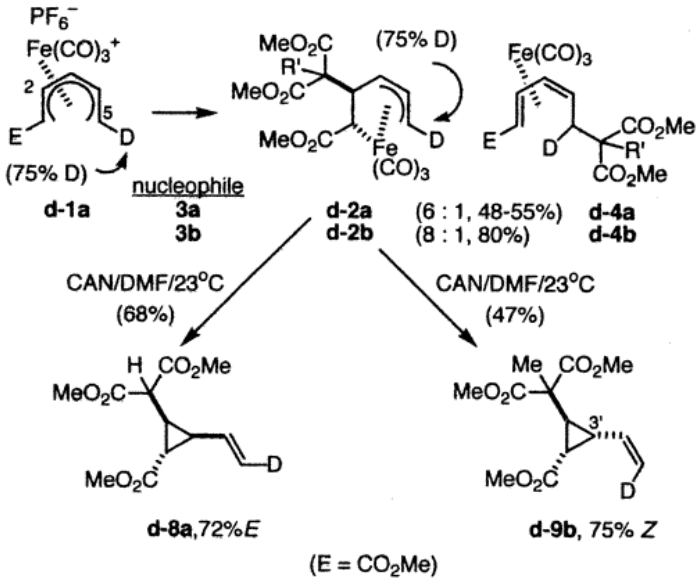
comparison, oxidative decomplexation of **d-3b** gave **d-9b**; ^{1}H NMR integration of the vinyl methylene protons (δ 5.17 ppm, d, *J* = 17.1 Hz, 0.25H; δ 5.01 ppm, d, *J* = 10.7 Hz, 0.75H) indicated the product to be 75% *Z*. Thus, inversion of configuration at the 3ʻ vinylcyclopropyl carbon is accompanied by an inversion in the stereochemistry about the C═C double bond. These results are consistent with the mechanism proposed in Scheme 4.



Scheme 6

Oxidative decomplexation of **2c**/**c**ʻ, **2d**/**d**ʻ, or **14** (prepared from the reaction of **1b** with the anion of nitromethane)[10b] with excess CAN gave the vinylcyclopropanes **8c**/**8c**ʻ, **8d**/**8d**ʻ, and **8g**, respectively (Scheme 7). Vinylcyclopropanes **8c**/**8c**ʻ and **8d**/**8d**ʻ are each formed as a 1:1 mixture of diastereomers at the indicated (*) carbon. Upon chromatography, the ratio of **8c**:**8c**ʻ changed to ca. 5:1 due to epimerization at the relatively acidic active methylene carbon. Comparison of the ^{13}C NMR spectral data for **8a** and **9b** with those of **8c**/**8c**ʻ, **8d**/**8d**ʻ, and **8g** indicated that these latter cyclopropanes have the same relative configurations about the ring as **8a**. In particular, signals for the vinyl and cyclopropane carbons of general structure **8** appear at ca. δ 131, 119, 29, 26, and 25 ppm, while those of **9b** appear at ca. δ 134, 117, 31, 28, and 24 ppm.

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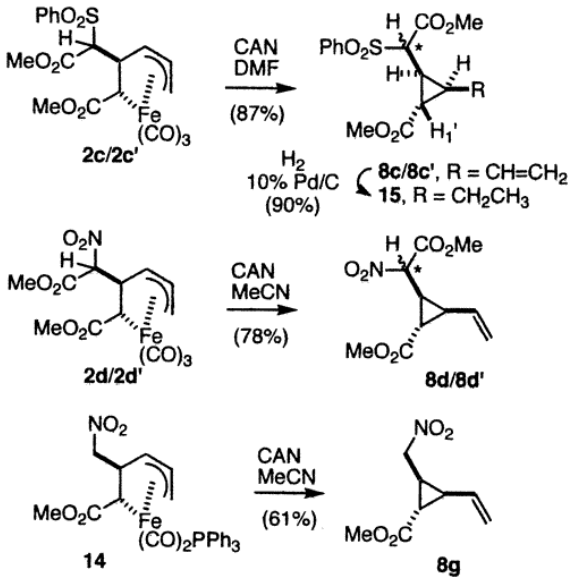

Scheme 7

Catalytic hydrogenation of **8c**/**8c'** (5:1) in the presence of 10% Pd/C gave **15**, as a mixture of diastereomers (ca. 5:1, Scheme 7). The cyclopropane ring was not cleaved under these conditions. The structure of **15** was assigned on the basis of its ^{1}H NMR spectral data. In particular, the signal for H1' of the major diastereomer appears at δ 1.55 ppm (dd, *J* = 5.0, 5.0 Hz). The magnitudes of these couplings are consistent with two *trans* cyclopropane hydrogens (i.e., H2' and H3'). This stereochemical assignment of **15** corroborates the assignment of **8c**/**c'**. The relative configurations about the cyclopropane rings in **8c**, **8d**, and **8g** are consistent with an oxidatively induced reductive elimination with retention of stereochemistry at the centers being coupled.

Attempted oxidative decomplexation of **2f** gave a complex mixture of unidentified products. The oxidation of **2f** may be complicated by initial oxidation at the *N*-acetamido group rather than at iron.

Preparation of (Carboxycyclopropyl)glycines and Analogues.[20]

L-Glutamic acid (Chart 1) is the major excitatory neurotransmitter for a wide variety of receptors in mammalian

systems.[21] The selective activation of different glutamate receptors may depend on recognition of a particular conformer of this flexible molecule. For this reason, the synthesis and evaluation of conformationally restricted 2-(2'-carboxycyclopropyl)glycines has led to the discovery of ligands with mGluR specificity.[22] In particular the extended conformation, as exemplified by compounds **16a–c** (Chart 1), is believed to be a requirement for binding to the mGluR1 and mGluR2 receptors, while the presence and electronic nature of the 3'-substituent may distinguish between agonist and antagonist activity.[22d] Pedregal et al. reported the synthesis of 2-(3'-alkyl-2'-carboxycyclopropyl)glycines **17a–c** in which the 3'-alkyl substituent was *trans* with respect to the glycine functionality.[23] Additionally, the cyclopropylchromane oxime **18** has been found to be an mGluR1 antagonist.[24]

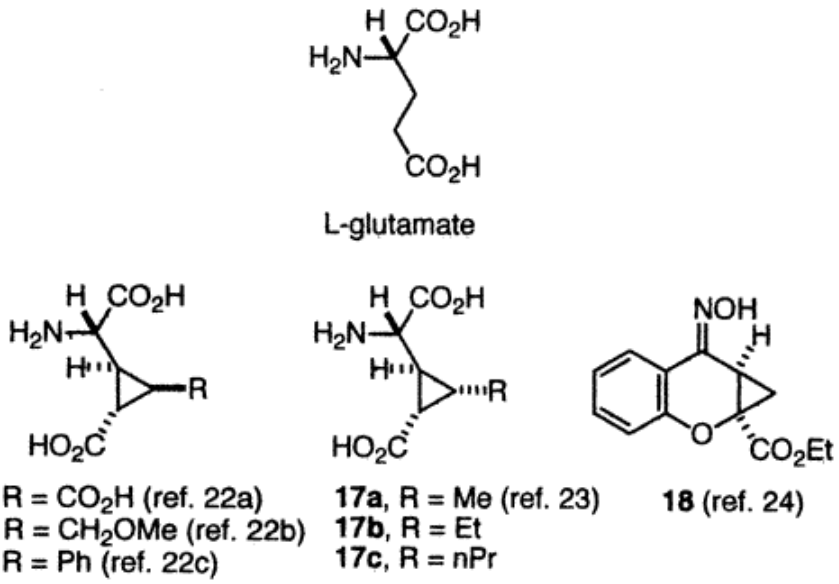

Chart 1

The vinylcyclopropane carboxylate **8d**/**8d'** was envisioned to be a versatile starting point for the preparation of conformationally restricted glutamate analogues. Toward this end, reaction of *rac*-**8d**/**8d'** with H_2/Raney nickel proceeded with reduction of both the nitro and the vinyl substituents to afford an inseparable mixture of diastereomeric glycine methyl esters, *rac*-**19**/**19'** (Scheme 8). Reaction of *rac*-**19**/**19'** with benzophenone imine[25] gave a mixture of crystalline imines *rac*-**20** and *rac*-**21** which were readily separable by column chromatography. The stereochemistry about the cyclopropane

