Functionalized Carbocycles by Tandem Dealkoxycarbonylation–Michael Addition Reactions

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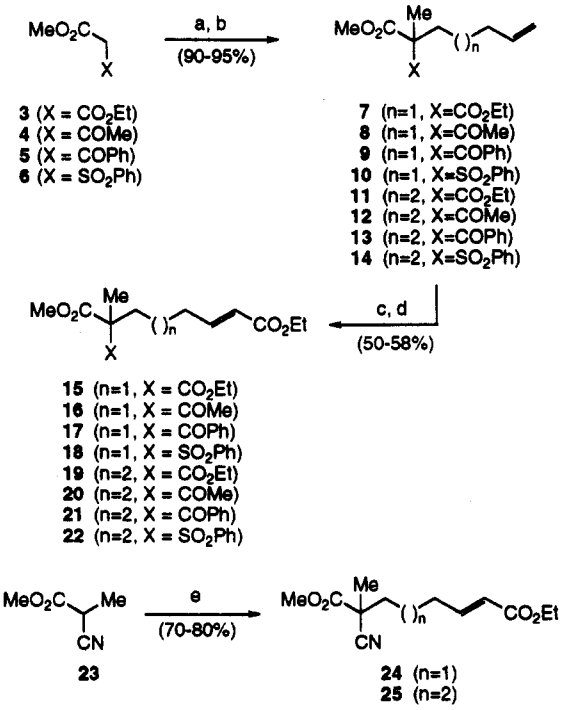
A tandem dealkoxycarbonylation–Michael addition reaction has been developed as a synthetic route to highly functionalized carbocycles. Methyl esters, activated toward decarboxylation by an electron-withdrawing group at C-2 and tethered by a three- or four-carbon chain to an acrylate Michael acceptor, have been prepared and used as the cyclization substrates. Treatment of these compounds with LiCl in HMPA at 120 °C for 4 h results in selective S_N2 dealkylation of the methyl esters, decarboxylation, and cyclization of the intermediate anions by a Michael addition to the pendant acrylate moiety. This affords 45–90% of the cyclopentane- and cyclohexaneacetic esters substituted at C-2 by an electron-withdrawing group. Moderate to excellent selectivity (3:1–99:1) in favor of the product having the electron-withdrawing group trans to the acetic ester side chain is observed. The reaction works best for the preparation of five-membered rings, and cyclizations proceed most cleanly from substrates which cyclize through a tertiary carbanion. Synthetic and mechanistic details as well as optimization studies and product structure proofs are presented.

Introduction

Decarboxylation reactions initiated by S_N2 dealkylation of activated esters hold an important place in organic synthesis allowing removal of a directing group after alkylation or acylation.[2,3] Recently, several reports have appeared describing synthetic transformations which utilize the intermediate anion generated in this reaction when run under anhydrous aprotic conditions. These include simple alkylations,[4] ring contractions,[5] alkylative spiroannulations,[6] olefin synthesis by Wittig[7] and elimination[8] processes, ketene thioacetal formation,[9] enamino ketone generation,[10] and heterocycle formation by O-alkylation of geometrically constrained conjugated enols.[11] Additionally, a preliminary report of our work on the synthesis of spirocycles by a tandem dealkoxycarbonylation–Michael addition reaction has appeared.[12] We present here our results on the use of a dealkoxycarbonylation–Michael addition tandem for the preparation of highly substituted five- and six-membered carbocycles.

Synthesis of Cyclization Substrates. The synthetic route used to prepare the cyclization substrates began with the active methylene compounds methyl ethyl malonate (3),[13] methyl acetoacetate (4), methyl benzoylacetate (5)[14] and methyl (phenylsulfonyl)acetate (6)[15] (Scheme I). Alkylation of these compounds with 4-pentenyl iodide or 5-hexenyl iodide followed by methyl iodide (NaH/DMF)[16] afforded the α-substituted ω-alkenyl methyl esters 7–14. Finally, the acrylate ester moiety was introduced

Scheme I[a]



[a] (a) NaH, DMF, $ICH_2(CH_2)_nCH_2CH{=}CH_2$ (n = 1,2); (b) NaH, DMF, MeI; (c) O_3, CH_2Cl_2, −78 °C, MeSMe, −78 → 20 °C; (d) $Ph_3P{=}CHCO_2Et$, PhH, 80 °C; (e) NaH, DMF, (*E*)-$BrCH_2(CH_2)_n$-$CH_2CH{=}CHCO_2Et$ (n = 1, 2).

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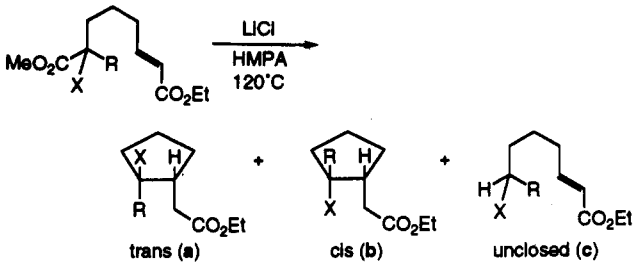
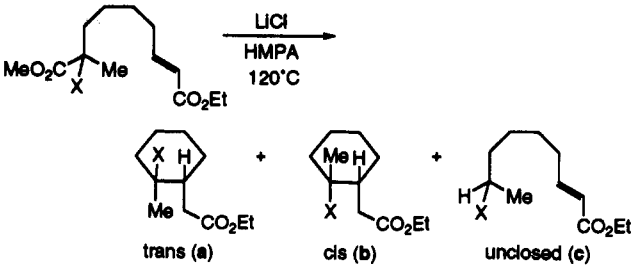
Table I. Synthesis of Cyclopentaneacetic Esters



substrate	R	X	product	a:b:c[a]	yield[b] (%)
15	Me	CO_2Et	26	74:26:0	64
16	Me	COMe	27	93:7:0	94
17	Me	COPh	28	89:11:0	78
18	Me	SO_2Ph	29	99:1:0	91
24	Me	CN	30	77:23:0	67

[a] Product ratios determined by GC of crude product. [b] Yields refer to isolated purified products.

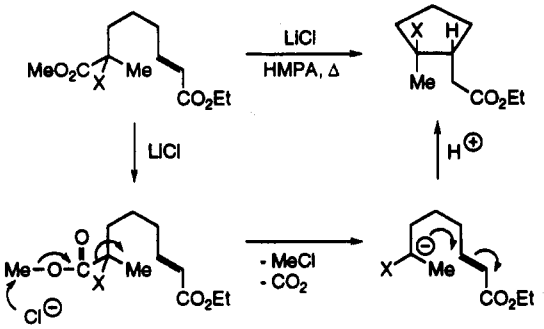
Table II. Synthesis of Cyclohexaneacetic Esters



substrate	X	product	a:b:c[a]	yield[b] (%)
19	CO_2Et	31	40:10:26	c
20	COMe	32	64:12:24	55
21	COPh	33	74:2:24	76
22	SO_2Ph	34	80:5:15	82
25	CN	35	69:15:16	45

[a] Product ratios determined by GC of crude product. [b] Yields refer to isolated purified products. [c] Product was a complex mixture from which no pure material could be isolated. Assay and identification were accomplished by coinjection of the crude product mixture with independently synthesized material.

Scheme II



by (1) ozonolysis with reductive workup and (2) Wittig olefination.[17] Overall yields of **15–22** using this route were 45–55%. An alternative synthesis, involving sequential alkylation of the active methylene compound with methyl iodide followed by ethyl (*E*)-6-iodo-2-hexenoate[17a] or ethyl (*E*)-7-iodo-2-heptenoate,[17a] afforded comparable yields. This second approach was successfully used on (±)-methyl 2-cyanopropionate[18] for the preparation of cyano substrates **24** and **25** which were not accessible using the ozonolysis route.

