2,2,3-Trisubstituted Tetrahydrofurans and 2*H*-Tetrahydropyrans by Tandem Demethoxycarbonylation−Michael Addition Reactions

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A tandem demethoxycarbonylation−Michael addition reaction has been developed as a synthetic route to highly functionalized five- and six-membered oxygen heterocycles. Methyl esters, activated toward decarboxylation by a C-2 ethoxycarbonyl group and tethered by a three- or four-atom chain to an acrylate Michael acceptor, have been prepared and used as the cyclization substrates. Treatment of these compounds with lithium chloride in DMEU (1,3-dimethyl-2-imidazolidinone) at 120 °C for 4−8 h results in chemoselective S_N2 dealkylation of the methyl esters, decarboxylation, and cyclization of the intermediate enolates by a Michael addition to the pendent acrylate moiety. This affords tetrahydrofuran and 2*H*-tetrahydropyran derivatives in 60−90% yields with diastereoselectivities up to 7.5:1 in favor of the product having the C-2 ethoxycarbonyl group trans to the C-3 acetic ester side chain. The reaction works best for the preparation of five- and six-membered rings, and cyclizations proceed most cleanly from substrates which cyclize through a tertiary enolate. Synthetic and mechanistic details are presented.

Introduction

Decarboxylation reactions initiated by S_N2 dealkylation of activated esters occupy an important place in organic synthesis, providing a mild method for the removal of a directing group after alkylation or acylation.[2] Early work by others[3] has described several tandem reaction processes which capture the intermediate enolate generated in this reaction when run under aprotic conditions. Reports from this laboratory have further demonstrated the use of a tandem demethoxycarbonylation−Michael addition sequence for the preparation of carbocycles,[4] lactones, and lactams.[5] Our recent efforts have focused on extending this methodology to the synthesis of oxygen heterocycles. Tetrahydrofurans and 2*H*-tetrahydropyrans are widely distributed in nature and are key structural components of a variety of ionophores[6] and polyether antibiotics.[7] Additionally, aryl-fused systems are important substructures found in naturally occurring antioxidants[8] and in several drug compounds.[9,10] We present here our results on the use of the demethoxycarbonylation−Michael addition reaction for the preparation of highly substituted tetrahydrofuran and 2*H*-tetrahydropyran derivatives.

Synthesis of Cyclization Substrates

The synthesis of precursors to simple functionalized tetrahydrofurans is outlined in Scheme 1. The starting alkoxyacetic esters **1**−**3** were prepared by treatment of 3-buten-1-ol derivatives[11] with chloroacetic acid in the presence of 2 equiv of NaH[12] followed by esterification under basic conditions.[13,14] Conversion to the mixed malonate esters **4**−**6** was accomplished by treatment of the alkoxyacetic esters with 2 equiv of LDA at −78 °C followed by methyl chloroformate.[15] Methylation,[16,17] ozonolysis,[4a] and Wittig olefination[4a] then furnished the cyclization substrates **10**−**12**. A similar sequence was

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(1) Undergraduate research participants: P.B.J. (1991−1993); E.D.D. (1991−1995). This work was taken, in large part, from the senior research thesis of E.D.D.

(2) For reviews of S_N2 ester cleavage, see: (a) McMurry, J. *Org. React.* **1976**, *24*, 187−224. (b) Krapcho, A. P. *Synthesis* **1982**, 805−822, 893−914.

(3) Related dealkoxycarbonylation-initiated processes: (a) Ring contraction: Takei, S.; Kawano, Y. *Tetrahedron Lett.* **1975**, 4389−4392. (b) Alkylative spiroannulation: Eilerman, R. G.; Willis, B. J. *J. Chem. Soc., Chem. Commun.* **1981**, 30−32. (c) Heterocycle formation by *O*-alkylation of geometrically constrained conjugated enols: Böhrer, G.; Böhrer, P.; Knorr, R. *Chem. Ber.* **1990**, *123*, 2167−2172.

(4) (a) Bunce, R. A.; Dowdy, E. D.; Jones, P. B.; Holt, E. M. *J. Org. Chem.* **1993**, *58*, 7143−7148. (b) Bunce, R. A.; Schilling, C. L., III. *J. Org. Chem.* **1995**, *60*, 2748−2752. (c) Bunce, R. A.; Harris, C. R. *Synth. Commun.* **1996**, *26*, 1969−1975. (d) Bunce, R. A.; Peeples, C. J.; Holt, E. M. 203rd National ACS Meeting, San Francisco, CA, April 1992, Abstract no. 6.

(5) Bunce, R. A.; Schilling, C. L., III. *Tetrahedron* **1997**, *53*, 9477−9486.

(6) Dobler, M. *Ionophores and Their Structures*; Wiley: New York, 1981.

(7) Westley, J. W., Ed. *Polyether Antibiotics: Naturally Occurring Acid Ionophores*; Marcel Dekker: New York, 1982; Vol. 1−2.

(8) Ellis, G. P.; Lockhart, I. M., Eds. *Chromans and Tocopherols*; Wiley: New York, 1981.

(9) See for example: (a) Lednicer, D.; Mitscher, L. A. *The Organic Chemistry of Drug Synthesis*; Wiley: New York, 1977, *1*, 286−292; **1980**, *2*, 314−322; **1984**, *3*, 109−115. (b) Lednicer, D.; Mitscher, L. A.; Georg, G. I. *The Organic Chemistry of Drug Synthesis*; Wiley: New York, 1990; Vol. 4, 209−211. (c) Wolff, M. E., Ed. *Berger's Medicinal Chemistry and Drug Discovery*, 5th ed.; Wiley: New York, 1995; Vol. 1, 986−989.

(10) Witiak, D. T.; Loh, W.; Feller, D. R.; Baldwin, J. R.; Newman, H. A. I.; Sober, C. L.; Cavestri, R. C. *J. Med. Chem.* **1979**, *22*, 699−705.

(11) Several of the 3-buten-1-ol and 4-penten-1-ol derivatives have been described previously, see Bunce, R. A.; Bennett, M. J. *Synth. Commun.* **1993**, *23*, 1009−1020.

(12) (a) Glover, S. A.; Golding, S. L.; Goosen, A.: McCleland, C. W. *J. Chem. Soc., Perkin Trans. 1* **1983**, 2479−2483. (b) See also, Gershon, H.; Shanks, L.; DeAngelis, A. *J. Pharm. Sci.* **1979**, *68*, 82−84.

(13) Degenhardt, C. R. *J. Org. Chem.* **1980**, *45*, 2763−2766.

(14) Details of the preparation of **1**−**3** and **13**−**16** can be found in the Supporting Information.

(15) Rathke, M. W.; Deitch, J. *Tetrahedron Lett.* **1971**, 2953−2956.

(16) Inomata, K.; Aoyama, S.; Kotake, H. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 930−932.

(17) Methylation in a separate step was found to be superior to direct methylation of the crude malonate anion.

(18) Jameson, D. L.; Hilgen, S. E.; Hummel, C. E.; Pichla, S. L. *Tetrahedron Lett.* **1989**, *30*, 1609−1612.

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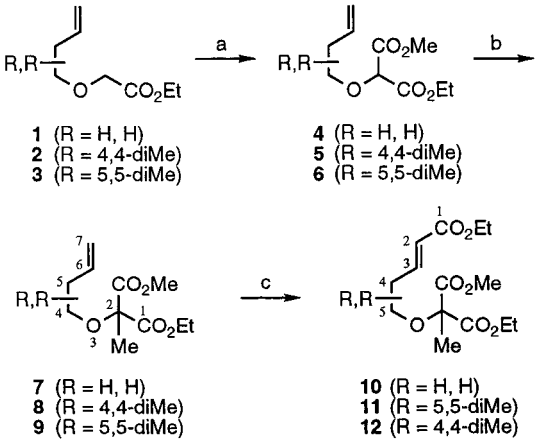
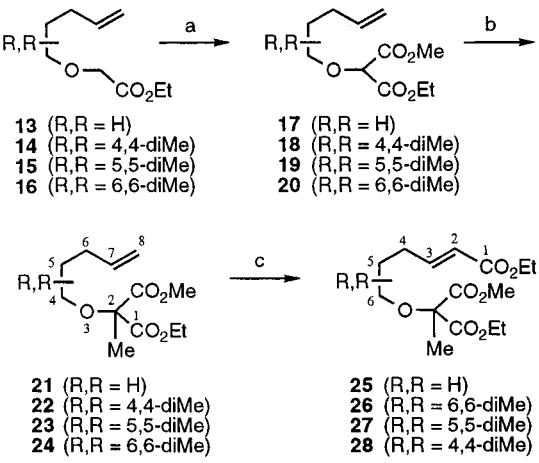
Scheme 1[a]



[a] Key: (a) 2 LDA, THF, −78 °C; $ClCO_2Me$, 56−68%; (b) NaH, DMF; CH_3I, 88−98%; (c) O_3, CH_2Cl_2, −78 °C; Me_2S, −78 → 20 °C; $Ph_3P{=}CHCO_2Et$, PhH, 80 °C, 50−56%.