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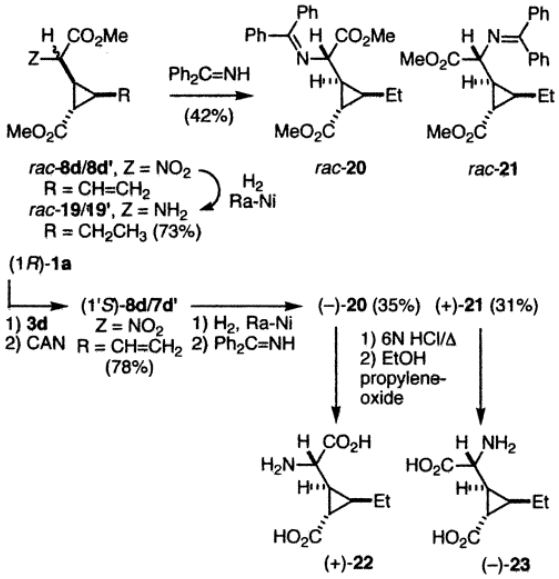
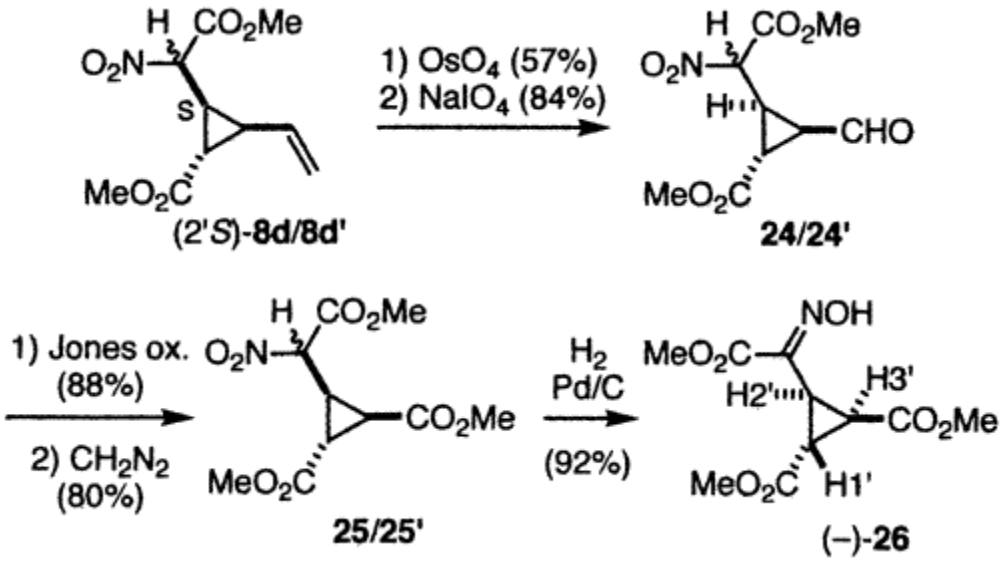
ring of *rac*-**21** was assigned on the basis of its ^{1}H NMR spectral data. In particular, the signals for H1‵ and H2‵ appear at δ 1.35 (dd, *J* = 4.8, 4.8 Hz) and 2.33 (*J* = 4.6, 9.4, 9.4 Hz) ppm, respectively. Since *rac*-**20** is diastereomeric with *rac*-**21** at the exocyclic stereocenter, it was also assigned the same relative stereochemistry about the cyclopropane ring.



Scheme 8

To prepare optically active (carboxycyclopropyl)glycines, it was necessary to begin with optically active cation **1a**. Reaction of (1*R*)-**1a**[26] with the anion derived from methyl nitroacetate, followed by treatment with CAN, gave (2‵*S*)-**8d**/**d‵** (Scheme 9). The 2‵*S* absolute configuration was assigned on the basis that nucleophilic attack occurs on the *exo*-face of the pentadienyl ligand (cf. Figure 1) and that this configuration is not affected during the oxidatively induced reductive elimination. Reduction of (2‵*S*)-**8d**/**8d‵**, followed by formation of the diphenylmethylene imines and chromatographic separation, gave (−)-**20** and (+)-**21**. Individual examination of (−)-**20** and (+)-**21** in the presence of a chiral shift reagent [Eu(hfc)$_3$, $CDCl_3$] gave evidence of separation of the glycine methyl ester signals; integration of these signals indicated that both were >80% ee. The 2*S* configuration of (−)-**20** was assigned by comparison of the sign of its specific rotation with that of a series of 13 *N*-diphenylmethylene imines of l-amino acids.[27] Separate hydrolysis of (−)-**20** and (+)-**21**, followed by generation of the free base by treatment with propylene oxide, gave

(+)-**22** and (−)-**23**, respectively. The spectral data for **22** and **23** are distinctive compared to those of the known[23] diastereomer **17b** (R = Et).



Scheme 9

To generate functional group diversity, further manipulation of **8d**/**8d'** was also explored (Scheme 9). Dihydroxylation of (2'*S*)-**8d**/**8d'**, followed by glycol cleavage, gave a mixture of cyclopropylcarboxaldehydes **24**/**24'**, which are diastereomeric at the C2 carbon. Jones oxidation of **24**/**24'** followed by treatment with diazomethane gave a mixture of cyclopropane diesters **25**/**25'**, which are likewise diastereomeric at C2. Catalytic semireduction[28] of the nitro group of **25**/**25'** with H_2 over Pd/C gave the oxime (−)-**26** as a single optically active compound. The relative stereochemistry about the cyclopropane ring of **26** was assigned on the basis of its ^{1}H NMR spectral data. In particular, the signals for H1', H2', and H3' appear at δ 2.77 (dd, *J* = 4.8, 6.5 Hz), 2.63 (dd, *J* = 5.0, 9.3 Hz), 2.56 (dd, *J* = 6.5, 9.3 Hz) ppm. The oxime **26** is a hybrid between the mGluR2 agonist **16a**[22b] and the mGluR1 antagonist **19**.[24]

In summary, a novel iron-mediated methodology for the stereoselective preparation of 1,2,3-trisubstituted cyclopropanes was developed. The relative stereochemistry at the three cyclopropane centers is established by nucleophilic attack on the pentadienyl ligand on the face opposite iron and subsequent oxidatively induced reductive

elimination with retention of configuration. This methodology was applied to the enantioselective synthesis of 2-(2`-carboxycyclopropyl)glycines and analogues.

Experimental Section

General Data.

All ^{1}H NMR and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively. For diastereomeric mixtures, the diastereomeric ^{13}C NMR signals are noted in brackets. Melting points were obtained on a melting point apparatus and are uncorrected. Elemental analyses were obtained from Midwest Microlabs, Ltd., Indianapolis, IN, and high-resolution mass spectra were obtained from the Nebraska Center for Mass Spectrometry and the Washington University Resource for Mass Spectroscopy. Spectrograde solvents were used without purification with the exception of tetrahydrofuran, which was distilled from sodium benzophenone ketyl. Unless otherwise noted, all organic extracts were dried over $MgSO_4$ prior to concentration on a rotary evaporator. The compounds **1a**,[26] (1*R*)-**1a**,[26] **2a**,[10a] **2b**,[10a] and **15**[10b] were prepared by literature procedures.

Deuterated Iron Cation d-1a.