Results and Discussion

The results of our study of the tandem dealkoxycarbonylation–Michael addition reaction are given in Tables I and II. The optimized reaction conditions utilize dry hexamethylphosphoramide (HMPA) containing 4 equiv of lithium chloride at a temperature of 120 °C (±5 °C) for 4 h. Anhydrous 1-methyl-2-pyrrolidinone (NMP) and 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (DMPU) were also explored as solvents for the reaction; of these, NMP appears to be the best substitute but yields, in most cases, proved inferior to those obtained in HMPA. The reaction gives optimum yields of cyclized products using substrate concentrations of *ca.* 0.1 M on scales up to 10 mmol; higher concentrations or larger reaction scales result in reduced selectivity and lower yields of cyclized material.

The mechanism of the reaction involves initial attack by chloride ion at the methyl ester in an S_N2-type reaction (Scheme II). This generates gaseous methyl chloride and a carboxylate anion activated toward decarboxylation by the anion-stabilizing X group. At 120 °C, the carboxylate group is spontaneously lost to afford the anion which cyclizes by a Michael addition on the pendant acrylate ester. In all cases, the methyl ester is selectively cleaved to initiate the reaction tandem. This would be expected based upon established relative rate data for the S_N2 reaction.[19] The method works best for the preparation of five-membered rings; six-membered rings are produced in lower yield and more uncyclized material is recovered, presumably due to a combination of electronic, torsional, and entropic factors. In the five-ring cases, cyclizations can be carried out on substrates which decarboxylate to tertiary (R = Me) or secondary carbanions (R = H) though tertiary carbanions generally give higher yields and cleaner products. The cyclohexane closures are limited exclusively to cases proceeding through a tertiary carbanion.

Cyclized product structures were established by independent synthesis and X-ray structure determination. The cis[20] and trans[21] five-membered methylated cyclic diesters (**26a** and **26b**, respectively) were independently synthesized using literature methods. The cis and trans assignments for the six-membered cyclic diesters were also confirmed by independent synthesis.[22] Finally, the relative stereochemistry of the trans five- and six-membered cyclic sulfones **29a** and **34a**, respectively, were confirmed by X-ray crystallographic determination.[23] In all cases, the major product corresponded to the trans isomer.

The trans selectivity of the reaction is of considerable interest, and both steric and electronic arguments must be invoked to account for the observed results. In the phenylsulfonyl-substituted substrate (X = SO_2Ph), steric

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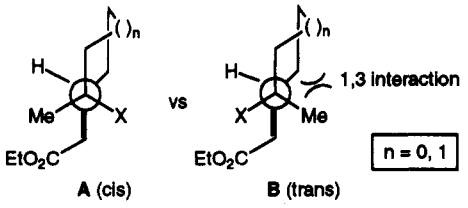
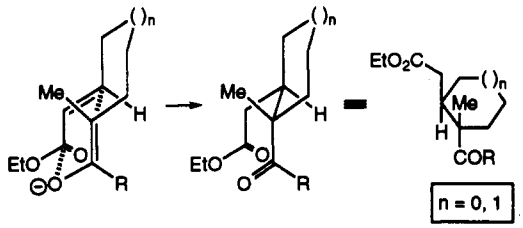
Chart I



Scheme III



factors would appear to predominate. In other substrates, where X is sterically smaller than methyl,[24] analysis of the steric interactions which develop during ring closure suggests that the major cyclization product derives from the more congested transition state (Chart I). Evaluation of the transition states leading to cis and trans products (**A** and **B**, respectively) reveals a destabilizing 1,3 interaction between the larger methyl and the C-3 methylene in the developing ring of the trans product. In these cases, other factors must control the ring closure. Calculations[25] have shown that secondary orbital interactions, similar to those used to rationalize the endo rule in the Diels–Alder reaction, may play an important role in ring closures of this type. In a compact chair transition state (Scheme III), the dominant interaction involves the HOMO of the enolate (Michael donor) and the LUMO of the *s*-cis α,β-unsaturated ester carbonyl (Michael acceptor). This overlap stabilizes the transition state leading to the trans product and, thus, governs the outcome of the reaction.[26] The degree of selectivity observed would vary according to the extent of delocalization in the donor anion and the ability of the anion-stabilizing group to interact with the LUMO of the acrylate acceptor.

In summary, we have developed and optimized a procedure for the synthesis of highly functionalized cyclopentane- and cyclohexaneacetic esters using a tandem dealkoxycarbonylation-Michael addition strategy. The procedure is simple and yields products with useful selectivities. Comparison with established methods for the synthesis of similar compounds shows that the current procedure is considerably shorter and easier to perform. We are continuing our exploration of this valuable reaction for the synthesis of more highly functionalized carbocyclic and heterocyclic structures. Several related procedures are also under development.

Experimental Section

Solvents were purified in the following manner: DMF, HMPA, and NMP were stored under nitrogen over 4-Å molecular sieves, THF was distilled from $LiAlH_4$, and diisopropylamine was distilled from CaH_2. Other reagents were used as a received from the vendors. Ethyl (triphenylphosphoranylidene)acetate was prepared by the literature method.[27] All reactions were run under dry N_2. Unless otherwise indicated, the saturated NH_4Cl, saturated $NaHCO_3$, 5% $Na_2S_2O_3$, saturated NaCl, and 0.5–1.0 M HCl used in workup procedures refer to aqueous solutions. Reactions were monitored by one of the following methods: (1) TLC on hard-layer silica gel GF plates (Analtech) using UV or phosphomolybdic acid detection or (2) capillary GC with FI detection (SE-30 column, 6-m × 0.25-mm i.d., 0.25-μm film thickness) programmed between 50 and 300 °C. Preparative separations were performed using one of the following methods: (1) PTLC on 20- × 20-cm silica gel GF plates (Analtech), (2) flash chromatography[28] on silica gel (Grace, grade 62, 60–200 mesh) containing UV-active phosphor (Sylvania no. 2282), (3) flash vacuum chromatography[29] on silica gel (60–200 mesh), or (4) HPLC using a Waters 510 pump and a silica gel Dynamax-60A (Rainin) preparative column. Band elution, where appropriate, was monitored using a hand-held UV lamp. Melting points are uncorrected. IR spectra are referenced to polystyrene. ^1H NMR and ^{13}C NMR spectra were measured at 300 and 75 MHz, respectively, and are referenced to internal $(CH_3)_4Si$. High-resolution mass spectra (HRMS, EI/DP) were obtained at 70 eV. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN.

Representative Procedure for the Preparation of α-Substituted ω-Alkenyl Esters: Methyl (±)-2-(Ethoxycarbonyl)-2-methyl-6-heptenoate (7). The general procedure of Inomata[16] was adapted. To a stirred suspension of 2.45 g (102 mmol) of oil-free NaH in 50 mL of DMF was added dropwise 14.6 g (100 mmol) of ethyl methyl malonate in 50 mL of DMF. The resulting solution was stirred for 20 min at rt before a solution of 14.9 g (102 mmol) of 5-bromopentene in 50 mL of DMF was added dropwise over 20 min. The reaction was stirred at 50–60 °C for 12 h and then quenched with 0.5 M HCl and ether extracted (3×). The combined organic layers were washed with 0.5 M HCl, H_2O, $NaHCO_3$, $Na_2S_2O_3$, and NaCl. The organic layer was dried ($MgSO_4$), concentrated *in vacuo*, and vacuum distilled to give 18.0 g (84.1 mmol, 84%) of methyl (±)-2-(ethoxycarbonyl)-6-heptenoate as a light yellow oil, bp 63–64 °C (0.5 mmHg).