Scheme 2[a]



[a] Key: (a) 2 LDA, THF, −78 °C; $ClCO_2Me$, 59−65%; (b) NaH, DMF; CH_3I, 88−92%; (c) O_3, CH_2Cl_2, −78 °C; Me_2S, −78 → 20 °C; $Ph_3P{=}CHCO_2Et$, PhH, 80 °C, 40−56%.

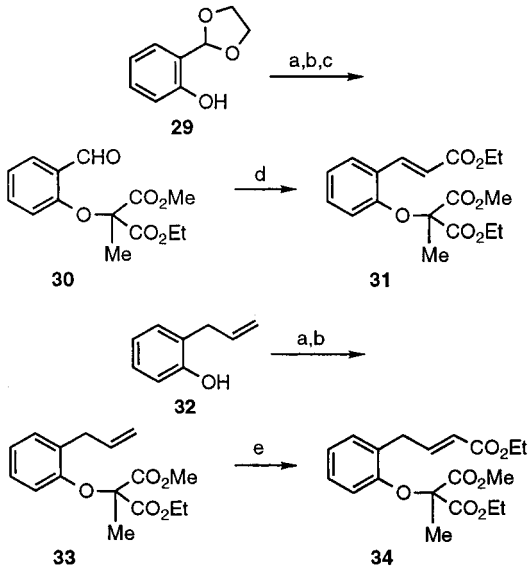
used to prepare 2*H*-tetrahydropyran precursors **25**−**28** from substituted 4-penten-1-ols (Scheme 2).[11,14]

The synthesis of starting materials for the aryl-fused oxygen heterocycles is given in Scheme 3. The 2,2,3-trisubstituted 2,3-dihydrobenzofuran precursor **31** was generated by Wittig olefination of aldehyde **30**, prepared in three steps from 2-(2-hydroxyphenyl)-1,3-dioxolane (**29**).[18] Compound **34** for the synthesis of the 2,2,3-trisubstituted 3,4-dihydro-2*H*-1-benzopyran system was prepared using an ozonolysis−Wittig protocol on alkene **33** which is available in two steps from 2-(2-propenyl)-phenol (**32**).

Results and Discussion

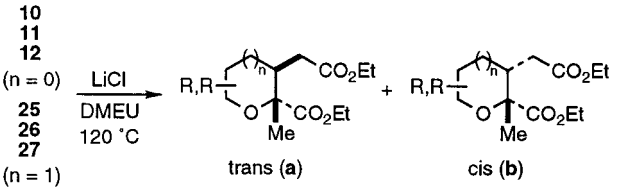
The results of our tandem demethoxycarbonylation−Michael synthesis of oxygen heterocycles are summarized in Tables 1 and 2. The optimized reaction conditions involve heating each substrate in dry DMEU (1,3-dimethyl-2-imidazolidinone)[19] containing 4−6 equiv of lithium chloride at 120 ± 5 °C for 4−8 h. The reaction also proceeds in HMPA, as reported in our earlier

Scheme 3[a]



[a] Key: (a) NaH, DMF, $MeO_2CCHClCO_2Et$; (b) NaH, DMF, MeI, 81−83%; (c) TsOH, acetone, 74%; (d) $Ph_3P{=}CHCO_2Et$, PhH, 80 °C, 74%; (e) O_3, CH_2Cl_2, −78 °C; Me_2S, −78 → 20 °C; $Ph_3P{=}CHCO_2Et$, PhH, 80 °C, 55%.

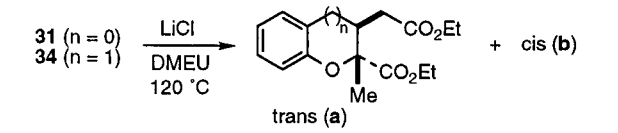
Table 1. Synthesis of Monocyclic Oxygen Heterocycles



substrate	n	R,R	product	R,R	**a**:**b**[a]	% yield[b]
10	0	H,H	**35**	H,H	76:24	67
11	0	5,5-diMe	**36**	5,5-diMe	60:40	67
12	0	4,4-diMe	**37**	4,4-diMe	84:16	60
25	1	H,H	**38**	H,H	88:12	93
26	1	6,6-diMe	**39**	6,6-diMe	81:19	75
27	1	5,5-diMe	**40**	5,5-diMe	81:19	72

[a] Ratios represent the percentage of the crude reaction mixture containing the indicated isomer. [b] Yields refer to isolated purified products (**a**+**b**).

Table 2. Synthesis of Aryl-Fused Oxygen Heterocycles



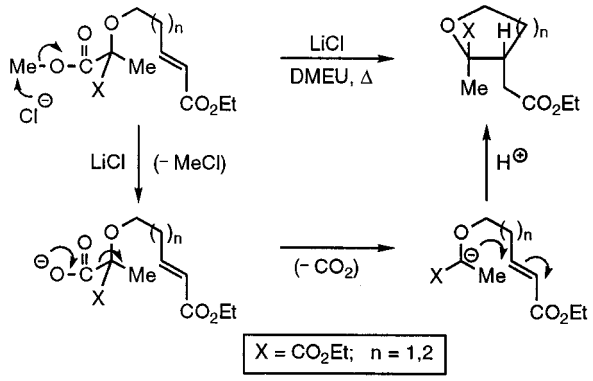
substrate	*n*	product	**a**:**b**[a]	% yield[b]
31	0	**42**	84:16	84
34	1	**43**	80:20[c]	76

[a] Ratios represent the percentage of the crude reaction mixture containing the indicated isomer. [b] Yields refer to isolated purified products (**a**+**b**). [c] Minor isomer contained 5−7% of the noncyclized product resulting from demethoxycarbonylation and double bond migration.

work,[4a,b] but the current procedure is less hazardous and gives slightly better diastereoselectivity. The reaction provides optimum yields of cyclized products using substrate concentrations of ca. 0.1 M on scales up to 5 mmol; higher concentrations or larger reaction scales

(19) Barker, B. J.; Rosenfarb, J.; Caruso, J. A. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 503−507.

Scheme 4



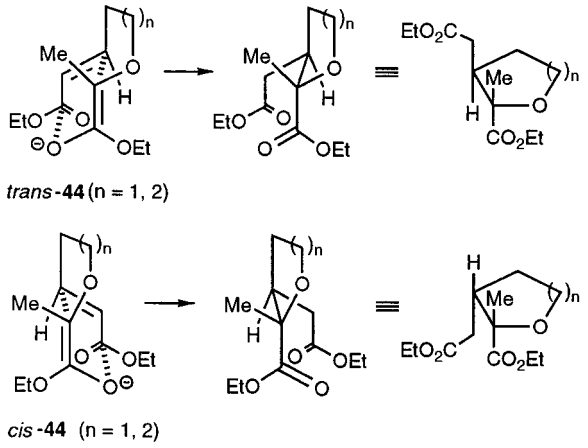
result in reduced selectivity and lower yields of cyclized material. Product purification can be effected by preparative thin-layer chromatography or flash chromatography, and generally isomers are easily separated.

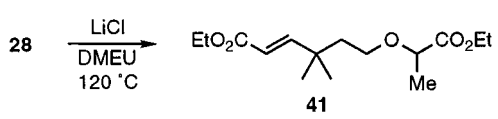
Product structures were established by spectroscopic correlation with compounds previously prepared and characterized in the carbocycle series.[4a] IR spectroscopy indicated the loss of the conjugated double bond. ^{1}H NMR spectra confirmed the absence of the methoxycarbonyl group and the acrylate double bond. As in our earlier carbocycle work,[4a] the trans isomer showed the C-2 methyl upfield by 0.08−0.18 ppm and the C-3 methine downfield by 0.32−0.75 ppm relative to the cis isomer. These observations are in agreement with the shielding−deshielding characteristics of the nearby carbonyl-containing functionality. Additionally, the trans isomer exhibited two doublets of doublets for the side chain methylene group; these signals were not always distinguishable in the cis isomer. ^{13}C NMR gave a correct accounting of the different types of carbons and corroborated the IR and ^{1}H NMR assignments. Finally, exact molecular mass measurements and elemental analyses of the products were consistent with the structures proposed.

The reaction tandem is initiated by chemoselective S_N2-type dealkylation of the methyl ester[2,20] to generate gaseous methyl chloride and a carboxylate anion activated toward decarboxylation by the α-ethoxycarbonyl group. At 120 °C, the carboxylate moiety is spontaneously lost to afford the enolate, which cyclizes by a favorable 5- or 6-[*enolexo*]-*exo-trig*[22] Michael addition on the pendent acrylate ester (see Scheme 4). As noted previously,[4] the best yields of cyclized products are obtained when the decarboxylation proceeds through a tertiary enolate, and when closure occurs to give a five- or six-membered ring.