To a solution of tricarbonyl(methyl 6-oxo-2,4-hexadienoate)iron[26] (1.50 g, 5.36 mmol) in dry THF (45 mL) was added $NaBD_4$ (0.289 g, 6.43 mmol). The solution was stirred for 30 min, and then diluted with water (10 mL). The mixture was extracted with ether, and the combined extracts were concentrated. The residue was purified by column chromatography (SiO_2, hexanes:ethyl acetate = 3:1) to afford tricarbonyl(methyl 6-deuterio-6-hydroxy-2,4-hexadienoate)iron (**d-7**) as a yellow solid (1.00 g, 66%): ^{1}H NMR ($CDCl_3$) δ 5.83 (dd, *J* = 5.0, 8.1 Hz, 1H), 5.39 (dd, *J* = 5.1, 8.7 Hz, 1H), 3.70 (m) and 3.65 (s) (total 4H), 1.41 (t, *J* = 7.7 Hz, 1H), 1.07 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 172.7, 85.7, 83.9, 63.3 (t, J_{CD} = 22 Hz), 62.3, 51.6, 45.8. To a cold solution of HPF_6 (1.0 mL, 60% solution) in Ac_2O (2.5 mL) was added a solution of **d-7** (0.91 g, 3.2 mmol) in Ac_2O (2 mL) at 0 °C. The mixture was stirred for 20 min, during which time a bright yellow precipitate formed. The mixture was

added to a large excess of ether (300 mL) and the precipitate collected by vacuum filtration and dried in vacuo to afford **d-1a** as a bright yellow powder (0.86 g, 65%): mp 134−140 °C; ^{1}H NMR (CD_3NO_2) δ 7.30 (t, *J* = 6.9 Hz, 1H), 6.75 (dd, *J* = 7.2, 10.9 Hz, 1H), 6.44 (dd, *J* = 6.8, 12.7 Hz, 1H), 4.09 (d, *J* = 9.9 Hz, 0.25H), 3.89 (s, 3H), 2.62 (m, 1.75H); ^{13}C NMR (CD_3NO_2) δ 197.3, 197.1, 169.9, 108.0, 107.7, 99.8, 70.4 (t, J_{CD} = 26 Hz), 66.6, 54.7. Anal. Calcd for $C_{10}H_8DO_5FePF_6$: C, 29.22; H, 2.45. Found: C, 29.29; H, 2.38.

Deuterated Dimethyl Malonate−π-Allyliron Complex d-2a.

To a solution of lithium dimethyl malonate (1.87 mmol, freshly prepared from dimethyl malonate and *n*-butyllithium) in THF (10 mL) at 0 °C was added solid cation **d-1a** (0.70 g, 1.7 mmol) in one portion. The mixture was stirred at 0 °C for 1 h and then warmed to rt. Water (10 mL) was added, and the mixture was extracted with ethyl acetate. The combined organic extracts were concentrated. The residue was purified by column chromatography (SiO_2, hexanes:ethyl acetate = 10:1) to afford a mixture of **d-2a** and **d-4a** (ca. 6:1, 0.38 g, 56%).

Data for **d-2a**: ^{1}H NMR (C_6D_6) δ 4.16 (t, *J* = 7.1 Hz, 1H), 4.08 (dt, *J* = 10.7, 8.3 Hz, 1H), 3.71 (dd, *J* = 6.8, 12.2 Hz, 1H), 3.51, 3.28, and 3.22 (3 s, 9H), 2.81 (d, *J* = 10.7 Hz, 1H), 2.73 (d, *J* = 9 Hz, 0.25H), 1.84 (d, *J* = 12.5 Hz, 0.75H), 0.16 (d, *J* = 8.6 Hz, 1H); FAB-HRMS *m*/*z* 398.0269 (calcd for $C_{15}H_{16}DO_9Fe$ (M + H$^+$) *m*/*z* 398.0284). Data for **d-4a**: ^{1}H NMR (partial, C_6D_6) δ 5.75 (m, 1H), 4.55 (m, 1H), 3.26, 3.24, 3.23 (3 s), 2.26 (m, 1H), 2.21 (d, *J* = 8.5 Hz, 1H); ^{13}C NMR (partial, $CDCl_3$) δ 173.0, 171.9, 171.8, 92.6, 86.7, 60.3, 55.0, 45.9, 19.9. This compound was only characterized as a mixture with **d-2a**.

Deuterated Dimethyl Methylmalonate−π-Allyliron Complex d-2b.

To a solution of lithium dimethyl methylmalonate (0.53 mmol, freshly prepared from dimethyl methylmalonate and *n*-butyllithium) in THF (10 mL) at 0 °C was added solid cation **d-1** (0.20 g, 0.48 mmol)

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in one portion. The mixture was stirred at 0 °C for 1 h. Water (10 mL) was added, and the mixture was extracted with ethyl acetate. The combined organic extracts were concentrated. The residue was purified by column chromatography (SiO_2, hexanes:ethyl acetate = 3:1) to afford a mixture of **d-2b** and **d-4b** (ca. 8:1, 0.16 g, 81%).

Data for **d-2b**: mp 125−129 °C; ^{1}H NMR (C_6D_6) δ 4.46 (t, *J* = 7.3 Hz, 1H), 4.22 (dd, *J* = 7.3, 10.4 Hz, 1H), 3.78 (dd, *J* = 7.4, 12.3 Hz, 1H), 3.50, 3.27, and 3.26 (3 s, 9H), 2.67 (d, *J* = 8.8 Hz, 0.3H), 1.96 (d, *J* = 12.2 Hz, 0.7H), 1.18 (s, 3H), 0.47 (d, *J* = 10.5 Hz, 1H); ^{1}H NMR ($CDCl_3$) δ 4.72 (t, *J* = 7.4 Hz, 1H), 4.58 (dd, *J* = 7.4, 12.1 Hz, 1H), 3.86 (dd, *J* = 7.5, 10.5 Hz, 1H), 3.69, 3.64 and 3.63 (3 s, 9H), 3.40 (d, *J* = 8.4 Hz, 0.3H), 2.32 (d, *J* = 12.2 Hz, 0.7H), 1.10 (s, 3H), 0.33 (d, *J* = 10.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 210.3, 209.5, 203.6, 179.9, 171.0, 170.9, 98.8, 65.4, 59.4, 53.5 (t), 52.3, 51.2, 45.4, 17.5, 13.5. Anal. Calcd for $C_{16}H_{17}DO_9Fe$: C, 46.74; H, 4.66. Found: C, 47.46; H, 4.79. Data for **d-4b**: ^{1}H NMR (partial, $CDCl_3$) δ 6.15 (m, 1H), 5.29 (m, 1H), 2.51 (m, 1H), 2.18 (d, *J* = 8.6 Hz, 1H), 1.35 (s, 3H); ^{13}C NMR (partial, $CDCl_3$) δ 173.0, 171.9, 171.8, 92.6, 86.7, 60.3, 55.0, 45.9, 19.9. This compound was only characterized as a mixture with **d-2b**.

Reaction of 1a with Methyl Phenylsulfonylacetate Anion.