To a stirred suspension of 1.25 g (52 mmol) of oil-free NaH in 25 mL of DMF was slowly added a 25-mL DMF solution of 10.7 g (50 mmol) of methyl (±)-2-(ethoxycarbonyl)-6-heptenoate. This solution was stirred for 45 min before 14.2 g (6.22 mL, 100 mmol) of methyl iodide was added dropwise. The resulting mixture was stirred at 50–60 °C overnight and then poured into 0.5 M HCl and ether extracted (3×). The combined organic layers were washed with 0.5 M HCl, H_2O, $NaHCO_3$, $Na_2S_2O_3$, and NaCl, dried ($MgSO_4$), and concentrated *in vacuo*. Vacuum distillation gave 10.8 g (47.5 mmol, 95%) of **7** as a colorless oil: bp 55–57 °C (0.3 mmHg); IR (thin film) 3078, 1739, 1643, 1380, 994, 911 cm^{-1}; ^1H NMR δ 5.78 (ddt, 1 H, J = 17.0, 10.3, 6.7 Hz), 5.01 (d, 1 H,

(23) Compound **29a** crystallizes in the monoclinic space group $P2_1/a$ with a = 13.484(5) Å, b = 9.817(4) Å, c = 12.199(3) Å, α = 90.0°, β = 93.78(3)°, γ = 90.0°, V = 1611.3(10) Å^3, and Z = 4. Final least-squares refinement using 1390 unique reflections with $I > 3.0\sigma(I)$ gave $R(R_w)$ = 6.2(8.2)%. Compound **34a** crystallizes in the triclinic space group $P\bar{1}$ with a = 11.192(3) Å, b = 11.217(3) Å, c = 15.686(8) Å, α = 106.20(3)°, β = 102.04(3)°, γ = 108.33(3)°, V = 1697.6(10) Å^3, and Z = 4. Final least-squares refinement using 3371 unique reflections with $I > 3.0\sigma(I)$ gave $R(R_w)$ = 6.7(8.9)%. Final refinement involved anisotropic thermal parameters for non-hydrogen atoms and fixed hydrogen positions. Atomic coordinates for **29a** and **34a** have been deposited with the Cambridge Crystallographic Data Centre. The coordinates can be obtained on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

(24) Based upon studies of cyclohexane derivatives, Me is sterically larger than CN, CO_2Et, and COMe, approximately isosteric with COPh, and sterically smaller than SO_2Ph; see: (a) Hirsch, J. A. *Top. Stereochem.* **1967**, *1*, 199–222. (b) Jensen, F. R.; Bushweller, C. H. *Adv. Alicyclic Chem.* **1971**, *3*, 139–194.

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J = 17.0 Hz), 4.96 (d, 1 H, J = 10.3 Hz), 4.18 (q, 2 H, J = 7.1 Hz), 3.71 (s, 3 H), 2.06 (q, 2 H, J = 7.1 Hz), 1.87 (m, 2 H), 1.41 (s, 3 H), 1.33 (m, 2 H), 1.24 (t, 3 H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 172.9, 172.2, 138.1, 114.9, 61.1, 53.6, 52.3, 35.0, 33.8, 23.6, 19.9, 14.0; HRMS m/e for $C_{11}H_{17}O_3$ ($M^+ - OCH_3$) calcd 197.1178, found 197.1181.

Other compounds prepared using this procedure, though on different scales, are given below. Compounds reported without boiling points were purified by flash chromatography[28] eluted with increasing concentrations of ether in hexanes.

Methyl (±)-2-acetyl-2-methyl-6-heptenoate (8): 18.4 g (92.7 mmol, 97%); bp 57–58 °C (0.5 mmHg); IR (thin film) 3082, 1755, 1725, 1648, 1630, 1380, 1360, 998, 918 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.78 (ddt, 1H, J = 17.0, 10.3, 6.7 Hz), 5.01 (d, 1 H, J = 17.0 Hz), 4.96 (d, 1 H, J = 10.3 Hz), 3.73 (s, 3 H), 2.14 (s, 3 H), 2.06 (q, 2 H, J = 7.0 Hz), 1.89 (m, 1 H), 1.78 (m, 1 H), 1.34 (s, 3 H), 1.27 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 205.5, 173.5, 137.9, 115.0, 59.5, 52.3, 34.2, 33.8, 26.0, 23.5, 18.8; HRMS m/e for $C_{10}H_{15}O_2$ ($M^+ - OCH_3$) calcd 167.1072, found 167.1075.

Methyl (±)-2-benzoyl-2-methyl-6-heptenoate (9): 12.2 g (47.1 mmol, 94%); bp 116–122 °C (0.5 mmHg); IR (thin film) 3080, 1745, 1690, 1648, 1604, 1585, 1380, 996, 919 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.81 (d, 2 H, J = 7.4 Hz), 7.51 (t, 1 H, J = 7.3 Hz), (7.41, 2 H, J = 7.6 Hz), 5.71 (ddt, 1 H, J = 17.1, 10.3, 6.8 Hz), 4.96 (d, 1 H, J = 17.1 Hz), 4.92 (d, 1 H, J = 10.3 Hz), 3.62 (s, 3 H), 2.03 (m, 4 H), 1.53 (s, 3 H), 1.29 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 197.2, 174.7, 137.9, 135.5, 132.5, 128.4, 128.2, 114.8, 56.7, 52.2, 35.7, 33.7, 23.0, 21.0; HRMS m/e for $C_{15}H_{17}O_2$ ($M^+ - OCH_3$) calcd 229.1229, found 229.1231.

Methyl (±)-2-methyl-2-(phenylsulfonyl)-6-heptenoate (10): 13.2 g (44.5 mmol, 94.5%); IR (thin film) 3080, 1742, 1646, 1590, 1385, 1318, 1155, 998, 920 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.82 (d, 2 H, J = 7.8 Hz), 7.68 (t, 1 H, J = 7.6 Hz), 7.55 (t, 2 H, J = 7.8 Hz), 5.73 (ddt, 1 H, J = 16.9, 10.2, 6.6 Hz), 4.99 (d, 1 H, J = 16.9 Hz), 4.96 (d, 1 H, J = 10.2 Hz), 3.68 (s, 3 H), 2.21 (m, 1 H), 2.05 (m, 2 H), 1.86 (m, 1 H), 1.58 (s, 3 H), 1.46 (m, 1 H), 1.21 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 168.5, 137.3, 135.6, 134.0, 130.2, 128.6, 115.3, 73.0, 52.8, 33.5, 32.2, 23.6, 16.3; HRMS m/e for $C_{14}H_{17}O_3S$ ($M^+ - OCH_3$) calcd 265.0898, found 265.0903.