The preparation of simple oxygen heterocycles proceeded in 60−90% yields with diastereoselectivities up to 7.5:1 in favor of the product isomer having the C-2 ethoxycarbonyl group trans to the C-3 acetic ester side chain. This outcome differs from our carbocycle work[4a] where ester-activated substrates gave unimpressive results and often produced substantial quantities of decarboxylated, uncyclized material. Among the compounds studied, only hindered substrate **28** gave a significant amount of uncyclized product **41**. The improved yields and selectivities in the current study may derive in part from a *gem*-dimethyl effect (if this moiety does not hinder the Michael addition) or an oxygen atom effect, both of which should facilitate ring formation.[20] Aryl-fused systems were also produced in good yield, benefiting from the proximity of the rigidly held reacting partners;[5] substrate **34**, however, gave 5−7% of the noncyclized product derived from demethoxycarbonylation and double bond migration along with the desired heterocycle **43**.

Scheme 5





The trans selectivity observed in the ring closure is of considerable interest and merits further discussion. Since steric interactions alone would tend to disfavor the trans product,[4a] electronic factors must control the reaction. Calculations by others[21] have suggested 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 (Scheme 5). In chair transition state *trans*-**44**, the dominant interaction would involve the HOMO of the enolate (Michael donor) and the LUMO of the *s-cis* α,β-unsaturated ester carbonyl (Michael acceptor). This overlap would stabilize the transition state leading to the trans product, and thus, govern the outcome of the reaction.[22] The lower selectivity observed in the five- (vs the six-) membered ring closures contrasts with observations in the carbocycle series and likely derives from the greater strain required to align the interacting π systems for optimum orbital overlap. This strain should increase as the distance between the interacting π systems decreases. In the current substrates, the two C−O single bonds (each ca. 0.10−0.15 Å shorter than a comparable C−C bond)[23] would shorten the connecting chain sufficiently to inhibit overlap of the interacting donor and acceptor moieties, particularly in five-membered ring closures. Finally, transition state *cis*-**44** should be dis-

(20) (a) For a general review of factors effecting ring closure reactions: Illuminati, G.; Mandolini, L. *Acc. Chem. Res* **1981**, *14*, 95−102. (b) *gem*-Dimethyl effect: Allinger, N. L.; Zalkow, V. *J. Org. Chem.* **1960**, *25*, 701−704. (c) Oxygen atom effect: Dale, J. *Tetrahedron* **1974**, *30*, 1683−1694. Presumably, both of these these factors also increased the rate of cyclization.

(21) (a) Smith, M. B. *Organic Synthesis*; McGraw-Hill: New York, 1994; p 132. (b) Isaacs, N. S. *Physical Organic Chemistry*; Wiley: New York, 1987; p 287.

(22) (a) Baldwin, J. E.; Luche, M. J. *Tetrahedron* **1982**, *38*, 2939−2947.

(23) Sevin, A.; Tortajada, J.; Pfau, M. *J. Org. Chem.* **1986**, *51*, 2671−2675.

favored relative to *trans*-**44** due to additional strain required to achieve chairlike overlap as well as unfavorable interactions between the enolate methyl and C-4 of the developing rings.

The aryl ring in the benzofuran ring closure precludes a chairlike transition state since the ether oxygen, the aromatic ring, and the acrylate acceptor would remain essentially coplanar during the reaction. In this extended π system, steric interaction between the enolate methyl and the acrylate group should force the enolate to rotate out of planarity. Once the enolate moiety tilts out of plane, the trans product should become favored since formation of the cis isomer would require the methyl to rotate past the C−H at the acrylate terminus. In the benzopyran case, overlap between the aromatic ring and the acrylate is eliminated, a chair transition state is again possible, and the trans product should predominate. This structure, however, positions the enolate α-carbon in close proximity to the benzylic methylene, giving rise to competitive double bond migration by proton exchange.

In summary, we have developed and optimized a procedure for the preparation of highly functionalized tetrahydrofuran- and 2*H*-tetrahydropyran-3-acetic esters using a tandem demethoxycarbonylation−Michael addition strategy. The cyclization substrates are readily available, the procedure is simple, and the products are furnished in good yields with useful selectivities. We are continuing our exploration of this reaction for the synthesis of other functionalized ring structures. Several related procedures are also under development.

Experimental Section

DMF (BaO, 20 mmHg), DMEU (CaH_2, 0.5 mmHg), and diisopropylamine (CaH_2) were distilled from the indicated desiccant and stored over 4-Å molecular sieves under N_2; THF was distilled from $LiAlH_4$ under N_2. Other reagents were used as received. All reactions were run under dry N_2 in oven-dried glassware. Unless otherwise indicated, the NH_4Cl (5%), $NaHCO_3$ (5%), $Na_2S_2O_3$ (5%), NaCl (saturated), NaOH (0.02 M), and HCl (0.5−1 M) 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-cm × 20-cm silica gel GF plates (Analtech), (2) flash vacuum chromatography[26] on silica gel (Grace, grade 62, 60−200 mesh), or (3) flash chromatography[27] on silica gel (60−200 mesh) mixed with Sylvania no. 2282 UV-active phosphor. Band elution, where appropriate, was monitored using a hand-held UV lamp. Melting points are uncorrected. IR spectra are referenced to polystyrene. ^{1}H NMR and ^{13}C NMR spectra were measured in $CDCl_3$ at 300 or 400 MHz and at 75 or 100 MHz, respectively, and are referenced to internal $(CH_3)_4Si$. High-resolution mass spectra (HRMS, EI/DP) were obtained at 70 eV. Elemental analyses are ±0.3%.

Representative Methoxycarbonylation Procedure: Ethyl Methyl (±)-(3-Butenoxy)propanedioate (4). The general procedure of Rathke and Deitch[15] was adapted and carried out 4× on a 25 mmol scale. LDA (50 mmol) was generated at −78 °C in 75 mL of THF from 5.25 g (7.27 mL, 52.0 mmol) of diisopropylamine and 31.3 mL of 1.6 M *n*-BuLi in hexanes (50.0 mmol). To the stirred solution of LDA was added a solution of 3.95 g (25.0 mmol) of **1** in 25 mL of THF dropwise during 15 min. The mixture was stirred at −78 °C for 15 min, and a solution of 2.36 g (1.93 mL, 25.0 mmol) of methyl chloroformate in 10 mL of THF was added dropwise over a period of 10 min. The reaction was stirred for 10 min at −78 °C and quenched with 50 mL of 1 M HCl. The mixture was warmed to 20 °C, the organic layer was separated, and the aqueous phase was extracted with ether (2×). The combined organic extracts were washed with H_2O, 5% $NaHCO_3$, and saturated NaCl, dried ($MgSO_4$), and concentrated under vacuum. The product from the four runs was purified by vacuum distillation to afford 12.1 g (56.1 mmol, 56%) of **4** as a colorless oil: bp 74−76 °C (0.5 mmHg); IR (thin film) 3085, 1758, 1648, 1005, 924 cm^{-1}; ^{1}H NMR δ 5.83 (ddt, 1 H, J = 17.1, 10.3, 6.8 Hz), 5.11 (d, 1 H, J = 17.1 Hz), 5.06 (d, 1 H, J = 10.3 Hz), 4.52 (s, 1 H), 4.27 (q, 2 H, J = 7.2 Hz), 3.81 (s, 3 H), 3.65 (t, 2 H, J = 6.8 Hz), 2.43 (q, 2 H, J = 6.8 Hz), 1.30 (t, 3 H, J = 7.2 Hz); ^{13}C NMR δ 166.9, 166.4, 134.0, 116.9, 79.0, 70.6, 61.9, 52.7, 33.7, 13.9; HRMS *m*/*z* Calcd for $C_{10}H_{16}O_5$: 216.0997. Found: 216.0992.

The following compounds were prepared by the same procedure. The yields are based on four runs using 25 mmol (100 mmol total) of the ester.

Ethyl Methyl (±)-(1,1-Dimethyl-3-butenoxy)propanedioate (5): 15.3 g (62.5 mmol, 62.5%) from **2**; bp 82−84 °C (0.5 mmHg); IR (thin film) 3080, 1775, 1750, 1644, 1390, 1372, 920 cm^{-1}; ^{1}H NMR δ 5.85 (ddt, 1 H, J = 16.5, 10.7, 7.1 Hz), 5.06 (m, 2 H), 4.66 (s, 1 H), 4.24 (m, 2 H), 3.79 (s, 3 H), 2.30 (d, 2 H, J = 7.1 Hz), 1.29 (t, 3 H, J = 7.2 Hz), 1.21 (s, 6 H); ^{13}C NMR δ 168.4, 167.9, 133.8, 117.8, 78.6, 72.3, 61.8, 52.6, 45.3, 25.1, 25.0, 13.9; HRMS *m*/*z* Calcd for $C_{12}H_{20}O_5$: 244.1311. Found: 244.1305.