To a solution of methyl phenylsulfonylacetate (0.205 mL, 1.22 mmol) in THF (20 mL) at 0 °C was added a solution of *n*-butyllithium in hexanes (0.74 mL, 1.6 M, 1.16 mmol). The mixture was stirred for 30 min at 0 °C. Solid cation **1** (500 mg, 1.22 mmol) was added in one portion, and the mixture was stirred for 1 h at 0 °C and 1 h at rt. Distilled water (5 mL) was added and the mixture then poured into brine (10 mL) and extracted with ether. The combined ethereal layers were concentrated. Crystallization from ether gave a **2c/2c`** as a yellow solid (343 mg, 62%). The filtrate was concentrated, and the residue was purified by column chromatography ($SiO_2$, hexanes:ethyl acetate = 4:1) to afford additional **2c/c`** as a yellow solid (114 mg, 20%): mp 112−120 °C; ^{13}C NMR ($CDCl_3$) δ 209.7 [209.6], 209.4 [209.3], 203.0, 179.4 [178.9], 164.6 [163.8], 137.8 [136.7], 134.4, 129.5 [129.2], 128.9, 97.0 [97.4], 78.2 [76.8], 61.3, [57.9], 55.0 [54.4], 53.0 [52.7], 51.6 [51.4], 36.7 [36.6], 13.1 [9.1]. Anal. Calcd

for $C_{19}H_{18}O_9SFe$: C, 47.72; H, 3.79. Found: C, 48.25; H, 4.08. Data for **2c**: ^{1}H NMR ($CDCl_3$) δ 7.90−7.85 (m, 2H), 7.75−7.68 (m, 1H), 7.60−7.50 (m, 2H), 4.60 (m, 1H), 4.28 (t, *J* = 7.1 Hz, 1H), 3.97 (td, *J* = 7.8, 10.7 Hz, 1H), 3.76 (s, 3H), 3.67 (s and m, 4H), 3.54 (d, *J* = 10.7 Hz, 1H), 2.55 (dd, *J* = 2.9, 11.9 Hz, 1H), 0.52 (d, *J* = 8.3 Hz, 1H). Data for **2c`**: ^{1}H NMR ($CDCl_3$) δ 7.90−7.85 (m, 2H), 7.75−7.68 (m, 1H), 7.60−7.50 (m, 2H), 4.74 (t, *J* = 7.0 Hz, 1H), 4.62 (m, 1H), 4.05 (td, *J* = 8.0, 10.9 Hz, 1H), 3.65 (s and m, 5H), 3.44 (s, 3H), 2.42 (dd, *J* = 2.9, 15.5 Hz, 1H), −0.11 (d, *J* = 8.7 Hz, 1H).

Reaction of 1a with Diethyl Acetamidomalonate Anion.

To a solution of diethyl acetamidomalonate (159 mg, 0.74 mmol) in THF (15 mL) at 0 °C was added a solution of *n*-butyllithium in hexanes (0.36 mL, 1.6 M, 0.58 mmol), and this mixture was stirred for 20 min. Solid cation **1** (250 mg, 0.61 mmol) was added in one portion, and the reaction mixture was stirred for 1 h at 0 °C. Distilled water (5 mL) was added, and the mixture was extracted with ether. The combined ethereal extracts were concentrated. The residue was purified by column chromatography (SiO_2, hexanes:ethyl acetate = 4:1) to afford **2f** as a yellow oil (278 mg, 95%): ^{1}H NMR ($CDCl_3$) δ 6.38 (s, 1H), 4.90 (t, *J* = 7.5 Hz, 1H), 4.57 (td, *J* = 8.1, 12.2 Hz, 1H), 4.31−4.12 (m, 4H), 4.03 (qd, *J* = 7.0, 10.9 Hz, 1H), 3.63 (s, 3H), 3.41 (br d, *J* = 8.7 Hz, 1H), 2.35 (dd, *J* = 2.2, 12.5 Hz, 1H), 1.96 (s, 3H), 1.27 and 1.22 (2 t, *J* = 7.0 Hz, 6H), 0.27 (d, *J* = 10.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 210.3, 209.4, 203.6, 179.3, 169.0, 166.9, 166.3, 98.7, 70.0, 65.8, 62.7, 53.1, 51.2, 44.8, 23.1, 13.9, 13.7, 11.6; FAB-LRMS *m/z* 488 (calcd for $C_{19}H_{23}NO_{10}FeLi$ *m/z* 488).

Reaction of 1a with Ethyl N-(Diphenylmethylene)glycinate Anion.

To a solution of ethyl *N*-(diphenylmethylene)glycinate (179 mg, 0.67 mmol) in THF (15 mL) at 0 °C was added a solution of *n*-butyllithium in hexanes (0.36 mL, 1.6 M, 0.58 mmol). The resultant bright yellow solution was stirred for 30 min at 0 °C. Solid cation **1** (250 mg, 0.61 mmol) was added in one portion, and the mixture was stirred for 1 h at 0°C. Distilled water (5 mL) was added, and the mixture was extracted with ether. The combined ethereal layers were

concentrated. The residue was purified by column chromatography (SiO_2, hexanes:ethyl acetate = 10:1) to afford a 1:1 mixture of diastereomeric complexes **2e**/**2e`** as a yellow oil (54.3 mg, 18%): ^{1}H NMR ($CDCl_3$) δ 7.69 (d, *J* = 6.7 Hz, 1H), 7.51−7.29 (m, 7H), 7.15 (m, 2H), 4.50 (m, 2H), 4.06 (q, *J* = 7.5 Hz, 1H), 4.15 (q, *J* = 7.5 Hz, 1H), 3.88 (m, 1H), 3.64 and 3.59 (2 s, 3H total), 3.56 (d, *J* = 8.2 Hz, 0.5H), 3.49 (d, *J* = 8.4 Hz, 0.5H), 3.38 (d, *J* = 7.5 Hz, 0.5H), 3.27 (d, *J* = 8.4 Hz, 0.5H), 2.18 (dd, *J* = 1.7, 12.3 Hz, 0.5H), 1.97 (dd, *J* = 2.2, 11.9 Hz, 0.5H), 1.27 and 1.18 (2 t, *J* = 7.2 Hz, 3H total), 0.14 (d, *J* = 9.1 Hz, 0.5H), 0.08 (d, *J* = 8.7 Hz, 0.5H). This compound was not further characterized.

Reaction of rac-*1a with Methyl Nitroacetate Anion.*

To a solution of methyl nitroacetate (135 μL, 1.46 mmol) in THF (20 mL) was added a solution of *n*-butyllithium (724 mL, 1.6 M in THF, 1.16 mmol), and this mixture was stirred for 20 min at 0 °C. Solid cation *rac*-**1** (500 mg, 1.22 mmol) was added in one portion. The reaction mixture was stirred at 0 °C for 20 min, then distilled water (5 mL) was added, and the mixture was warmed to rt. The mixture was extracted with distilled ether (4 × 15 mL). The combined ethereal fractions were concentrated to afford a solid. The solid was collected by vacuum filtration and washed with cold ether to afford *rac*-**2d** (129 mg, 30%). The filtrate was concentrated and purified by column chromatography (silica gel, 0.35−0.07 mm, hexanes:ethyl acetate = 8:1) to afford *rac*-**2d`** as a yellow solid (48.4 mg, 11%), followed by a mixture of *rac*-**2d**/**2d`** as a yellow oil (135 mg, 31%) and finally a diastereomeric mixture of diene complexes *rac*-**4d** (30.0 mg, 7%). Data for *rac*-**2d**: mp 89−91 °C; ^{1}H NMR ($CDCl_3$) δ 4.70 (ddd, *J* = 7.1, 8.3, 12.5 Hz, 1H), 4.47 (t, *J* = 10.8 Hz, 1H), 4.51−4.45 (m, 1H), 4.12 (ddd, *J* = 7.1, 8.7, 10.7 Hz, 1H), 3.70 and 3.69 (2 s and m, 7H), 2.49 (dd, *J* = 2.9, 12.5 Hz, 1H), 0.22 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 209.4, 209.1, 202.7, 178.9, 162.7, 98.8, 91.6, 58.4, 55.2, 53.4, 51.7, 39.7, 9.1. Anal. Calcd for $C_{13}H_{13}NO_7Fe$: C, 40.76; H, 3.42; N, 3.65. Found: C, 40.55; H, 3.36; N, 3.50. Data for *rac*-**2d`**: mp 125−130 °C dec; ^{1}H NMR ($CDCl_3$) δ 4.70 (ddd, *J* = 7.0, 8.7, 12.5 Hz, 1H), 4.55 (t, *J* = 7.2 Hz, 1H), 4.48 (d, *J* = 10.2 Hz, 1H), 4.17 (ddd, *J* = 7.1, 8.2, 10.1 Hz, 1H), 3.83 (s, 3H), 3.68 (s and m, 4H), 2.50 (dd, *J* = 2.8, 12.5 Hz, 1H), 0.21 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ

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209.4, 209.0, 202.8, 178.9, 163.0, 98.4, 91.7, 58.4, 54.5, 53.5, 51.7, 39.9, 9.0. Anal. Calcd for $C_{13}H_{13}NO_7Fe$: C, 40.76; H, 3.42; N, 3.65. Found: C, 40.85; H, 3.50; N, 3.60. Data for *rac*-**4d**: ^{1}H NMR ($CDCl_3$) δ 6.08 (m, 1H), 5.31 (m, 1H), 5.11 (dd, *J* = 4.1, 10.3 Hz, 0.5H), 4.93 (dd, *J* = 5.9, 8.8 Hz, 0.5H), 3.83 (s, 3H), 3.70 (s, 3H), 2.67 (ddd, *J* = 4.2, 8.6, 14.8 Hz, 0.5 H), 2.49 (m, 1.5H), 2.12 (m, 1H), 1.96 (m, 0.5H), 1.80 (ddd, *J* = 5.2, 10.4, 15.3 Hz, 0.5H); ^{13}C NMR ($CDCl_3$) δ 172.6, 163.9, 93.9, 89.2 (89.1), 85.2, 53.8, 51.9 (51.1), 50.3, 46.2 (46.1), 30.9 (30.5). This compound was not further characterized.