Methyl (±)-2-(ethoxycarbonyl)-2-methyl-7-octenoate (11): 13.6 g (56.0 mmol, 93%); bp 69–71 °C (0.3 mmHg); IR (thin film) 3079, 1738, 1642, 1378, 992, 911 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.78 (ddt, 1 H, J = 17.0, 10.3, 6.7 Hz), 4.99 (d, 1 H, J = 17.0 Hz), 4.94 (d, 1 H, J = 10.3 Hz), 4.18 (q, 2 H, J = 7.1 Hz), 3.71 (s, 3 H), 2.05 (q, 2 H, J = 7.1 Hz), 1.86 (m, 2 H), 1.40 (m, 2 H), 1.40 (s, 3 H), 1.26 (m, 2 H), 1.24 (t, 3 H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 173.0, 172.3, 138.6, 114.5, 61.1, 53.6, 52.3, 35.3, 33.4, 29.0, 23.7, 19.8, 14.0; HRMS m/e for $C_{12}H_{18}O_3$ ($M^+ - CH_3OH$) calcd 210.1256, found 210.1257.

Methyl (±)-2-acetyl-2-methyl-7-octenoate (12): 9.63 g (45.4 mmol, 98%); IR (thin film) 3080, 1750, 1720, 1647, 1625, 1380, 1360, 998, 918 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.78 (ddt, 1 H, J = 17.0, 10.3, 6.7 Hz), 4.99 (d, 1 H, J = 17.0 Hz), 4.94 (d, 1 H, J = 10.3 Hz), 3.73 (s, 3 H), 2.14 (s, 3 H), 2.05 (q, 2 H, J = 7.1 Hz), 1.89 (m, 1 H), 1.75 (m, 1 H), 1.39 (m, 2 H), 1.33 (s, 3 H), 1.19 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 205.6, 173.5, 138.5, 114.5, 59.6, 52.3, 34.6, 33.3, 29.1, 26.0, 23.6, 18.8; HRMS m/e for $C_{11}H_{17}O_2$ ($M^+ - OCH_3$): calcd 181.1229, found 181.1234.

Methyl (±)-2-benzoyl-2-methyl-7-octenoate (13): 12.7 g (46.2 mmol, 97.5%); IR (thin film) 3078, 1746, 1690, 1647, 1603, 1587, 1380, 997, 915 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.82 (d, 2 H, J = 7.4 Hz), 7.52 (t, 1 H, J = 7.3 Hz), 7.41 (t, 2 H, J = 7.4 Hz), 5.73 (ddt, 1 H, J = 17.0, 10.3, 6.8 Hz), 4.94 (d, 1 H, J = 17.0 Hz), 4.90 (d, 1 H, J = 10.3 Hz), 3.63 (s, 3 H), 2.02 (m, 4 H), 1.52 (s, 3 H), 1.37 (m, 2 H), 1.19 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 197.4, 174.9, 138.5, 135.5, 132.6, 128.5, 128.3, 114.4, 56.8, 52.3, 36.1, 33.3, 29.0, 23.1, 21.0; HRMS m/e for $C_{16}H_{19}O_2$ ($M^+ - OCH_3$) calcd 243.1385, found 243.1389.

Methyl (±)-2-methyl-2-(phenylsulfonyl)-7-octenoate (14): 13.6 g (43.8 mmol, 97%); IR (thin film) 3080, 1740, 1645, 1590, 1385, 1320, 1150, 995, 920 cm^{-1}; ^{1}H NMR (thin film) δ 7.82 (d, 2 H, J = 7.1 Hz), 7.68 (t, 1 H, J = 7.4 Hz), 7.56 (t, 2 H, J = 7.9 Hz), 5.74 (ddt, 1 H, J = 17.0, 10.3, 6.6 Hz), 4.97 (d, 1 H, J = 17.0 Hz), 4.93 (d, 1 H, J = 10.3 Hz), 3.68 (s, 3 H), 2.22 (m, 1 H), 2.02 (m, 2 H), 1.84 (m, 1 H), 1.57 (s, 3 H), 1.40 (m, 3 H), 1.10 (m, 1 H); ^{13}C NMR (thin film) δ 168.6, 138.1, 135.7, 134.1, 130.3, 128.6, 114.7, 73.1, 52.9, 33.2, 32.5, 28.7, 23.7, 16.3; HRMS m/e for $C_{15}H_{19}O_3S$ ($M^+ - OCH_3$) calcd 279.1055, found 279.1071.

Representative Ozonolysis–Wittig Procedure: 1-Ethyl Methyl (±)-(*E*)-7-(Ethoxycarbonyl)-7-methyl-2-octenedioate (15). The general procedure of Bunce[17] was used. A 300-mL CH_2Cl_2 solution of 8.21 g (36.0 mmol) of **7** was cooled to −78 °C and treated with ozone until the solution turned light blue. The reaction was quenched at −78 °C with 5.08 g (6.00 mL, 81.8 mmol) of dimethyl sulfide, warmed to rt, stirred for 3 h, and concentrated *in vacuo*. To the resulting light yellow oil was added 150 mL of benzene and 15.0 g (43.2 mmol) of ethyl (triphenylphosphoranylidene)acetate. The solution was refluxed for 12 h and then cooled and concentrated to afford a tan semisolid mass. The residue was loaded on top of a 10- × 10-cm plug of silica gel in a sintered glass frit, and 2 L of 15% ether in hexanes was poured through under aspirator vacuum.[29] Concentration of the filtrate afforded the crude diester as a light yellow oil. The crude product was diluted with ether, washed with $NaHCO_3$ and NaCl, dried ($MgSO_4$), concentrated *in vacuo*, and fractionated through a 15-cm Vigreux column (1.5 cm-i.d.) at reduced pressure to afford **15** as a colorless oil: 5.27 g (17.6 mmol, 49%); bp 116–120 °C (0.5 mmHg); *E*:*Z* 93:7, IR (thin film) 1740, 1660, 1375 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.93 (dt, 1 H, J = 15.7, 6.8 Hz), 5.82 (d, 1 H, J = 15.7 Hz), 4.18 (q, 4 H, J = 7.1 Hz), 3.72 (s, 3 H), 2.22 (m, 2 H), 1.88 (m, 2 H), 1.42 (m, 2 H), 1.41 (s, 3 H), 1.28 (t, 3 H, J = 7.1 Hz), 1.24 (t, 3 H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 172.6, 171.9, 166.4, 148.0, 121.7, 61.2, 60.1, 53.5, 52.4, 35.0, 32.1, 22.8, 19.8, 14.1, 13.9; HRMS m/e for $C_{13}H_{18}O_5$ ($M^+ - C_2H_5OH$) calcd 254.1154, found 254.1158.

Other compounds prepared using this procedure, though on different scales, are given below. The compounds were purified by flash chromatography[28] on silica gel eluted with increasing concentrations of ether in hexanes.

1-Ethyl methyl (±)-(*E*)-7-acetyl-7-methyl-2-nonenedioate (16): 4.55 g (16.9 mmol, 52%); *E*:*Z* 92:8, IR (thin film) 1750, 1735, 1658, 1375 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.96 (dt, 1 H, J = 15.7, 6.9 Hz), 5.82 (d, 1 H, J = 15.7 Hz), 4.18 (q, 2 H, J = 7.1 Hz), 3.74 (s, 3 H), 2.22 (m, 2 H), 2.14 (s, 3 H), 1.90 (m, 1 H), 1.78 (m, 1 H), 1.36 (m, 2 H), 1.35 (s, 3 H), 1.29 (t, 3 H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 205.2, 173.2, 166.4, 147.9, 121.8, 60.1, 59.4, 52.3, 34.2, 32.1, 26.0, 22.8, 18.8, 14.1; HRMS m/e for $C_{12}H_{20}O_4$ ($M^+ - CH_2CO$) calcd 228.1362, found 228.1358.