Ethyl Methyl (±)-(2,2-Dimethyl-3-butenoxy)propanedioate (6): 14.7 g (60.1 mmol, 60%) from **3**; bp 65−67 °C (0.2 mmHg); IR (thin film) 3085, 1755, 1649, 1395, 1370, 983, 920 cm^{-1}; ^{1}H NMR δ 5.87 (dd, 1 H, J = 17.5, 10.8 Hz), 5.04 (d, 1 H, J = 17.5 Hz), 4.99 (d, 1 H, J = 10.8 Hz), 4.47 (s, 1 H), 4.26 (m, 2 H), 3.80 (s, 3 H), 3.35 (s, 2 H), 1.30 (t, 3 H, J = 7.1 Hz), 1.07 (s, 6 H); ^{13}C NMR δ 167.0, 166.5, 144.9, 112.0, 79.8, 79.6, 61.8, 52.6, 38.0, 23.7 (2), 13.9; HRMS *m*/*z* Calcd for $C_{12}H_{20}O_5$: 244.1311. Found: 244.1310.

Ethyl Methyl (±)-(4-Pentenoxy)propanedioate (17): 13.3 g (58 mmol, 58%) from **13**; bp 84−86 °C (0.5 mmHg); IR (thin film) 3085, 1758, 1648, 1003, 920 cm^{-1}; ^{1}H NMR δ 5.80 (ddt, 1 H, J = 17.2, 10.3, 6.8 Hz), 5.03 (d, 1 H, J = 17.2 Hz), 4.97 (d, 1 H, J = 10.3 Hz), 4.49 (s, 1 H), 4.27 (q, 2 H, J = 7.1 Hz), 3.81 (s, 3 H), 3.60 (t, 2 H, J = 6.8 Hz), 2.16 (q, 2 H, J = 6.8 Hz), 1.77 (quintet, 2 H, J = 6.8 Hz), 1.30 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 167.0, 166.4, 137.7, 114.9, 79.1, 70.7, 61.9, 52.6, 29.8, 28.4, 13.9; HRMS *m*/*z* Calcd for $C_{11}H_{18}O_5$: 230.1154. Found: 230.1149.

Ethyl Methyl (±)-(1,1-Dimethyl-4-pentenoxy)propanedioate (18): 17.0 g (65.8 mmol, 66%) from **14**; bp 92−94 °C (0.5 mmHg); IR (thin film) 3082, 1776, 1750, 1648, 1390, 1375, 1000, 912 cm^{-1}; ^{1}H NMR δ 5.81 (ddt, 1 H, J = 17.1, 10.3, 6.8 Hz), 5.02 (d, 1 H, J = 17.1 Hz), 4.93 (d, 1 H, J = 10.3 Hz), 4.62 (s, 1 H), 4.25 (m, 2 H), 3.79 (s, 3 H), 2.15 (m, 2 H), 1.61 (m, 2 H), 1.29 (t, 3 H, J = 7.2 Hz), 1.22 (s, 6 H); ^{13}C NMR δ 168.4, 167.9, 138.5, 114.2, 78.5, 72.2, 61.7, 52.6, 39.7, 28.0, 25.2, 25.1, 13.9; HRMS *m*/*z* Calcd for $C_{13}H_{22}O_5$: 258.1467. Found: 258.1458.

Ethyl Methyl (±)-(2,2-Dimethyl-4-pentenoxy)propanedioate (19): 15.1 g (58.5 mmol, 58.5%) from **15**; bp 88−89 °C (0.5 mmHg); IR (thin film) 3078, 1774, 1750, 1642, 1380, 1368,

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1000, 918 cm^{-1}; ^1H NMR δ 5.81 (ddt, 1 H, J = 17.0, 10.8, 7.5 Hz), 5.02 (m, 2 H), 4.44 (s, 1 H), 4.27 (m, 2 H), 3.80 (s, 3 H), 3.27 (s, 2 H), 2.07 (d, 2 H, J = 7.5 Hz), 1.30 (t, 3 H, J = 7.1 Hz), 0.93 (s, 6 H); ^{13}C NMR δ 167.1, 166.6, 134.9, 117.2, 79.6 (2), 61.8, 52.6, 43.2, 34.9, 24.1 (2), 14.0; HRMS *m/z* Calcd for $C_{13}H_{22}O_5$: 258.1467. Found: 258.1477.

Ethyl Methyl (±)-(3,3-Dimethyl-4-pentenoxy)propanedioate (20): 16.8 g (65.1 mmol, 65%) from **16**; bp 83−84 °C (0.5 mmHg); IR (thin film) 3084, 1760, 1644, 1385, 1370, 981, 915 cm^{-1}; ^1H NMR δ 5.76 (dd, 1 H, J = 17.8, 10.4 Hz), 4.92 (m, 2 H), 4.46 (s, 1 H), 4.27 (m, 2 H), 3.81 (s, 3 H), 3.56 (t, 2 H, J = 7.5 Hz), 1.73 (t, 2 H, J = 7.5 Hz), 1.30 (t, 3 H, J = 7.1 Hz), 1.02 (s, 6 H); ^{13}C NMR δ 167.0, 166.5, 147.4, 110.8, 79.2, 68.7, 61.9, 52.7, 41.0, 35.4, 26.9 (2), 13.9; HRMS *m/z* Calcd for $C_{13}H_{22}O_5$: 258.1467. Found: 258.1471.

Representative Methylation Procedure: Ethyl Methyl (±)-(3-Butenoxy)methylpropanedioate (7). The general alkylation procedure of Inomata and co-workers was used.[16,17] To a suspension of 1.22 g (51.0 mmol) of oil-free NaH in 75 mL of DMF was added a solution of 10.8 g (50.0 mmol) of **4** in 25 mL of DMF dropwise with stirring. The mixture was stirred for 30 min, and a solution of 10.7 g (4.67 mL, 75.0 mmol) of methyl iodide in 10 mL of DMF was added dropwise. The reaction was heated at 50 °C for 12 h, cooled, quenched with 5% NH_4Cl, and extracted with ether (3×). The combined organic extracts were washed with H_2O, 5% $Na_2S_2O_3$, and saturated NaCl, dried ($MgSO_4$), and concentrated under vacuum. Final purification by vacuum distillation afforded 10.2 g (44.5 mmol, 89%) of **7** as a colorless oil: bp 72−74 °C (0.2 mmHg); IR (thin film) 3085, 1752, 1648, 1376, 998, 920 cm^{-1}; ^1H NMR δ 5.82 (ddt, 1 H, J = 17.2, 10.3, 6.9 Hz), 5.08 (d, 1 H, J = 17.2 Hz), 5.03 (d, 1 H, J = 10.3 Hz), 4.25 (q, 2 H, J = 7.2 Hz), 3.79 (s, 3 H), 3.58 (t, 2 H, J = 6.9 Hz), 2.38 (q, 2 H, J = 6.9 Hz), 1.64 (s, 3 H), 1.29 (t, 3 H, J = 7.2 Hz); ^{13}C NMR δ 169.8, 169.2, 134.5, 116.5, 81.7, 65.5, 61.7, 52.5, 34.3, 20.6, 13.9; HRMS *m/z* Calcd for $C_{11}H_{18}O_5$: 230.1154. Found: 230.1150.

The following compounds were prepared on varying scales using the same procedure. Purification was achieved by vacuum distillation or silica gel flash chromatography eluted with ether in hexanes.

Ethyl Methyl (±)-(1,1-Dimethyl-3-butenoxy)methylpropanedioate (8): 11.2 g (43.4 mmol, 97%) from **5**; bp 79−81 °C (0.5 mmHg); IR (thin film) 3080, 1750, 1645, 1390, 1372, 1000, 920 cm^{-1}; ^1H NMR δ 5.95 (ddt, 1 H, J = 17.1, 10.3, 7.2 Hz), 5.04 (m, 2 H), 4.22 (q, 2 H, J = 7.1 Hz), 3.76 (s, 3 H), 2.32 (d, 2 H, J = 7.2 Hz), 1.74 (s, 3 H), 1.28 (t, 3 H, J = 7.1 Hz), 1.25 (s, 6 H); ^{13}C NMR δ 171.4, 170.8, 134.8, 117.2, 80.3, 78.7, 61.6, 52.5, 48.6, 26.7, 26.6, 23.0, 13.8; HRMS *m/z* Calcd for $C_{13}H_{22}O_5$: 258.1467. Found: 258.1469.

Ethyl Methyl (±)-(2,2-Dimethyl-3-butenoxy)methylpropanedioate (9): 9.78 g (37.9 mmol, 91%) from **6**; used without further purification; IR (thin film) 3085, 1750, 1648, 1393, 1373, 985, 919 cm^{-1}; ^1H NMR δ 5.87 (dd, 1 H, J = 17.5, 10.7 Hz), 5.01 (d, 1 H, J = 17.5 Hz), 4.97 (d, 1 H, J = 10.7 Hz), 4.24 (q, 2 H, J = 7.1 Hz), 3.77 (s, 3 H), 3.28 (s, 2 H), 1.61 (s, 3 H), 1.28 (t, 3 H, J = 7.1 Hz), 1.04 (s, 6 H); ^{13}C NMR δ 170.0, 169.3, 145.5, 111.5, 81.5, 74.0, 61.5, 52.4, 37.7, 23.8 (2), 20.7, 14.0; HRMS *m/z* Calcd for $C_{13}H_{22}O_5$: 258.1464. Found: 258.1460.