Oxidative Decomplexation of 2a.

To a solution of **2a** (750 mg, 1.89 mmol) in DMF (50 mL) at rt was added in one portion solid CAN (3.11 g, 5.67 mmol). After 10 min, an additional portion of CAN (3.11 g, 5.67 mmol) was added, and after a further 10 min a final portion of CAN (4.15 g, 7.56 mmol) was added. The reaction mixture was stirred for 3 h, poured into water (20 mL), and extracted with ether. The combined extracts were washed with water, followed by brine, dried, and concentrated. The residue was purified by chromatography (SiO_2, hexanes:ethyl acetate = 10:1) to give a mixture of **8a** and **9a** (>10:1) as a colorless oil (340 mg, 70%): ^{1}H NMR (C_6D_6) δ 5.26 (ddd, *J* = 7.5, 9.9, 17.1 Hz, 1H), 4.93 (d, *J* = 17.1 Hz, 1H), 4.88 (d, *J* = 11.4 Hz, 1H), 3.27, 3.26, and 3.25 (3 s, 9H), 3.04 (d, *J* = 11.0 Hz, 1H), 2.57 (ddd, *J* = 4.9, 9.6, 11.1 Hz, 1H), 2.33 (dt, *J* = 4.9, 8.5 Hz, 1H), 1.76 (apparent t, *J* = 4.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 172.4, 168.8, 168.1, 131.9, 118.9, 52.9, 52.7, 52.1, 50.3, 28.9, 25.9, 25.2; EI-HRMS *m/z* 256.0949 (calcd for $C_{12}H_{16}O_6$ *m/z* 256.0947).

Oxidative Decomplexation of 2b.

To a solution of **2b** (0.12 g, 0.29 mmol) in DMF (15 mL) at rt was added in one portion solid CAN (1.75 g, 3.19 mmol). The reaction mixture was stirred for 3 h, poured into water (20 mL), and extracted with CH_2Cl_2 (3 × 25 mL). The combined extracts were concentrated. The residue was purified by chromatography (SiO_2, hexanes:ethyl acetate = 3:1) to give **9b** as translucent oil (44 mg, 56%): ^{1}H NMR (C_6D_6) δ 6.14 (ddd, *J* = 8.8, 10.2, 17.1 Hz, 1H), 5.18 (dd, *J* = 1.8, 17.1 Hz, 1H), 5.02 (dd, *J* = 1.8, 10.2 Hz, 1H), 3.31, 3.22, and 3.21 (3

s, 9H), 2.61 (dd, *J* = 5.9, 6.6 Hz, 1H), 2.18 (dd, *J* = 5.9, 9.3 Hz, 1H), 2.00 (dt, *J* = 6.7, 9.0 Hz, 1H), 1.23 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 171.3, 171.1, 133.8, 117.2, 52.8, 52.7, 51.8, 31.5, 27.9, 24.2, 18.5; EI-HRMS *m*/*z* 270.1096 (calcd for $C_{13}H_{18}O_6$ *m*/*z* 270.1103).

Oxidative Decomplexation of d-2a.

To a solution of **d-2a** (120 mg, 0.30 mmol) in DMF (10 mL) at rt was added in one portion solid CAN (1.66 g, 3.02 mmol). The reaction mixture was stirred for 3 h, poured into water (20 mL), and extracted with ether. The combined extracts were washed with water, followed by brine, dried, and concentrated. The residue was purified by chromatography (SiO_2, hexanes:ethyl acetate = 10:1) to give a mixture of **d-8a** and **d-3a** (>10:1) as a colorless oil (40 mg, 52%) followed by recovered **d-2a** (30 mg): ^{1}H NMR (C_6D_6) δ 5.26 (dd, *J* = 7.8, 16.8 Hz, 1H), 4.93 (d, *J* = 16.8 Hz, 0.72H), 4.88 (d, *J* = 10.5 Hz, 0.28H), 3.27, 3.26, and 3.25 (3 s, 9H), 3.04 (d, *J* = 11.0 Hz, 1H), 2.61 (ddd, *J* = 4.9, 9.1, 14.2 Hz, 1H), 2.33 (dt, *J* = 4.9, 8.5 Hz, 1H), 1.76 (apparent t, *J* = 4.9 Hz, 1H); EI-HRMS *m*/*z* 257.1010 (calcd for $C_{12}H_{15}DO_6$ *m*/*z* 257.1010).

Oxidative Decomplexation of d-2b.

To a solution of **d-2b** (0.16 g, 0.39 mmol) in DMF (15 mL) at rt was added in one portion solid CAN (2.13 g, 3.89 mmol). The reaction mixture was stirred for 3 h, poured into water (20 mL), and extracted with ether. The combined extracts were washed with water, followed by brine, dried, and concentrated. The residue was purified by chromatography (SiO_2, hexanes:ethyl acetate = 10:1) to give **d-9b** as translucent oil (50 mg, 46%): ^{1}H NMR (C_6D_6) δ 6.14 (m, 1H), 5.17 (d, *J* = 17.1 Hz, 0.25H), 5.01 (d, *J* = 10.5 Hz, 0.75H), 3.31, 3.22, and 3.21 (3 s, 9H), 2.61 (t, *J* = 6.8 Hz, 1H), 2.18 (dd, *J* = 5.9, 9.3 Hz, 1H), 2.00 (dt, *J* = 6.7, 9.0 Hz, 1H), 1.23 (s, 3H); EI-HRMS *m*/*z* 271.1158 (calcd for $C_{13}H_{17}DO_6$ *m*/*z* 271.1166).

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Methyl 2-(2'-Methoxycarbonyl-3'-vinylcyclopropyl)-2-phenylsulfonylacetate (8c/ 8c').

To a solution of **2c**/**2c'** (1.92 g, 4.02 mmol) in DMF (100 mL) at rt was added, over a 30 min period, solid CAN (22.03 g, 40.02 mmol) in three portions. The reaction mixture was stirred for 3 h, poured into water (100 mL), and extracted with ether. The combined extracts were washed with water, dried, and concentrated. The residue was purified by chromatography (SiO_2, hexanes:ethyl acetate = 4:1) to give **8c**/**8c'** as an oil (1.181 g, 87%): IR (neat, cm^{-1}) 1739; ^1H NMR (300 MHz, $CDCl_3$) δ 7.90−7.85 (m, 2H), 7.75−7.68 (m, 1H), 7.61−7.54 (m, 2H), 5.50 (ddd, *J* = 7.5, 10.1, 17.1 Hz, 1H), 5.27−5.19 (m, 2H), 3.77 and 3.71 (2 s, 6H), 3.64 (d, *J* = 10.7 Hz, 1H), 2.25 (br q, *J* = 7.3 Hz, 1H), 2.00−1.96 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.5, 165.4, 136.6, 134.5, 130.9, 129.4, 129.0, 119.8, 69.6, 53.2, 52.1, 28.1, 25.7, 24.0; FAB-HRMS *m/z* 339.0890 (calcd for $C_{16}H_{18}O_6SH^+$ *m/z* 339.0902).