1-Ethyl methyl (±)-(*E*)-7-benzoyl-7-methyl-2-octenedioate (17): 5.32 g (16.0 mmol, 51.5%); *E*:*Z* 93:7, IR (thin film) 1740, 1721, 1689, 1658, 1600, 1580, 1370 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.81 (d, 2 H, J = 7.4 Hz), 7.54 (t, 1 H, J = 7.3 Hz), 7.43 (t, 2 H, J = 7.4 Hz), 6.89 (dt, 1 H, J = 15.6, 6.9 Hz), 5.80 (d, 1 H, J = 15.6 Hz), 4.18 (q, 2 H, J = 7.1 Hz), 3.65 (s, 3 H), 2.20 (q, 2 H, J = 7.2 Hz), 2.04 (m, 2 H), 1.54 (s, 3 H), 1.34 (m, 2 H), 1.28 (t, 3 H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 197.2, 174.7, 166.6, 148.1, 135.4, 132.7, 128.5, 128.3, 121.8, 60.2, 56.7, 52.4, 35.9, 32.2, 22.4, 21.1, 14.2; HRMS m/e for $C_{18}H_{21}O_4$ ($M^+ - OCH_3$) calcd 301.1439, found 301.1424.

1-Ethyl methyl-(±) (*E*)-7-methyl-7-(phenylsulfonyl)-2-octenedioate (18): 9.19 g (25.0 mmol, 50%); *E*:*Z* 96:4; mp 79–81 °C; IR (thin film) 1730, 1660, 1588, 1372, 1315, 1150 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.82 (d, 2 H, J = 7.3 Hz), 7.69 (t, 1 H, J = 7.4 Hz), 7.56 (t, 2 H, J = 7.4 Hz), 6.88 (dt, 1 H, J = 15.6, 6.9 Hz), 5.81 (d, 1 H, J = 15.6 Hz), 4.18 (q, 2 H, J = 7.2 Hz), 3.68 (s, 3 H), 2.23 (m, 3 H), 1.89 (m, 1 H), 1.58 (s, 3 H), 1.56 (m, 1 H), 1.30 (m, 1 H), 1.29 (t, 3 H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 168.3, 166.2, 147.2, 135.4, 134.1, 130.2, 128.6, 122.0, 72.8, 60.1, 52.9, 32.1, 31.8, 22.9, 16.4, 14.1; HRMS m/e for $C_{16}H_{18}O_5S$ ($M^+ - C_2H_5OH$) calcd 322.0875, found 322.0869.

1-Ethyl methyl (±)-(*E*)-8-(ethoxycarbonyl)-8-methyl-2-nonenedioate (19): 5.31 g (16.9 mmol, 47%); 96:4 *E*:*Z*, IR (thin film) 1740, 1660, 1375 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.93 (dt, 1 H, J = 15.6, 6.9 Hz), 5.81 (d, 1 H, J = 15.6 Hz), 4.18 (2q, 4 H, J = 7.1 Hz), 3.72 (s, 3 H), 2.21 (m, 2 H), 1.84 (m, 3 H), 1.47 (m, 2 H), 1.40 (s, 3 H), 1.29 (t, 3 H, J = 7.1 Hz), 1.26 (m, 1 H), 1.24 (t, 3 H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 172.7, 172.1, 166.5, 148.6, 121.4, 61.1, 60.0, 53.4, 52.2, 35.1, 31.7, 28.0, 23.7, 19.8, 14.1, 13.9; HRMS m/e for $C_{14}H_{20}O_5$ ($M^+ - C_2H_5OH$) calcd 268.1311, found 268.1308.

1-Ethyl methyl (±)-(*E*)-8-acetyl-8-methyl-2-nonenedioate (20): 4.03 g (14.2 mmol, 50.5%); *E*:*Z* 93:7, IR (thin film) 1748, 1722, 1658, 1370 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.93 (dt, 1 H, J = 15.6,

6.9 Hz), 5.80 (d, 1 H, J = 15.6 Hz), 4.18 (q, 2 H, J = 7.2 Hz), 3.73 (s, 3 H), 2.20 (m, 2 H), 2.14 (s, 3 H), 1.88 (m, 1 H), 1.76 (m, 1 H), 1.48 (m, 2 H), 1.34 (s, 3 H), 1.29 (t, 3 H, J = 7.2 Hz) 1.24 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 205.4, 173.4, 166.6, 148.6, 121.5, 60.1, 59.5, 52.3, 34.5, 31.8, 28.2, 26.1, 23.7, 18.8, 14.2; HRMS m/e for $C_{13}H_{22}O_4$ ($M^+ - CH_2CO$) calcd 242.1518, found 242.1506.

1-Ethyl methyl (±)-(*E*)-8-benzoyl-8-methyl-2-nonenedioate (21): 5.67 g (16.4 mmol, 54%); *E*:*Z* 95:5; IR (thin film) 1742, 1726, 1690, 1660, 1601, 1585, 1372 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.81 (d, 2 H, J = 7.5 Hz), 7.53 (t, 1 H, J = 7.3 Hz), 7.42 (t, 2 H, J = 7.6 Hz), 6.90 (dt, 1 H, J = 15.6, 6.9 Hz), 5.77 (d, 1 H, J = 15.6 Hz), 4.17 (q, 2 H, J = 7.1 Hz), 3.63 (s, 3 H), 2.17 (q, 2 H, J = 6.8 Hz), 2.03 (m, 2 H), 1.53 (s, 3 H), 1.45 (m, 2 H), 1.28 (t, 3 H, J = 7.1 Hz), 1.24 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 197.1, 174.7, 166.4, 148.5, 135.3, 132.6, 128.4, 128.2, 121.4, 60.0, 56.6, 52.3, 35.9, 31.6, 28.1, 23.2, 20.9, 14.1; HRMS m/e for $C_{19}H_{23}O_4$ ($M^+ - OCH_3$) calcd 315.1596, found 315.1601.

1-Ethyl methyl (±)-(*E*)-8-methyl-8-(phenylsulfonyl)-2-nonenedioate (22): 6.95 g (18.2 mmol, 47.5%); *E*:*Z* 97:3, IR (thin film) 1730, 1660, 1590, 1374, 1315, 1152 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.82 (d, 2 H, J = 7.3 Hz), 7.69 (t, 1 H, J = 7.4 Hz), 7.56 (t, 2 H, J = 7.5 Hz); 6.89 (dt, 1 H, J = 15.6, 6.9 Hz), 5.79 (d, 1 H, J = 15.6 Hz), 4.18 (q, 2 H, J = 7.1 Hz), 3.68 (s, 3 H), 2.20 (m, 3 H), 1.85 (m, 1 H), 1.57 (s, 3 H), 1.46 (m, 2 H), 1.37 (m, 1 H), 1.28 (t, 3 H, J = 7.1 Hz), 1.13 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 168.4, 166.4, 148.1, 135.5, 134.1, 130.2, 128.6, 121.6, 72.9, 60.0, 52.9, 32.2, 31.5, 27.8, 23.8, 16.3, 14.1; HRMS m/e for $C_{17}H_{20}O_5S$ ($M^+ - C_2H_5OH$) calcd 336.1031, found 336.1038.