Ethyl Methyl (±)-Methyl(4-pentenoxy)propanedioate (21): 11.3 g (46.3 mmol, 89%) from **17**; bp 88−89 °C (0.5 mmHg); IR (thin film) 3085, 1750, 1648, 1377, 1000, 919 cm^{-1}; ^1H NMR δ 5.81 (ddt, 1 H, J = 17.2, 10.3, 7.0 Hz), 5.03 (d, 1 H, J = 17.2 Hz), 4.95 (d, 1 H, J = 10.3 Hz), 4.25 (q, 2 H, J = 7.1 Hz), 3.79 (s, 3 H), 3.52 (t, 2 H, J = 6.6 Hz), 2.14 (q, 2 H, J = 7.0 Hz), 1.72 (quintet, 2 H, J = 7.0 Hz), 1.63 (s, 3 H), 1.29 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 169.9, 169.2, 138.0, 114.6, 81.6, 65.3, 61.6, 52.5, 29.9, 29.0, 20.5, 13.9; HRMS *m/z* Calcd for $C_{12}H_{20}O_5$: 244.1310. Found: 244.1309.

Ethyl Methyl (±)-(1,1-Dimethyl-4-pentenoxy)methylpropanedioate (22): 10.8 g (39.7 mmol, 88%) from **18**; bp 70−72 °C (0.3 mmHg); IR (thin film) 3085, 1752, 1650, 1390, 1375, 1000, 913 cm^{-1}; ^1H NMR δ 5.84 (ddt, 1 H, J = 17.1, 10.2, 6.8 Hz), 5.02 (d, 1 H, J = 17.1 Hz), 4.92 (d, 1 H, J = 10.2 Hz), 4.22 (q, 2 H, J = 7.1 Hz), 3.76 (s, 3 H), 2.21 (m, 2 H), 1.72 (s, 3 H), 1.62 (m, 2 H), 1.28 (t, 3 H, J = 7.1 Hz), 1.27 (s, 6 H); ^{13}C NMR δ 171.5, 170.9, 139.1, 113.9, 80.2, 78.7, 61.6, 52.5, 43.2, 28.3, 27.0 (2), 22.9, 13.8; HRMS *m/z* Calcd for $C_{14}H_{24}O_5$: 272.1464. Found: 272.1459.

Ethyl Methyl (±)-(2,2-Dimethyl-4-pentenoxy)methylpropanedioate (23): 10.9 g (40.0 mmol, 88%) from **19**; bp 84−87 °C (0.5 mmHg); IR (thin film) 3078, 1750, 1642, 1398, 1370, 998, 915 cm^{-1}; ^1H NMR δ 5.82 (ddt, 1 H, J = 17.3, 10.7, 7.5 Hz), 4.99 (m, 2 H), 4.23 (q, 2 H, J = 7.1 Hz), 3.77 (s, 3 H), 3.19 (s, 2 H), 2.03 (d, 2 H, J = 7.5 Hz), 1.61 (s, 3 H), 1.28 (t, 3 H, J = 7.1 Hz), 0.89 (s, 6 H); ^{13}C NMR δ 170.1, 169.4, 135.2, 116.4, 81.4, 73.6, 61.5, 52.4, 43.4, 34.5, 24.1 (2), 20.7, 14.0; HRMS *m/z* Calcd for $C_{14}H_{24}O_5$: 272.1464. Found: 272.1462.

Ethyl Methyl (±)-(3,3-Dimethyl-4-pentenoxy)methylpropanedioate (24): 9.98 g (36.7 mmol, 92%) from **20**; used without further purification; IR (thin film) 3083, 1750, 1643, 1385, 1375, 982, 914 cm^{-1}; ^1H NMR δ 5.76 (dd, 1 H, J = 17.8, 10.4 Hz), 4.90 (m, 2 H), 4.25 (m, 2 H), 3.78 (s, 3 H), 3.49 (t, 2 H, J = 7.7 Hz), 1.69 (t, 2 H, J = 7.7 Hz), 1.63 (s, 3 H), 1.29 (t, 3 H, J = 7.1 Hz), 1.01 (s, 6 H); ^{13}C NMR δ 170.7, 169.3, 147.6, 110.6, 81.8, 63.3, 61.7, 52.5, 41.7, 35.5, 27.0 (2), 20.5, 14.0; HRMS *m/z* Calcd for $C_{14}H_{24}O_5$: 272.1464. Found: 272.1463.

Representative Ozonolysis−Wittig Procedure: Ethyl (±)-(*E*)-5-(1-(Ethoxycarbonyl)-1-(methoxycarbonyl)-ethoxy)-2-pentenoate (10). The procedure of Bunce and co-workers[4a] was used. A solution of 9.20 g (40.0 mmol) of **7** in 300 mL of CH_2Cl_2 was cooled to −78 °C and treated with O_3 until the solution turned a light blue color. The reaction was quenched at −78 °C with 6.20 g (7.33 mL, 100 mmol) of Me_2S, warmed to 20 °C, stirred for 3 h, and concentrated under vacuum. To the resulting light yellow oil was added 250 mL of benzene and 20.9 g (60.0 mmol) of ethyl (triphenylphosphoranylidene)acetate.[28] The solution was refluxed for 12 h and then cooled and concentrated under vacuum to afford a tan semisolid mass. The residue was layered on top of a 10 cm × 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. Concentration of the filtrate afforded the crude product as a viscous yellow oil. This oil was flash chromatographed on a 50 cm × 2.5 cm silica gel column eluted with increasing concentrations of ether in hexanes. The major band gave 7.19 g (20.8 mmol, 59.5%) of **10** as a colorless oil: IR (thin film) 1750, 1735, 1658, 1375 cm^{-1}; ^1H NMR δ 6.96 (dt, 1 H, J = 15.7, 6.8 Hz), 5.90 (d, 1 H, J = 15.7 Hz), 4.26 (q, 2 H, J = 7.2 Hz), 4.18 (q, 2 H, J = 7.2 Hz), 3.79 (s, 3 H), 3.67 (t, 2 H, J = 6.6 Hz), 2.53 (q, 2 H, J = 6.7 Hz), 1.64 (s, 3 H), 1.29 (t, 6 H, J = 7.2 Hz); ^{13}C NMR δ 167.7, 169.1, 166.3, 144.9, 123.0, 81.8, 64.4, 61.8, 60.1, 52.6, 32.7, 20.8, 14.2, 14.0; HRMS *m/z* Calcd for $C_{14}H_{22}O_7$: 302.1364. Found: 302.1358. Anal. Calcd for $C_{14}H_{22}O_7$: C, 55.62; H, 7.28. Found: C, 55.64; H, 7.25.

The following compounds were prepared on varying scales using the same procedure. Purification was achieved by silica gel flash chromatography eluted with ether in hexanes.

Ethyl (±)-(*E*)-5-(1-(Ethoxycarbonyl)-1-(methoxycarbonyl)ethoxy)-5-methyl-2-hexenoate (11): 7.95 g (24.1 mmol, 56%) from **8**; IR (thin film) 1750, 1730, 1660, 1392, 1374 cm^{-1}; ^1H NMR δ 7.11 (dt, 1 H, J = 15.7, 7.5 Hz), 5.84 (d, 1 H, J = 15.7 Hz), 4.28−4.17 (complex, 4 H), 3.77 (s, 3 H), 2.46 (d, 2 H, J = 7.5 Hz), 1.74 (s, 3 H), 1.29 (m, 12 H); ^{13}C NMR δ 171.3, 170.6, 166.3, 145.2, 123.7, 80.4, 78.4, 61.7, 60.1, 52.6, 47.1, 26.9, 26.8, 23.1, 14.2, 13.8; HRMS *m/z* Calcd for $C_{16}H_{26}O_7$: 330.1678. Found: 330.1675. Anal. Calcd for $C_{16}H_{26}O_7$: C, 58.18; H, 7.88. Found: C, 58.12; H, 7.93.

Ethyl (±)-(*E*)-5-(1-(Ethoxycarbonyl)-1-(methoxycarbonyl)ethoxy)-4,4-dimethyl-2-pentenoate (12): 4.74 g (14.4 mmol, 50%) from **9**; IR (thin film) 1749, 1722, 1651, 1392, 1370, 985 cm^{-1}; ^1H NMR δ 6.98 (d, 1 H, J = 16.0 Hz), 5.82 (d, 1 H, J = 16.0 Hz), 4.24 (q, 2 H, J = 7.1 Hz), 4.19 (q, 2 H, J = 7.1 Hz), 3.77 (s, 3 H), 3.38 (s, 2 H), 1.61 (s, 3 H), 1.29 (t, 3 H, J = 7.1 Hz), 1.28 (t, 3 H, J = 7.1 Hz), 1.10 (s, 6 H); ^{13}C NMR δ

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169.8, 169.2 167.1, 155.2, 118.9, 81.6, 73.3, 61.7, 60.2, 52.5, 37.9, 23.7 (2), 21.0, 14.3, 14.0; HRMS *m/z* Calcd for $C_{16}H_{26}O_7$: 330.1678. Found: 330.1676. Anal. Calcd for $C_{16}H_{26}O_7$: C, 58.18; H, 7.88. Found: C, 58.39; H, 7.96.