Methyl 2-(2'-Methoxycarbonyl-3'-vinylcyclopropyl)-2-nitroacetate (rac-8d/8d').

To a mixture of diastereomeric complexes *rac*-**2c**/**2c'** (159 mg, 0.41 mmol) in anhydrous CH_3CN (15 mL) at rt was added, over a 30 min period, solid CAN (2.27 g, 4.10 mmol) in three portions. The reaction mixture was poured into water (10 mL) and extracted with ether. The combined extracts were washed with water, dried, and concentrated. The residue was purified by column chromatography (silica gel 0.35−0.07 mm, hexanes:ethyl acetate = 10:1) to give a mixture of *rac*-**8d**/**d'** as a colorless oil (77.8 mg, 78%): ^1H NMR ($CDCl_3$) δ 5.74−5.58 (m, 1H), 5.32−5.26 (m, 2H), 4.71 and 4.67 (2 d, *J* = 10.6 Hz, total 1H), 3.86 (2 s, total 3H), 3.73 and 3.72 (2 s, total 3H), 2.52−2.47 (m, 2H), 2.04 (t, *J* = 5.0 Hz, 1H), ^{13}C NMR ($CDCl_3$) δ 171.1, 163.5, 130.6 [129.9], 120.6 [120.2], 86.5 [85.6], 53.9 [53.8], 52.3, 29.1 [28.3], 26.3 [25.4], 24.5 [24.3]; FAB-HRMS *m/z* 244.0827 (calcd for $C_{10}H_{14}NO_6$ (M + H^+) *m/z* 244.0821).

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Methyl (2-Nitromethyl-3-vinylcyclopropane)carboxylate (8g).

To a solution of **14**[10b] (360 mg, 0.617 mmol) in CH_3CN (20 mL) at rt was added, over a 30 min period, solid CAN (3.50 g, 6.39 mmol) in three portions. The reaction mixture was stirred for 2 h, poured into ether (200 mL), and washed with brine. The ether layer was dried and concentrated. The residue was purified by chromatography (SiO_2, hexanes:ethyl acetate = 3:1) to give **8g** as an oil (70 mg, 61%): ^{1}H NMR (300 MHz, C_6D_6) δ 4.92 (ddd, *J* = 7.2, 9.6, 17.4 Hz, 1H), 4.81−4.74 (m, 2H), 3.39 (ABdd, 7.8, 14.4 Hz, 2H), 3.24 (s, 3H), 2.10 (ddd, *J* = 4.8, 6.9, 9.0 Hz, 1H), 1.93 (dtd, *J* = 4.8, 7.8, 9.2 Hz, 1H), 1.41 (t, *J* = 4.9 Hz, 1H); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.61 (ddd, *J* = 7.2, 10.5, 17.4 Hz, 1H), 5.27 (td, *J* = 1.0, 17.1 Hz, 1H), 5.24 (td, *J* = 1.0, 10.2 Hz, 1H), 4.38 (d, *J* = 7.8 Hz, 2H), 3.71 (s, 3H), 2.31 (m, 1H), 2.28 (dtd, *J* = 4.8, 7.8, 9.6 Hz, 1H), 1.90 (t, *J* = 4.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.7, 130.9, 119.7, 73.5, 52.2, 28.9, 24.8, 23.4; EI-HRMS *m*/*z* 186.0762 (calcd for $C_8H_{13}NO_4H^+$ *m*/*z* 186.0766).

p-Nitrobenzoate 10.

To a solution of **8b** (0.20 g, 0.70 mmol) in dry THF (10 mL) at 0 °C was added a solution of BH_3·THF (0.74 mL, 1.0 M in THF, 0.74 mmol). The mixture was stirred at 0 °C for 1 h and then treated with 1.0 M KOH (0.93 mL) and 30% H_2O_2 (0.74 mL). After 1 min, the mixture was poured into brine (25 mL) and extracted with ether (2 × 25 mL). The combined etheral extracts were washed with water, followed by brine, dried, and concentrated. The residue was purified by chromatography (SiO_2, hexanes:ethyl acetate = 3:1) to give recovered **8b** (40 mg) followed by a colorless oil (70 mg, 40% based on consumed **8b**): ^{1}H NMR (C_6D_6) δ 3.58 (m, 2H), 3.35, 3.24 and 3.23 (3 s, 9H), 2.52 (br s, OH), 2.27 (dd, *J* = 5.4, 7.2 Hz, 1H), 1.98−1.75 (m, 3H), 1.38 (m, 1H), 1.18 (s, 3H); ^{13}C NMR (C_6D_6) δ 171.8, 62.0, 53.5, 52.3, 51.4, 31.3, 30.2, 22.8, 21.3, 18.4. To a solution of the above alcohol (0.19 g, 0.66 mmol) in pyridine (4 mL) at rt was added *p*-nitrobenzoyl chloride (0.14 g, 0.76 mmol). The reaction mixture was stirred for 3 h, then poured into water (25 mL), and extracted with ether (2 × 25 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ (20 mL), followed by brine (20 mL), dried, and

concentrated. The residue was purified by chromatography (SiO_2, hexanes:ethyl acetate = 1:1) to give **10** as an oil (0.18 g, 62%). Recrystallization (hexanes−ethyl acetate) gave a white solid: mp 67−68 °C; ^{1}H NMR (C_6D_6) δ 7.83−7.76 (AB qt, 4H), 4.30−4.13 (m, 2H), 3.33, 3.30, and 3.28 (3 s, 9H), 2.20 (dd, *J* = 5.5, 7.0 Hz, 1H), 2.04 (m, 2H), 1.93 (dd, *J* = 5.4, 9.1 Hz, 1H), 1.34 (dd, *J* = 7.0, 9.1 Hz, 1H), 1.21 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 171.6, 171.3, 171.2, 164.4, 150.5, 135.6, 130.6, 123.4, 65.3, 53.2, 52.3, 51.5, 31.5, 25.9, 21.9, 21.7, 18.6. Anal. Calcd for $C_{20}H_{23}NO_{10}$: C, 54.92; H, 5.30. Found: C, 55.27; H, 5.41.

Methyl 2-(2'-Methoxycarbonyl-3'-ethylcyclopropyl)-2-phenylsulfonylacetate (15).

To a solution of **8c**/**c'** (300 mg, 0.887 mmol) in methanol (10 mL) in a 50 mL heavy-walled reaction vessel was added 10% Pd/C (20 mg). The mixture was shaken for 1 h in a Parr hydrogenation apparatus under H_2 pressure (45 psi). After removal of the excess H_2 gas, the reaction mixture was filtered and concentrated. The residue was purified by chromatography (hexanes:ethyl acetate = 4:1) to give **15** as a colorless oil which solidified upon standing (273 mg, 90%): mp 69−87 °C; ^{1}H NMR ($CDCl_3$) δ 7.94−7.82 (m, 2H), 7.72−7.64 (m, 1H), 7.51−7.50 (2H), 3.79 and 3.67 (2 s, 6H), 3.64 (d, *J* = 11.6 Hz, 1H), 1.77 (ddd, *J* = 4.8, 9.0, 11.4 Hz, 1H), 1.55 (t, *J* = 5.0 Hz, 1H), 1.52−1.42 (m, 1H), 1.40−1.18 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 172.4, 165.9, 136.5, 134.4, 129.5, 128.9, 69.7, 53.2, 51.9, 27.6, 25.8, 23.5, 20.9, 13.4. Anal. Calcd for $C_{16}H_{20}O_6S$: C, 56.46; H, 5.92. Found: C, 56.28; H, 6.06.

Methyl 2-[3'-Ethyl-2'-(methoxycarbonyl)cyclopropyl]glycinate (rac-19/19').