Representative Procedure for the Alkylation of Methyl (±)-2-Cyanopropanoate with Ethyl (*E*)-ω-Iodo-2-alkenoates: 1-Ethyl Methyl (±)-7-Cyano-7-methyl-2-octenedioate (24). The general procedure for Inomata[16] was used. The anion of methyl (±)-2-cyanopropanoate was generated at 25 °C on a 25 mmol scale using NaH/DMF and treated with 25.3 mmol of ethyl (*E*)-6-iodo-2-hexenoate. The reaction was warmed at 50 °C for 8 h and worked up as described for the synthesis of **7**. The product was purified by flash chromatography[28] on silica gel eluted with increasing concentrations of ether in hexane. The yield was 4.86 g (19.2 mmol, 77%) of **24** as a colorless oil: IR (thin film) 2235, 1748, 1720, 1655, 1370 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.91 (dt, 1 H, J = 15.6, 6.8 Hz), 5.84 (d, 1 H, J = 15.6 Hz), 4.19 (q, 2 H, J = 7.1 Hz), 3.83 (s, 3 H), 2.26 (q, 2 H, J = 7.0 Hz), 1.96 (m, 1 H), 1.77 (m, 2 H), 1.61 (s, 3 H), 1.56 (m, 1 H), 1.29 (t, 3 H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 169.1, 166.2, 147.0, 122.3, 119.6, 60.2, 53.5, 43.6, 37.4, 31.3, 23.7, 23.4, 14.1; HRMS m/e for $C_{11}H_{14}NO_3$ ($M^+ - OCH_2CH_3$) calcd 208.0983, found 208.0968.

1-Ethyl methyl-(±)-8-cyano-8-methyl-2-nonenedioate (25): 4.73 g (17.7 mmol, 71%); IR (thin film) 2235, 1748, 1720, 1653, 1368 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.93 (dt, 1 H, J = 15.7, 6.9 Hz), 5.82 (d, 1 H, J = 15.7 Hz), 4.18 (q, 2 H, J = 7.2 Hz), 3.83 (s, 3 H), 2.22 (m, 2 H), 1.94 (m, 1 H), 1.77 (m, 1 H), 1.60 (s, 3 H), 1.53 (m, 4 H), 1.29 (t, 3 H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 169.8, 166.5, 148.0, 121.8, 119.8, 60.2, 53.5, 43.7, 37.9, 31.7, 25.7, 24.9, 23.5, 14.2; HRMS m/e for $C_{12}H_{16}NO_3$ ($M^+ - OCH_2CH_3$) calcd 222.1130, found 222.1130.

Representative Procedure for the Tandem Dealkoxycarbonylation–Michael Reaction: Ethyl (±)-(1*S,2*R**)-2-Acetyl-2-methylcyclopentane-1-acetate (27a).** To a flame-dried three-necked round-bottomed flask, equipped with magnetic stirring, a reflux condenser, a rubber septum, and a drying tube, was added 340 mg (8.0 mmol) of dry LiCl and 540 mg (2.0 mmol) of **16**. HMPA (10 mL) was added via syringe, and the reaction mixture was stirred at rt to dissolve the LiCl. Once homogeneous, the reaction was heated for 4 h in an oil bath which had been preheated to 120 °C (±5 °C). The reaction was cooled, added to 0.5 M HCl, and extracted with ether (3×). The combined organic layers were washed with 0.5 M HCl, H_2O, and NaCl, dried ($MgSO_4$), and concentrated *in vacuo*. The crude product was purified by PTLC, eluting with increasing concentrations of ether in hexane, to afford 365 mg (1.72 mmol, 86%) of **27a**; the cis isomer (**27b**), which comprised 7% of the crude reaction mixture, could not be isolated in pure form. The spectral data for **27a** were as follows: IR (thin film) 1742, 1710, 1380 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.10 (q, 2 H, J = 7.2 Hz), 2.66 (m, 1 H), 2.37 (dd, 1 H, J = 15.3, 5.7 Hz), 2.18 (complex, 4 H), 2.00 (m, 2 H), 1.71 (m, 2 H), 1.53 (m, 1 H), 1.38 (m, 1 H), 1.25 (t, 3 H, J = 7.2 Hz), 1.05 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 212.5, 172.8, 60.2, 56.7, 41.5, 37.7, 35.4, 30.6, 25.4, 22.2, 17.5, 14.1; HRMS m/e for $C_{12}H_{20}O_3$ calcd 212.1412, found 212.1412.

Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.92; H, 9.43. Found: C, 67.62; H, 9.54.

Other compounds prepared using this procedure, though on different scales, are given below. The compounds were purified by PTLC[30] and eluted with increasing concentrations of ether in hexanes; the diesters were purified by HPLC using 5% ethyl acetate in hexanes.

Ethyl (±)-(1R*,2S*)-2-(ethoxycarbonyl)-2-methylcyclopentane-1-acetate (26a): 583 mg (2.41 mmol, 45%); IR (thin film) 1742, 1380 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.13 (q, 2 H, J = 7.0 Hz), 2.65 (m, 1 H), 2.50 (dd, 1 H, J = 15.1, 4.9 Hz), 2.16 (dd, 2 H, J = 15.1, 10.2 Hz), 2.01 (sextet, 1 H, J = 6.5 Hz), 1.70 (quintet, 2 H, J = 6.5 Hz), 1.60 (m, 1 H), 1.30 (m, 1 H), 1.25 (t, 6 H, J = 7.0 Hz), 1.07 (s, 3 H); ^{13}C NMR (CDCl3) δ 177.6, 173.0, 60.4, 60.2, 50.7, 43.0, 38.1, 35.6, 30.3, 22.0, 17.8, 14.2 (2); HRMS m/e for $C_{11}H_{17}O_3$ ($M^+ - OCH_2CH_3$) calcd 197.1178, found 197.1180.

Anal. Calcd for $C_{13}H_{22}O_4$: C, 64.46; H, 9.09. Found: C, 64.74; H, 9.20.

Ethyl (±)-(1S*,2S*)-2-(ethoxycarbonyl)-2-methylcyclopentane-1-acetate (26b): 171 mg (0.71 mmol, 13%); IR (thin film) 1738, 1375 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.05 (q, 2 H, J = 7.0 Hz), 4.04 (q, 2 H, J = 7.0 Hz), 2.40 (m, 1 H), 2.18–2.03 (complex, 3 H), 1.91 (m, 1 H), 1.75 (m 1 H), 1.59 (m, 1 H), 1.46 (m, 2 H), 1.18 (s, 3 H), 1.18 (2t, 6 H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 176.4, 173.1, 60.3, 60.2, 51.8, 47.2, 37.4, 35.9, 31.4, 23.9, 22.5, 14.2(2); HRMS m/e for $C_{11}H_{17}O_3$ ($M^+ - OCH_2CH_3$) calcd 197.1178, found 197.1185.

Anal. Calcd for $C_{13}H_{22}O_4$: C, 64.46; H, 9.09. Found: C, 64.77; H, 9.21.

Ethyl (±)-(1R*,2S*)-2-benzoyl-2-methylcyclopentane-1-acetate (28a): 608 mg (2.22 mmol, 70%); IR (thin film) 1740, 1680, 1601, 1584, 1382 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.78 (d, 2 H, J = 7.2 Hz), 7.43 (m, 3 H), 4.13 (q, 2 H, J = 7.1 Hz), 2.98 (m, 1 H), 2.57 (dd, 1 H, J = 15.0, 4.7 Hz), 2.22 (m, 1 H), 2.16 (dd, 1 H, J = 15.0, 10.0 Hz), 2.08–1.65 (complex, 4 H), 1.39 (m, 1 H), 1.25 (t, 3 H, J = 7.1 Hz), 1.23 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 206.5, 173.0, 137.4, 131.2, 128.3, 127.2, 60.1, 55.8, 42.3, 38.2, 35.6, 29.7, 22.4, 20.0, 14.1; HRMS m/e for $C_{17}H_{22}O_3$ calcd 274.1569, found 274.1572.

Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.45; H, 8.03. Found: C, 74.08; H, 7.94.