Ethyl (±)-(*E*)-6-(1-(Ethoxycarbonyl)-1-(methoxycarbonyl)ethoxy)-2-hexenoate (25): 7.96 g (25.2 mmol, 56%) from **21**; IR (thin film) 1750, 1735, 1660, 1375 cm^{-1}; ^1H NMR δ 6.97 (dt, 1 H, J = 15.6, 6.8 Hz), 5.84 (d, 1 H, J = 15.6 Hz), 4.25 (q, 2 H, J = 7.1 Hz), 4.18 (q, 2 H, J = 7.1 Hz), 3.79 (s, 3 H), 3.56 (t, 2 H, J = 6.5 Hz), 2.33 (q, 2 H, J = 7.2 Hz), 1.79 (quintet, 2 H, J = 6.8 Hz), 1.63 (s, 3 H), 1.29 (2 t, 6 H, J = 7.1 Hz); ^{13}C NMR δ 169.7, 169.1, 166.4, 148.3, 121.5, 81.5, 64.8, 61.6, 59.9, 52.5, 28.4, 28.1, 20.6, 14.1, 13.9; HRMS *m/z* Calcd for $C_{15}H_{24}O_7$: 316.1521. Found: 316.1517. Anal. Calcd for $C_{15}H_{24}O_7$: C, 56.96; H, 7.59. Found: C, 57.19; H, 7.63.

Ethyl (±)-(*E*)-6-(1-(Ethoxycarbonyl)-1-(methoxycarbonyl)ethoxy)-6-methyl-2-heptenoate (26): 6.74 g (19.6 mmol, 52%) from **22**; IR (thin film) 1750, 1728, 1660, 1395, 1376 cm^{-1}; ^1H NMR δ 7.02 (dt, 1 H, J = 15.6, 6.8 Hz), 5.83 (d, 1 H, J = 15.6 Hz), 4.22 (q, 2 H, J = 7.1 Hz), 4.18 (q, 2 H, J = 7.1 Hz), 3.76 (s, 3 H), 2.42 (m, 2 H), 1.72 (s, 3 H), 1.67 (m, 2 H), 1.28 (s, 6 H), 1.28 (2 t, 6 H, J = 7.1 Hz); ^{13}C NMR δ 171.3, 170.7, 166.6, 149.5, 120.9, 80.2, 78.2, 61.6, 60.0, 52.5, 42.4, 27.0, 26.9, 26.7, 23.0, 14.2, 13.8; HRMS *m/z* Calcd for $C_{17}H_{28}O_7$: 344.1835. Found: 344.1843. Anal. Calcd for $C_{17}H_{28}O_7$: C, 59.30; H, 8.14. Found: C, 59.55; H, 8.20.

Ethyl (±)-(*E*)-6-(1-(Ethoxycarbonyl)-1-(methoxycarbonyl)ethoxy)-5,5-dimethyl-2-hexenoate (27): 5.57 g (16.2 mmol, 51%) from **23**; IR (thin film) 1750, 1728, 1658, 1396, 1372 cm^{-1}; ^1H NMR δ 6.99 (dt, 1 H, J = 15.6, 7.7 Hz), 5.83 (d, 1 H, J = 15.6 Hz), 4.24 (q, 2 H, J = 7.1 Hz), 4.18 (q, 2 H, J = 7.1 Hz), 3.78 (s, 3 H), 3.23 (s, 2 H), 2.21 (d, 2 H, J = 7.7 Hz), 1.62 (s, 3 H), 1.30 (t, 3 H, J = 7.1 Hz), 1.29 (t, 3 H, J = 7.1 Hz), 0.93 (s, 6 H); ^{13}C NMR δ 169.9, 169.3, 166.4, 146.6, 123.5, 81.4, 73.4, 61.6, 60.0, 52.4, 41.5, 35.2, 24.4 (2), 20.7, 14.2, 14.0; HRMS *m/z* Calcd for $C_{17}H_{28}O_7$: 344.1835. Found: 344.1839. Anal. Calcd for $C_{17}H_{28}O_7$: C, 59.30; H, 8.14. Found: C, 59.59; H, 8.17.

Ethyl (±)-(*E*)-6-(1-(Ethoxycarbonyl)-1-(methoxycarbonyl)ethoxy)-4,4-dimethyl-2-hexenoate (28): 2.48 g (7.21 mmol, 40%) from **24**; IR (thin film) 1750, 1729, 1659, 1394, 1372, 985 cm^{-1}; ^1H NMR δ 5.95 (d, 1 H, J = 13.1 Hz), 5.69 (d, 1 H, J = 13.1 Hz), 4.25 (q, 2 H, J = 7.1 Hz), 4.15 (q, 2 H, J = 7.1 Hz), 3.78 (s, 3 H), 3.56 (t, 2 H, J = 7.3 Hz), 1.89 (t, 2 H, J = 7.3 Hz), 1.63 (s, 3 H), 1.29 (t, 3 H, J = 7.1 Hz), 1.28 (t, 3 H, J = 7.1 Hz), 1.20 (s, 6 H); ^{13}C NMR δ 169.9, 169.4, 166.6, 152.9, 119.5, 81.8, 63.4, 61.8, 60.2, 52.3, 42.4, 36.0, 27.6 (2), 20.6, 14.1, 14.0; HRMS *m/z* Calcd for $C_{17}H_{28}O_7$: 344.1835. Found: 344.1841. Anal. Calcd for $C_{17}H_{28}O_7$: C, 59.30; H, 8.14. Found: C, 59.47; H, 8.16.

Ethyl Methyl (±)-(2-Formylphenoxy)methylpropanedioate (30). The general alkylation procedure of Inomata and co-workers was used.[16] To a suspension of 0.60 g (25.0 mmol) of oil-free NaH in 10 mL of DMF was added a solution of 4.08 g (24.6 mmol) of **29**[18] in 15 mL of DMF. To the clear solution was added 4.51 g (25.0 mmol) of ethyl methyl (±)-chloropropanedioate[29] in 15 mL of DMF. The reaction was stirred for 1 h at rt and for 8 h at 50 °C and then cooled, quenched with 5% NH_4Cl, and extracted with ether (3×). The combined organic extracts were washed with H_2O, 0.02 M NaOH (until the washes were colorless), H_2O, and saturated NaCl, dried (Na_2SO_4), and concentrated under vacuum. The crude ethyl methyl (±)-(2-formylphenoxy)propanedioate ethylene ketal (7.00 g) was isolated as a light yellow oil and used without further purification. IR (thin film) 1749, 1665, 1603, 1495, 759 cm^{-1}; ^1H NMR δ 7.57 (d, 1 H, J = 8.0 Hz), 7.29 (t, 1 H, J = 7.5 Hz), 7.08 (t, 1 H, J = 7.5 Hz), 6.86 (d, 1 H, J = 8.2 Hz), 6.30 (s, 1 H), 5.23 (s, 1 H), 4.29 (q, 2 H, J = 7.1 Hz), 4.13 (m, 2 H), 4.03 (m, 2 H), 3.83 (s, 3 H), 1.29 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 166.1, 165.4, 155.5, 130.3, 128.3, 127.6, 122.9, 114.0, 99.0, 77.8, 65.1, 62.3, 53.0, 13.7; HRMS *m/z* Calcd for $C_{15}H_{18}O_7$: 310.1052. Found: 310.1049.

The crude ethyl methyl (±)-(2-formylphenoxy)propanedioate ethylene ketal was alkylated with methyl iodide on a 22.5 mmol scale using the same procedure given for the preparation of **7**. The crude ethyl methyl (±)-(2-formylphenoxy)methylpropanedioate ethylene ketal (6.42 g) was isolated as a light yellow oil and used without further purification. IR (thin film) 1745, 1602, 1494, 1373, 752 cm^{-1}; ^1H NMR δ 7.56 (d, 1 H, J = 8.0 Hz), 7.24 (t, 1 H, J = 7.5 Hz), 7.09 (t, 1 H, J = 7.5 Hz), 6.88 (d, 1 H, J = 8.2 Hz), 6.25 (s, 1 H), 4.28 (q, 2 H, J = 7.1 Hz), 4.12 (m, 2 H), 4.02 (m, 2 H), 3.82 (s, 3 H), 1.73 (s, 3 H), 1.25 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 169.6, 168.8, 153.0, 130.1, 129.8, 127.4, 123.4, 118.4, 99.0, 83.0, 65.1, 62.2, 53.0, 19.9, 13.7; HRMS *m/z* Calcd for $C_{16}H_{20}O_7$: 324.1208. Found: 324.1202.