To a solution of diastereomers *rac*-**8d**/**d'** (272 mg, 1.12 mmol) in methanol (10 mL) in a 50 mL heavy-walled reaction vessel was added a slurry of Raney nickel (50 wt % in water, 0.5 mL). The mixture was shaken for 2 h in a Parr hydrogenation apparatus under H_2 pressure (45 psi). The reaction mixture was filtered through a filter aid, and the filter bed was washed with CH_2Cl_2. The filtrate was dried

and concentrated. The residue was purified by column chromatography (silica gel 0.35−0.07 mm, CH_2Cl_2:methanol = 20:1) to give a mixture of *rac*-**19**/**19'** as a colorless oil (176 mg, 73%): IR (neat) 3385, 3304, 2955, 1731 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.76 (s, 1.5H), 3.74 (s, 1.5H), 3.67 (s, 1.5H), 3.66 (s, 1.5H), 3.13 (d, *J* = 10.5 Hz, 0.5 H), 3.11 (d, *J* = 10.1 Hz, 0.5 H), 1.78−1.23 (m, 7H); ^{13}C NMR ($CDCl_3$) δ 175.0 [174.6], 174.0 [173.6], 53.3 [53.2], 52.2 [51.7], 32.4, 31.5, 30.0, 28.5, 25.1, 21.3 [20.5], 13.8 [13.7]; FAB-HRMS *m*/*z* 216.1237 (calcd for $C_{10}H_{18}NO_4$ ($M + H^+$) *m*/*z* 216.1236).

Methyl N-(Diphenylmethylene)-2-[3'-ethyl-2'-(methoxycarbonyl)cyclopropyl]glycinate (rac-20/21).

To a solution of diastereomers *rac*-**19**/**19'** (80.1 mg, 0.37 mmol) in CH_2Cl_2 (10 mL) was added benzophenone imine (83.0 mg, 0.457 mmol). The solution was heated at reflux for 14 h. After this time, TLC monitoring indicated disappearance of the starting material. The resultant solution was concentrated, and the residue was purified by column chromatography (silica gel 0.35−0.07 mm, hexanes:ethyl acetate = 10:1) to give *rac*-**20** (24.8 mg, 18%) followed by a mixture of *rac*-**20** and *rac*-**21** (13.9 mg, 10%) and finally *rac*-**21** (19.2 mg, 14%) all as colorless solids. Data for *rac*-**20**: mp 93−95 °C; ^1H NMR ($CDCl_3$) δ 7.64 (m, 2H), 7.40 (m, 6H), 7.21 (m, 2H), 3.82 (d, *J* = 9.4 Hz, 1H), 3.76 (s, 3H), 3.64 (s, 3H), 2.28 (ddd, *J* = 4.7, 9.5, 9.5 Hz, 1H), 1.54 (m, 1H), 1.24 (m, 1H), 0.97 (t, *J* = 4.8 Hz, 1H), 0.85 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 173.9, 171.6, 136.0, 130.5, 129.0, 128.8, 128.6, 128.1, 128.0, 64.1, 52.3, 51.7, 30.4, 29.3, 25.0, 21.5. 13.6. Anal. Calcd for $C_{23}H_{25}NO_4 \cdot {}^1/_4H_2O$: C, 71.95; H, 6.69; N, 3.65. Found: C, 72.13; H, 6.69; N, 3.60. Data for

rac-**21**: mp 73−74 °C; ^1H NMR ($CDCl_3$) δ 7.64 (m, 2H), 7.38 (m, 6H), 7.16 (m, 2H), 3.78 (d, *J* = 9.6 Hz, 1H), 3.73 (s, 3H), 3.66 (s, 3H), 2.33 (ddd, *J* = 4.6, 9.4, 9.4 Hz, 1H), 1.51 (m, 1H), 1.35 (dd, *J* = 4.8, 4.8 Hz, 1H), 1.20 (m, 1H), 1.01 (m, 1H), 0.91 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 174.0, 172.1, 170.6, 139.4, 135.9, 130.5, 129.0, 128.4, 128.1, 127.8, 64.5, 52.3, 51.7, 30.8, 28.6, 24.0, 20.7. 14.0. Anal. Calcd for $C_{23}H_{25}NO_4 \cdot {}^1/_4H_2O$: C, 71.95; H, 6.69; N, 3.65. Found: C, 71.95; H, 6.70; N, 3.63.

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Optically Active Methyl 2-(2‘-Methoxycarbonyl-3‘-vinylcyclopropyl)-2-nitroacetate [(2‘S)-8d/d‘].

Addition of the lithium salt of methyl nitroacetate to cation (1*R*)-**1a** (500 mg, 1.22 mmol) was carried out in a fashion similar to that of the addition of this anion to *rac*-**1a**. The residue was dissolved in anhydrous CH_3CN (30 mL), and solid CAN (6.35 g, 11.6 mmol) was added to the solution in three portions over a 30 min period. The reaction mixture was stirred for 1 h, and then poured into water (15 mL). The mixture was extracted with ether, and the combined ethereal extracts were washed with water (15 mL), dried, and concentrated. The residue was purified by column chromatography (silica gel 0.35−0.07 mm, hexanes:ethyl acetate = 10:1) to give a mixture of (2‘S)-**8d**/**d‘** as a colorless oil (151.5 mg, 54%). The ^{1}H NMR spectral data for this mixture were identical with those of the racemic material.

Preparation of (−)-20 and (+)-21.

To a solution of (2‘*S*)-**8d**/**d‘** (104 mg, 0.430 mmol) in methanol (15 mL) in a 50 mL heavy-walled vessel was added a slurry of Raney nickel (50 wt % in water, 0.25 mL). The mixture was shaken under H_2 pressure (45 psi) in a Parr hydrogenation apparatus for 2 h. The reaction mixture was filtered through a filter aid, and the filter bed was washed with CH_2Cl_2. The filtrate was dried and concentrated. The residue was dissolved in CH_2Cl_2 (10 mL), and benzophenone imine (89.3 μL, 0.52 mmol) was added. The reaction mixture was heated at reflux for 14 h, cooled, and concentrated. The residue was purified by column chromatography (silica gel 0.35−0.07 mm, hexanes:ethyl acetate = 10:1) to give (−)-**20** (57.7 mg, 35%) followed by (+)-**21** (50.7 mg, 31%) both as colorless solids. Data for (−)-**20:** mp 56−58 °C; $[\alpha]_D$ = −53 (*c* = 0.1, $CHCl_3$). The ^{1}H NMR spectral data for (−)-**20** were identical with those of *rac*-**20**.

Data for (+)-**21:** mp 86−87 °C; $[\alpha]_D$ = +99 (*c* = 0.1, $CHCl_3$). The ^{1}H NMR spectral data for (+)-**22** were identical with those of *rac*-**21**.

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(2S,1'S,2'S,3'R)-2-(3'-Ethyl-2'-carboxycyclopropyl)glycine [(+)-22].

A mixture of (−)-**20** (50 mg, 0.13 mmol) and hydrochloric acid (6 N, 5 mL) was heated at reflux for 14 h. The reaction mixture was concentrated under reduced pressure. The solid residue was dissolved in distilled water (5 mL) and extracted with CH_2Cl_2 (5 mL). The aqueous layer was concentrated under reduced pressure. The residue was dissolved in hydrochloric acid (1 N, 5 mL) and concentrated under reduced pressure to give the hydrochloride salt as a hygroscopic pale white solid (29.5 mg, 97%). A small sample of the hydrochloride salt was dissolved in a mixture of absolute ethanol (1 mL) and water (1 mL) and treated with propylene oxide (1 mL). After the solution was stirred for 15 min, the solvents were evaporated under reduced pressure, and the residue was dried under high vacuum to afford (+)-**22** as an off-white solid: mp 174−179 °C dec; $[\alpha]_D$ = +36 (*c* = 0.21, D_2O); ^{1}H NMR (D_2O) δ 3.47 (d, *J* = 11.2 Hz, 1H), 1.87−1.75 (m, 2H), 1.71−1.61 (m, 1H), 1.54 (t, *J* = 4.8 Hz, 1H), 1.32−1.17 (m, 1H), 1.05 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (D_2O) δ 179.3, 174.5, 56.5, 33.3, 30.9, 28.0, 23.7, 15.6; FAB-HRMS *m/z* 188.0929 (calcd for $C_8H_{14}NO_4$ (M + H^+) *m/z* 188.0923).