Ethyl (±)-(1R*,2S*)-2-(phenylsulfonyl)-2-methylcyclopentane-1-acetate (29a): 660 mg (2.13 mmol, 90%); mp 62–63 °C; IR (thin film) 1738, 1590, 1385, 1300, 1150 cm^{-1}; H NMR ($CDCl_3$) δ 7.92 (d, 2 H, J = 7.3 Hz), 7.66 (t, 1 H, J = 7.3 Hz), 7.56 (t, 2 H, J = 7.5 Hz), 4.13 (q, 2 H, J = 7.1 Hz), 2.94 (m, 1 H), 2.66 (dd, 1 H, J = 15.4, 3.0 Hz), 2.41 (m, 1 H), 2.13 (m, 1 H), 2.10 (dd, 1 H, J = 15.4, 11.7 Hz), 1.72–1.39 (complex, 4 H), 1.28 (s, 3 H), 1.26 (t, 3 H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 172.2, 136.2, 133.6, 130.2, 128.8, 69.4, 60.4, 39.4, 36.2, 35.8, 31.4, 22.0, 17.1, 14.1; HRMS m/e for $C_{16}H_{23}O_4S$ ($M^+ + 1$) calcd 311.1317, found 311.1313.

Anal. Calcd for $C_{16}H_{22}O_4S$: C, 61.94; H, 7.10. Found: C, 62.22; H, 7.22.

Ethyl (±)-(1R*,2S*)-2-cyano-2-methylcyclopentane-1-acetate (30a): 400 mg (2.05 mmol, 50%); IR (thin film) 2245, 1742, 1380 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.17 (q, 2 H, J = 7.2 Hz), 2.60 (m, 2 H), 2.24 (m, 2 H), 2.11 (m, 1 H), 1.88–1.72 (complex, 3 H), 1.30 (m, 1 H), 1.28 (t, 2 H, J = 7.2 Hz), 1.22 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 171.7, 125.0, 60.7, 44.7, 39.1, 38.8, 34.9, 29.0, 21.5, 18.8, 14.1; HRMS m/e for $C_{11}H_{17}NO_2$ calcd 195.1258, found 195.1257.

Anal. Calcd for $C_{11}H_{17}NO_2$: C, 67.69; H, 8.71. Found: C, 67.89; H, 8.82.

Ethyl (±)-(1S*,2S*)-2-cyano-2-methylcyclopentane-1-acetate (30b): 103 mg (0.53 mmol, 13%); IR (thin film) 2245, 1746, 1382 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.16 (q, 2 H, J = 7.2 Hz), 2.64 (dd, 1 H, J = 15.8, 4.3 Hz), 2.43 (dd, 1 H, J = 15.8, 9.4 Hz), 2.22 (m, 1 H), 2.09 (m, 2 H), 1.90–1.45 (complex, 4 H), 1.41 (s, 3 H), 1.27

(30) For non-UV active compounds, PTLC plates were visualized with I_2 vapor and bands were separated, cut from the plates, and extracted with ether. The ether extracts were washed with 5% $Na_2S_2O_3$ and saturated NaCl, dried ($MgSO_4$), and concentrated.

(t, 3 H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 172.1, 123.1, 60.6, 46.1, 42.8, 39.5, 36.3, 30.7, 23.2, 21.4, 14.2; HRMS m/e for $C_{11}H_{17}NO_2$ calcd 195.1258, found 195.1253.

Anal. Calcd for $C_{11}H_{17}NO_2$: C, 67.69; H, 8.71. Found: C, 67.91; 8.79.

Ethyl (±)-(1*R,2*S**)-2-acetyl-2-methylcyclohexane-1-acetate (32a)**: 160 mg (0.71 mmol, 33%); IR (thin film) 1740, 1705, 1375 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.11 (q, 2 H, J = 7.2 Hz), 2.44 (m, 1 H), 2.18 (s, 3 H), 2.09 (dd, 1 H, J = 15.1, 3.6 Hz), 1.95 (dd, 1 H, J = 15.1, 10.1 Hz), 1.72–1.56 (complex, 4 H), 1.51–1.10 (complex, 4 H), 1.25 (t, 3 H, J = 7.2 Hz), 1.06 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 213.5, 172.7, 60.2, 51.2, 37.0 (2), 35.4, 27.4, 25.0, 24.9, 20.9, 14.7, 14.1; HRMS m/e for $C_{13}H_{22}O_3$ calcd 226.1569, found 226.1564.

Anal. Calcd for $C_{13}H_{22}O_3$: C, 69.03; H, 9.73. Found: C, 69.21; H, 9.77.

Ethyl (±)-(1*S,2*S**)-2-acetyl-2-methylcyclohexane-1-acetate (32b)**: 27.1 mg (0.12 mmol, 6%); IR (thin film) 1740, 1708, 1380 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.11 (q, 2 H, J = 7.1 Hz), 2.54 (dd, 1 H, J = 15.9, 10.1 Hz), 2.30 (dd, 1 H, J = 15.9, 3.2 Hz), 2.08 (s, 3 H), 1.92 (m, 1 H), 1.70–1.51 (complex 4 H), 1.42–1.21 (complex 3 H), 1.25 (t, 3 H, J = 7.1 Hz), 1.22 (s, 3 H), 1.06 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 213.2, 171.9, 60.2, 50.7, 41.5, 35.7 (2), 27.2, 25.7, 24.2, 24.1, 22.6, 14.2; HRMS m/e for $C_{13}H_{22}O_3$ calcd 226.1569, found 226.1558.

Anal. Calcd for $C_{13}H_{22}O_3$: C, 69.03; H, 9.73. Found: C, 69.34; H, 9.79.

Ethyl (±)-(*E*)-8-acetyl-2-nonenoate (32c): 58.8 mg (0.26 mmol, 12%); IR (thin film) 1742, 1710, 1630, 1378 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.94 (dt, 1 H, J = 15.6, 6.9 Hz), 5.81 (d, 1 H, J = 15.6 Hz), 4.18 (q, 2 H, J = 7.1 Hz), 2.50 (sextet, 1 H, J = 6.8 Hz), 2.19 (q, 2 H, J = 7.0 Hz), 2.14 (s, 3 H), 1.64 (m, 2 H), 1.55–1.25 (complex, 4 H), 1.29 (t, 3 H, J = 7.1 Hz), 1.08 (d, 3 H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$) δ 212.6, 166.6, 148.8, 121.4, 60.1, 55.5, 47.0, 32.5, 31.9, 28.0, 26.7, 16.2, 14.2; HRMS m/e for $C_{13}H_{22}O_3$ calcd 226.1569, found 226.1572.

Anal. Calcd for $C_{13}H_{22}O_3$: C, 69.03; H, 9.73. Found: C, 69.24; H, 9.68.

Ethyl (±)-(1*R,2*S**)-2-benzoyl-2-methylcyclohexane-1-acetate (33a)**: 740 mg (2.57 mmol, 55%); IR (thin film) 1742, 1684, 1604, 1584, 1384 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.60 (d, 2 H, J = 7.4 Hz), 7.56 (m, 3 H), 4.10 (q, 2 H, J = 7.1 Hz), 2.77 (m, 1 H), 2.26 (dd, 1 H, J = 15.1, 3.4 Hz), 2.02 (dd, 1 H, J = 15.1, 10.3 Hz), 1.88–1.30 (complex, 8 H), 1.24 (t, 3 H, J = 7.1 Hz), 1.23 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 210.2, 172.9, 139.8, 130.3, 128.0, 127.1, 60.3, 51.5, 37.2, 37.1, 36.5, 27.5, 24.8, 21.2, 16.6, 14.2; HRMS m/e for $C_{18}H_{24}O_3$ calcd 288.1725, found 288.1727.