A solution of 6.42 g (19.8 mmol) of ethyl methyl (±)−(2-formylphenoxy)methylpropanedioate ethylene ketal in 100 mL of acetone was treated with 100 mg of *p*-TsOH and stirred at rt for 4 h. The reaction was concentrated, diluted with ether, washed with 5% $NaHCO_3$ and saturated NaCl, dried ($MgSO_4$), and concentrated under vacuum. The crude aldehyde was flash chromatographed on a 50 cm × 2.5 cm silica gel column eluted with increasing concentrations of ether in hexanes. Concentration of the major band gave 4.08 g (14.6 mmol, 60% from **29**) of aldehyde **30** as a light yellow oil. IR (thin film) 2875, 2761, 1741, 1688, 1595, 1488, 1373, 759 cm^{-1}; ^1H NMR δ 10.59 (s, 1 H), 7.88 (d, 1 H, J = 7.7 Hz), 7.48 (t, 1 H, J = 7.5 Hz), 7.15 (t, 1 H, J = 7.5 Hz), 6.93 (d, 1 H, J = 8.2 Hz), 4.29 (q, 2 H, J = 7.1 Hz), 3.84 (s, 3 H), 1.87 (s, 3 H), 1.25 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 190.1, 168.9, 168.1, 157.4, 135.1, 128.4, 127.8, 123.1, 117.8, 83.1, 62.5, 53.2, 20.7, 13.6; HRMS *m/z* Calcd for $C_{14}H_{16}O_6$: 280.0946. Found: 280.0941.

Ethyl Methyl (±)-(*E*)-(2-(2-(Ethoxycarbonyl)ethenyl)-phenoxy)methylpropanedioate (31). A solution of 4.05 g (14.5 mmol) of **30** in 150 mL of benzene was treated with 5.08 g (14.6 mmol) of ethyl (triphenylphosphoranylidene)acetate,[28] and the mixture was refluxed for 12 h. The solution was cooled and concentrated under vacuum to afford a tan semisolid mass. The residue was layered on top of a 10 cm × 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. Concentration of the filtrate afforded the crude product as a viscous yellow oil. This oil was flash chromatographed on a 50 cm × 2.5 cm silica gel column eluted with increasing concentrations of ether in hexanes. Concentration of the major band gave 3.75 g (10.7 mmol, 74%) of **31** as a light yellow oil. IR (thin film) 1749, 1711, 1626, 1595, 1488, 1373, 982, 759 cm^{-1}; ^1H NMR δ 8.08 (d, 1 H, J = 16.2 Hz), 7.56 (d, 1 H, J = 7.7 Hz), 7.25 (t, 1 H, J = 7.5 Hz), 7.06 (t, 1 H, J = 7.5 Hz), 6.85 (d, 1 H, J = 8.2 Hz), 6.64 (d, 1 H, J = 16.2 Hz), 4.31 (q, 2 H, J = 7.1 Hz), 4.27 (q, 2 H, J = 7.1 Hz), 3.85 (s, 3 H), 1.78 (s, 3 H), 1.34 (t, 3 H, J = 7.1 Hz), 1.28 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 169.4, 168.6, 167.4, 153.5, 139.7, 130.7, 129.0, 126.9, 123.2, 119.8, 117.9, 83.1, 62.5, 60.2, 53.1, 20.2, 14.1, 13.7; HRMS *m/z* Calcd for $C_{18}H_{22}O_7$: 350.1365. Found: 350.1367. Anal. Calcd for $C_{18}H_{22}O_7$: C, 61.71; H, 6.29. Found: C, 61.94; H, 6.34.

Ethyl Methyl (±)-Methyl(2-(2-propenyl)phenoxy)propanedioate (33). Compound **32** was alkylated with ethyl methyl (±)-chloropropanedioate[29] on a 22.5 mmol scale using the same procedure given to alkylate **29** in the preparation of **30**. Flash chromatography on a 100 cm × 2.5 cm silica gel column eluted with increasing concentrations of ether in hexanes gave 5.50 g (19.8 mmol, 88%) of ethyl methyl (±)-(2-(2-propenyl)phenoxy)propanedioate as a light yellow oil. IR (thin film) 1773, 1751, 1648, 1370, 996, 916, 755 cm^{-1}; ^1H NMR δ 7.15 (m, 2 H), 6.98 (t, 1 H, J = 7.4 Hz), 6.74 (d, 1 H, J = 8.1 Hz), 6.03 (ddt, 1 H, J = 17.0, 10.1, 6.8 Hz), 5.20 (s, 1 H), 5.09 (d, 1 H, J = 17.0 Hz), 5.05 (d, 1 H, J = 10.1 Hz), 4.30 (q, 2 H, J = 7.1 Hz), 3.84 (s, 3 H), 3.51 (d, 2 H, J = 6.8 Hz), 1.29 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 166.2, 165.6, 154.7, 136.6, 130.3,

(29) The general chlorination procedure of Budesinsky and co-workers was used; see Budesinsky, Z.; Budesinsky, M.; Svab, A. *Collect. Czech. Chem. Commun.* **1981**, *46*, 2254−2262. The yield was 86%, bp 88−89 °C (2 mmHg). IR (thin film) 1762, 1367 cm^{-1}; ^1H NMR δ 4.88 (s, 1 H), 4.30 (q, 2 H, J = 7.1 Hz), 3.85 (s, 3 H), 1.32 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 165.0, 164.4, 63.2, 55.1, 53.7, 13.8; HRMS *m/z* Calcd for $C_6H_9{}^{35}ClO_4$: 180.0190. Found: 180.0184.

129.9, 127.2, 122.6, 115.6, 112.3, 77.0, 62.3, 53.0, 34.2, 13.9; HRMS *m/z* Calcd for $C_{15}H_{18}O_5$: 278.1154. Found: 278.1144.

The crude ethyl methyl (±)-(2-(2-propenyl)phenoxy)propanedioate was alkylated with methyl iodide on a 19.8 mmole scale using the procedure described for the preparation of **7**. Flash chromatography on an 80 cm × 2.5 cm silica gel column eluted with increasing concentrations of ether in hexanes gave 4.76 g (16.3 mmol, 94%) of **33** as a light yellow oil. IR (thin film) 1746, 1635, 1367, 988, 909, 751 cm^{-1}; ^1H NMR δ 7.17 (d, 1 H, J = 7.4 Hz), 7.08 (m, 1 H), 6.98 (t, 1 H, J = 7.4 Hz), 6.78 (d, 1 H, J = 8.1 Hz), 5.99 (ddt, 1 H, J = 17.0, 10.1, 6.8 Hz), 5.06 (d, 1 H, J = 17.0 Hz), 5.04 (d, 1 H, J = 10.1 Hz), 4.27 (q, 2 H, J = 7.1 Hz), 3.82 (s, 3 H), 3.46 (d, 2 H, J = 6.8 Hz), 1.72 (s, 3 H), 1.25 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 169.7, 168.9, 152.3, 136.8, 132.1, 130.3, 126.8, 123.0, 117.3, 115.6, 82.6, 62.3, 53.1, 34.4, 20.2, 13.9; HRMS *m/z* Calcd for $C_{16}H_{20}O_5$: 292.1311. Found: 292.1304.

Ethyl Methyl (±)-(*E*)-(2-(3-(Ethoxycarbonyl)-2-propenyl)phenoxy)methylpropanedioate (34). This compound was prepared from **33** by the ozonolysis−Wittig procedure given for the preparation of **10**. Flash chromatography on an 80 cm × 2.5 cm silica gel column eluted with increasing concentrations of ether in hexanes gave 3.18 g (8.93 mmol, 55%) of **34** as a light yellow oil. IR (thin film) 1746, 1714, 1651, 1367, 980, 751 cm^{-1}; ^1H NMR δ 7.12 (m, 3 H), 6.98 (t, 1 H, J = 7.4 Hz), 6.77 (d, 1 H, J = 8.2 Hz), 5.82 (dt, 1 H, J = 15.5, 1.6 Hz), 4.27 (q, 2 H, J = 7.1 Hz), 4.16 (q, 2 H, J = 7.1 Hz), 3.82 (s, 3 H), 3.60 (dd, 2 H, J = 6.8, 1.6 Hz), 1.75 (s, 3 H), 1.26 (t, 3 H, J = 7.1 Hz), 1.24 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 169.5, 168.5, 166.6, 152.6, 147.0, 130.7, 129.5, 127.5, 123.0, 122.1, 116.8, 82.6, 62.3, 60.6, 53.1, 33.0, 20.5, 14.2 13.8; HRMS *m/z* Calcd for $C_{19}H_{24}O_7$: 356.1522. Found: 356.1509. Anal. Calcd for $C_{19}H_{24}O_7$: C, 64.04; H, 6.74. Found: C, 63.85; H, 6.75.