(2R,1'S,2'S,3'R)-2-(3'-Ethyl-2'-carboxycyclopropyl)glycine [(−)-23].

The hydrolysis of (+)-**21** (48.0 mg, 0.13 mmol) with hydrochloric acid was carried out in a fashion similar to that of the hydrolysis of (−)-**20**. The residue was redissolved in hydrochloric acid (1 N, 5 mL) and concentrated under reduced pressure to give the hydrochloride salt as a white solid (26.2 mg, 95%). A small sample of the hydrochloride salt was dissolved in a mixture of absolute ethanol (1 mL) and water (1 mL) and treated with propylene oxide (1 mL). After the solution was stirred for 15 min, the solvents were evaporated under reduced pressure, and the residue was dried under high vacuum to afford (−)-**23** as an off-white solid: $[\alpha]_D$ = −32 (*c* = 0.16, D_2O); ^{1}H NMR (D_2O) δ 3.41 (d, *J* = 10.6 Hz, 1H), 1.84−1.70 (m, 3H), 1.63−1.54 (m, 1H), 1.22−1.10 (m, 1H), 1.05 (t, *J* = 7.0 Hz, 3H); ^{13}C

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NMR (D_2O) δ 179.1, 175.0, 55.6, 31.5, 30.4, 28.5, 22.7, 15.7; FAB-HRMS *m/z* 188.0923 (calcd for $C_8H_{14}NO_4$ (M + H^+) *m/z* 188.0923).

Methyl 2-(2'-Formyl-3'-methoxycarbonylcyclopropyl)-2-nitroacetate [(1'S,2'R,3'R)-24/24'].

To a solution of (1'*S*)-**8d**/**d'** (460 mg, 1.89 mmol) in acetone (15 mL) and water (1 mL) was added *N*-methylmorpholine *N*-oxide, followed by a solution of OsO_4 in toluene (0.25 mL, ca. 2 M, ca. 0.05 mmol). The reaction mixture was stirred at rt for 18 h, until TLC monitoring (hexanes:ethyl acetate = 4:1) indicated the disappearance of the vinylcyclopropane. Solid Na_2SO_3 (2 g) was added, and the mixture was stirred for an additional 1 h. The reaction mixture was concentrated and purified by column chromatography (hexanes:ethyl acetate = 4:1) to afford a mixture of diols as a colorless oil (300 mg, 57% yield). To a solution of the above diol mixture (300 mg, 1.08 mmol) in CH_2Cl_2 (20 mL) and water (1 mL), cooled to 0 °C, was added solid $NaIO_4$ (290 mg, 2.20 mmol). The reaction mixture was stirred at 0 °C for 15 min, warmed to rt, and stirred for 1 h. Solid $MgSO_4$ (4 g) was added, and the mixture was stirred for 30 min, at which time it was filtered and concentrated. The residue was purified by column chromatography (hexanes:ethyl acetate = 4:1) to afford **24**/**24'** as a colorless oil (222 mg, 84%): ^{1}H NMR ($CDCl_3$) δ 9.96 (d, *J* = 7.0 Hz, 1H), 5.33 and 5.32 (2 d, *J* = 10.8 Hz, 1H total), 3.89, 3.84, 3.76, 3.75 (4 s, total 6H), 3.05−2.97 (m, 1H), 2.83−2.73 (m, 1H), 2.62 and 2.60 (2 t, *J* = 4.8 Hz, 1H total). This compound was used in the next step without further characterization.

Methyl 2-[2',3'-Bis(methoxycarbonyl)cyclopropyl)-2-nitroacetate [(2'S,3'S)-25/25'].

To a solution of aldehyde **24**/**24'** (222 mg, 0.907 mmol) in acetone (10 mL), cooled to 0 °C, was added a solution of Jones reagent (1.12 g of CrO_3 in 0.75 mL of concd H_2SO_4, 1.25 mL of water). The reaction mixture was stirred at 0 °C for 2 h, and then poured into 1 N HCl (40 mL). The mixture was extracted with CH_2Cl_2, and the combined extracts were dried and concentrated. The residue was purified by column chromatography (SiO_2, hexanes:ethyl acetate =

1:1) to afford the carboxylic acid as a colorless oil (200 mg, 88%). To a solution of the carboxylic acid (190 mg, 0.728 mmol) in ether (30 mL) was cautiously added an ethereal solution of diazomethane (prepared from MNNG and KOH) until the yellow color presisted. The reaction mixture was flushed with N_2 until colorless, and then dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO_2, hexanes−ethyl acetate = 1:1) to afford **25**/**25'** as a colorless oil (160 mg, 80%): ^{1}H NMR ($CDCl_3$) δ 5.54 (br d, *J* = 8.7 Hz) and 5.52 (d, *J* = 10.3 Hz, total 1H), 3.89, 3.88, 3.85, 3.77, 3.76, 3.75 (6 s, total 9H), 2.67−2.54 (m, 2H), 2.47 and 2.45 (2 d, *J* = 5.7 Hz, 1H total); ^{13}C NMR ($CDCl_3$) δ 170.0, 169.9, 164.3 [163.9], 84.3 [83.8], 54.1 [54.0], 53.0 [52.9], 52.7 [52.5], 26.9, 26.4, [26.3], 26.1, [25.5]. This compound was used in the next step without further characterization.

Methyl 2-[2',3'-Bis(methoxycarbonyl)cyclopropyl]-2-(hydroxyimino)acetate [(−)-26].

A solution of nitrocyclopropane **25**/**25'** (70 mg, 0.25 mmol) and 10% Pd/C (5 mg) in ethyl acetate (5 mL) was stirred under a balloon of H_2 for 7 h. The reaction mixture was filtered through a filter aid, and the filter bed was washed with ethyl acetate. The solvent was evaporated, and the residue was purified by column chromatography (SiO_2, hexanes:ethyl acetate = 4:1) to give (−)-**26** as a colorless oil (60 mg, 92%): $[\alpha]_D$ = −11 (*c* = 0.4, MeOH); IR (neat, cm^{-1}) 3320, 1720; ^{1}H NMR ($CDCl_3$) δ 3.85, 3.77, 3.67 (3 s, total 9H), 2.77 (dd, *J* = 4.8, 6.5 Hz, 1H), 2.63 (dd, *J* = 5.0, 9.3 Hz, 1H), 2.56 (dd, *J* = 6.5, 9.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 171.3, 170.3, 163.3, 146.3, 52.9, 52.7, 52.5, 27.5, 27.2, 22.4; FAB-HRMS *m*/*z* 260.0763 (calcd for $C_{10}H_{14}NO_7$ (M + H$^+$) *m*/*z* 260.0770).

Acknowledgment

We are grateful to Prof. Douglas Stephen (University of Windsor) for obtaining the X-ray crystal structure of **2c** and **2d'**. Mr. Nathaniel J. Wallock is acknowledged for obtaining spectral data for (+)-**22** and (−)-**23**. Financial support for this work was provided by the National Institutes of Health (Grant No. GM-42641), with partial financial support from the Petroleum Research Fund (Grant No. 34297-AC1). High-resolution mass spectral determinations were made at the Nebraska Center for Mass Spectrometry and the

Washington University Mass Spectrometry Resource, an NIH Research Resource (Grant No. P41RR0954).

Supporting Information Available

^{1}H and/or ^{13}C NMR spectra of **d-2a**, **2e/2e`**, **2f**, **4d**, **8a**, **d-8a**, **9b**, **d-9b**, **8c**/**8c`**, **8d**/**8d`**, **8g**, **19**/**19`**, (+)-**22**, (−)-**23**, **24**/**24`**, **25**/**25`**, and (−)-**26** and the X-ray data for **2c** and **2d`** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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