Anal. Calcd for $C_{18}H_{24}O_3$: C, 75.00; H, 8.33. Found: C, 74.70; H, 8.56.

Ethyl (±)-(*E*)-8-benzoyl-2-nonenoate (33c): 228 mg (0.79 mmol, 17%); IR (thin film) 1725, 1690, 1660, 1601, 1584, 1370, 975 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.95 (d, 2 H, J = 7.2 Hz), 7.56 (t, 1 H, J = 6.8 Hz), 7.47 (t, 2 H, J = 7.6 Hz), 6.93 (dt, 1 H, J = 15.6, 7.1 Hz), 5.79 (d, 1 H, J = 15.6 Hz), 4.17 (q, 2 H, J = 7.2 Hz), 3.46 (sextet, 1 H, J = 6.8 Hz), 2.17 (q, 2 H, J = 6.8 Hz), 1.82 (m, 2 H), 1.51–1.20 (complex, 4 H), 1.28 (t, 3 H, J = 7.2 Hz), 1.19 (d, 3 H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$) δ 204.1, 166.6, 148.9, 136.5, 132.8, 128.5, 128.1, 121.3, 60.0, 40.4, 33.2, 31.9, 28.0, 26.8, 17.3, 14.2; HRMS m/e for $C_{18}H_{24}O_3$ calcd 288.1725, found 288.1717.

Anal. Calcd for $C_{18}H_{24}O_3$: C, 75.00; H, 8.33. Found: C, 74.74; H, 8.27.

Ethyl (±)-(1*R,2*S**)-2-(phenylsulfonyl)-2-methylcyclohexane-1-acetate (34a)**: 780 mg (2.41 mmol, 64%); IR (thin film) 1740, 1589, 1380, 1300, 1150 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.81 (d, 2 H, J = 7.7 Hz), 7.59 (t, 1 H, J = 7.3 Hz), 7.49 (t, 2 H, J = 7.6 Hz), 4.07 (q, 2 H, J = 7.1 Hz), 3.51 (dd, 1 H, J = 15.8, 2.2 Hz), 2.32 (m, 1 H), 2.01 (dd, 1 H, J = 15.8, 11.2 Hz), 1.65 (m, 1 H), 1.52 (m, 4 H), 1.32 (s, 1.32 (s, 3 H), 1.20 (t, 3 H, J = 7.1 Hz), 1.05 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 172.6, 135.2, 133.5, 130.5, 128.6, 66.1, 60.3, 36.8, 35.7, 34.0, 29.1, 21.5, 14.2, 12.0; HRMS m/e for $C_{17}H_{25}O_4S$ (M^+ + 1) calcd 325.1473, found 325.1478.

Anal. Calcd for $C_{17}H_{24}O_4S$: C, 62.96; H, 7.41. Found: C, 62.64; H, 7.59.

Ethyl (±)-(*E*)-8-(phenylsulfonyl)-2-nonenoate (34c): 122 mg (0.38 mmol, 10%); IR (thin film) 1725, 1660, 1590, 1372, 1310, 1150, 975 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.88 (d, 2 H, J = 7.8 Hz), 7.67 (t, 1 H, J = 7.4 Hz), 7.57 (t, 2 H, J = 7.4 Hz), 6.90 (dt, 1 H, J = 15.6, 6.9 Hz), 5.78 (d, 1 H, J = 15.6 Hz), 4.18 (q, 2 H, J = 7.1 Hz), 3.01 (m, 1 H), 2.18 (q, 2 H, J = 6.5 Hz), 1.96 (m, 2 H), 1.48–1.30 (complex, 4 H), 1.29 (t, 3 H, J = 7.1 Hz), 1.26 (d, 3 H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$) δ 166.5, 148.3, 137.2, 133.6, 129.0, 128.9, 121.6, 60.1, 59.9, 31.6, 28.8, 27.6, 26.0, 14.2, 13.2; HRMS m/e for $C_{17}H_{24}O_4S$ calcd 324.1395, found 324.1383.

Anal. Calcd for $C_{17}H_{24}O_4S$: C, 62.96; H, 7.41. Found: C, 63.07; H, 7.39.

Ethyl (±)-(1*R,2*S**)-2-cyano-2-methylcyclohexane-1-acetate (35a)**: 47.5 mg (0.23 mmol, 28%); IR (thin film) 2245, 1745, 1380 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.15 (q, 2 H, J = 7.1 Hz), 2.59 (dd, 1 H, J = 15.0, 3.2 Hz), 2.32 (m, 1 H), 2.17 (dd, 1 H, J = 15.0, 10.6 Hz), 1.84–1.72 (complex, 3 H), 1.64 (m, 2 H), 1.49–1.22 (complex, 3 H), 1.28 (s, 3 H), 1.27 (t, 3 H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 171.9, 125.1, 60.6, 39.2, 36.2 (2), 35.9, 26.3, 25.2, 23.6, 20.6, 18.2, 14.1; HRMS m/e for $C_{12}H_{19}NO_2$ calcd 209.1416, found 209.1413.

Anal. Calcd for $C_{12}H_{19}NO_2$: C, 68.90; H, 9.09. Found: C, 69.03; H, 9.16.

Ethyl (±)-(1*S,2*S**)-2-cyano-2-methylcyclohexane-1-acetate (35b)**: 10.1 mg (0.05 mmol, 6%); IR (thin film) 2240, 1740, 1378 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.15 (q, 2 H, J = 7.1 Hz), 2.64 (dd, 1 H, J = 15.7, 4.1 Hz), 2.24 (dd, 1 H, J = 15.7, 9.1 Hz), 1.98 (dm, 1 H, J = 13.3 Hz), 1.82–1.59 (complex, 6 H), 1.42–1.32 (complex, 2 H), 1.35 (s, 3 H), 1.27 (t, 2 H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 172.4, 122.5, 60.7, 42.3, 38.7, 38.4, 37.2, 29.8, 25.3 (2), 23.2, 14.2; HRMS m/e for $C_{12}H_{19}NO_2$ calcd 209.1416, found 209.1422.

Anal. Calcd for $C_{12}H_{19}NO_2$: C, 68.90; H, 9.09. Found: C, 69.11; H, 9.17.

Ethyl (±)-(*E*)-8-cyano-2-nonenoate (35c): 9.7 mg (0.05 mmol, 6%); IR (thin film) 2250, 1730, 1662, 1376, 980 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.94 (dt, 1 H, J = 15.6, 6.9 Hz), 5.82 (dt, 1 H, J = 15.6, 1.5 Hz), 4.19 (q, 2 H, J = 7.1 Hz), 2.60 (m, 1 H), 2.24 (m, 2 H), 1.76–1.39 (complex, 6 H), 1.32 (d, 3 H, J = 7.1 Hz), 1.29 (t, 3 H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 166.5, 148.3, 122.8, 121.6, 60.1, 33.7, 31.8, 27.4, 26.5, 25.4, 17.9, 14.2; HRMS m/e for $C_{12}H_{19}NO_2$ calcd 209.1416, found 209.1422.

Anal. Calcd for $C_{12}H_{19}NO_2$: C, 68.90; H, 9.09. Found: 69.23; H, 9.18.

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Supplementary Material Available: High-field ^{1}H NMR and ^{13}C NMR spectra for 7–22, 24, and 25 (36 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.