Representative Procedure for the Tandem Demethoxycarbonylation−Michael Addition Reaction: Ethyl (±)-(2*R,3*S**)-2-(Ethoxycarbonyl)-2-methyltetrahydrofuran-3-acetate (35a) and Ethyl (±)−(2*R**,3*R**)-2-(Ethoxycarbonyl)-2-methyltetrahydrofuran-3-acetate (35b).** The general procedure of Bunce and co-workers[4a] was used. To a 25-mL three-necked round-bottomed flask, equipped with a magnetic stirrer, a reflux condenser, a rubber septum, and a drying tube were added 92 mg (2.2 mmol) of dry LiCl and 151 mg (0.50 mmol) of **10**. DMEU (5 mL) was added via syringe, and the reaction mixture was stirred at rt to dissolve the LiCl. Once homogeneous, the reaction was heated in an oil bath (preheated to 120 ± 5 °C) until GC indicated complete consumption of starting material (4−8 h). The reaction was cooled, quenched with 5% NH_4Cl, and extracted with ether (3×). The combined ether layers were washed with 5% NH_4Cl, H_2O, and saturated NaCl, dried ($MgSO_4$), and concentrated under vacuum. The crude product was purified by PTLC,[30] eluted with increasing concentrations of ethyl acetate in hexanes, to afford 62 mg (0.25 mmol, 51%) of **35a** and 18 mg (0.07 mmol, 16%) of **35b**. The spectral data for **35a** were: IR (thin film) 1740 cm^{-1}; ^1H NMR δ 4.25−4.12 (complex, 4 H), 4.01 (m, 1 H), 3.92 (m, 1 H), 2.81 (m, 1 H), 2.64 (dd, 1 H, J = 15.6, 4.8 Hz), 2.28 (dd, 1 H, J = 15.6, 10.5 Hz), 2.21 (m, 1 H), 1.70 (dq, 1 H, J = 12.3, 8.1 Hz), 1.31 (s, 3 H), 1.30 (t, 3 H, J = 7.1 Hz), 1.27 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 174.6, 172.1, 83.9, 66.9, 61.1, 60.5, 41.8, 34.9, 31.5, 19.6, 14.1 (2); HRMS *m/z* Calcd for $C_{12}H_{20}O_5$: 244.1311. Found: 244.1309. Anal. Calcd for $C_{12}H_{20}O_5$: C, 59.02; H, 8.20. Found: C, 59.27; H, 8.22.

The spectral data for the 2*R**,3*R** isomer **35b**: IR (thin film) 1740 cm^{-1}; ^1H NMR δ 4.20−4.05 (complex, 5 H), 3.90 (m, 1 H), 2.46 (dd, 1 H, J = 15.4, 4.1 Hz), 2.39 (m, 1 H), 2.20 (m, 1 H), 2.07 (dd, 1 H, J = 15.4, 10.2 Hz), 1.73 (m, 1 H), 1.42 (s, 3 H), 1.23 (t, 3 H, J = 7.1 Hz), 1.20 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 173.8, 172.0, 85.1, 67.7, 60.4, 60.3, 45.9, 35.6, 31.9, 21.8, 14.0 (2); HRMS *m/z* Calcd for $C_{12}H_{20}O_5$: 244.1311. Found: 244.1306. Anal. Calcd for $C_{12}H_{20}O_5$: C, 59.02; H, 8.20. Found: C, 58.94; H, 8.23.

The following compounds were prepared on varying scales using the same procedure. Purification was achieved by PTLC[30] eluted with increasing concentrations of ethyl acetate in hexanes.

Ethyl (±)-(2*R,3*S**)-2-(Ethoxycarbonyl)-2,5,5-trimethyltetrahydrofuran-3-acetate (36a):** 130 mg (0.48 mmol, 48%) from **11**; IR (thin film) 1740, 1388, 1375 cm^{-1}; ^1H NMR δ 4.25−4.11 (complex, 4 H), 3.06 (m, 1 H), 2.66 (dd, 1 H, J = 15.6, 4.8 Hz), 2.29 (dd, 1 H, J = 15.6, 10.3 Hz), 2.13 (dd, 1 H, J = 12.1, 6.8 Hz), 1.60 (t, 1 H, J = 12.1 Hz), 1.35 (s, 3 H), 1.28 (m, 12 H); ^{13}C NMR δ 174.7, 172.1, 84.0, 81.2, 61.0, 60.5, 44.0, 41.9, 34.9, 30.0, 28.2, 20.9, 14.1, 14.0; HRMS *m/z* Calcd for $C_{14}H_{24}O_5$: 272.1624. Found: 272.1623. Anal. Calcd for $C_{14}H_{24}O_5$: C, 61.76; H, 8.82. Found: C, 61.91; H, 8.85.

Ethyl (±)-(2*R,3*R**)-2-(Ethoxycarbonyl)-2,5,5-trimethyltetrahydrofuran-3-acetate (36b):** 53 mg (0.19 mmol, 19%) from **11**; IR (thin film) 1740, 1385, 1370 cm^{-1}; ^1H NMR δ 4.24−4.09 (complex, 4 H), 2.72 (m, 1 H), 2.52 (dd, 1 H, J = 15.9, 4.3 Hz), 2.11 (dd, 1 H, J = 15.9, 10.5 Hz). 2.06 (m, 1 H), 1.76 (t, 1 H, J = 12.4 Hz), 1.49 (s, 3 H), 1.44 (s, 3 H), 1.30 (t, 3 H, J = 7.1 Hz), 1.28 (t, 3 H, J = 7.1 Hz), 1.27 (s, 3 H); ^{13}C NMR δ 173.8, 172.0, 85.5, 81.8, 60.9, 60.6, 45.8, 44.2, 35.0, 29.8, 28.5, 24.9, 14.2 (2); HRMS *m/z* Calcd for $C_{14}H_{24}O_5$: 272.1624. Found: 272.1619. Anal. Calcd for $C_{14}H_{24}O_5$: C, 61.76; H, 8.82. Found: C, 61.95; H, 8.84.

Ethyl (±)-(2*R,3*R**)-2-(Ethoxycarbonyl)-2,4,4-trimethyltetrahydrofuran-3-acetate (37a):** 132 mg (0.49 mmol, 49%) from **12**; IR (thin film) 1734, 1389, 1373 cm^{-1}; ^1H NMR δ 4.24−4.11 (complex, 4 H), 3.65 (m, 2 H), 2.63 (dd, 1 H, J = 8.3, 6.9 Hz), 2.48−2.33 (complex, 2 H), 1.37 (s, 3 H), 1.29 (t, 3 H, J = 7.2 Hz), 1.27 (t, 3 H, J = 7.2 Hz), 1.02 (s, 3 H), 1.01 (s, 3 H); ^{13}C NMR δ 176.0, 172.2, 84.6, 79.9, 61.0, 60.6, 50.5, 42.0, 31.3, 24.4, 21.5, 20.9, 14.2, 14.1; HRMS *m/z* Calcd for $C_{14}H_{24}O_5$: 272.1624. Found: 272.1627. Anal. Calcd for $C_{14}H_{24}O_5$: C, 61.76; H, 8.82. Found: C, 61.88; H, 8.87.

The minor 2*R**,3*S** isomer **37b** could not be isolated free of contamination.

Ethyl (±)-(2*R,3*S**)-2-(Ethoxycarbonyl)-2-methyl-2*H*-tetrahydropyran-3-acetate (38a):** 220 mg (0.82 mmol, 82%) from **25**; IR (thin film) 1738, 1378 cm^{-1}; ^1H NMR δ 4.25 (m, 2 H), 4.14 (q, 2 H, J = 7.1 Hz), 3.78 (m, 2 H), 2.69 (m, 1 H), 2.59 (dd, 1 H, J = 15.3, 5.3 Hz), 2.30 (dd, 1 H, J = 15.3, 9.1 Hz), 1.80−1.50 (complex, 3 H), 1.44 (m, 1 H), 1.31 (t, 3 H, J = 7.1 Hz), 1.30 (s, 3 H), 1.26 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 173.8, 172.8, 79.0, 63.7, 61.1, 60.4, 34.9, 34.0, 25.2, 21.4, 21.0, 14.2, 14.1; HRMS *m/z* Calcd for $C_{13}H_{22}O_5$: 258.1467. Found 258.1466. Anal. Calcd for $C_{13}H_{22}O_5$: C, 60.47; H, 8.53. Found: C, 60.73; H, 8.59.

Ethyl (±)-(2*R,3*R**)-2-(Ethoxycarbonyl)-2-methyl-2*H*-tetrahydropyran-3-acetate (38b):** 30 mg (0.11 mmol, 11%) from **25**; IR (thin film) 1740, 1381 cm^{-1}; ^1H NMR δ 4.23 (q, 2 H, J = 7.1 Hz), 4.14 (q, 2 H, J = 7.1 Hz), 3.82 (m, 1 H), 3.72 (m, 1 H), 2.54 (m, 2 H), 2.14 (m, 1 H), 1.79 (m, 1 H), 1.62 (m, 2 H), 1.49 (m, 1 H), 1.46 (s, 3 H), 1.31 (t, 3 H, J = 7.1 Hz), 1.26 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 174.0, 173.0, 79.2, 64.3, 60.8, 60.4, 41.0, 36.5, 25.7, 24.9, 24.5, 14.3, 14.2; HRMS *m/z* Calcd for $C_{13}H_{22}O_5$: 258.1467. Found 258.1463. Anal. Calcd for $C_{13}H_{22}O_5$: C, 60.47; H, 8.53. Found: C, 60.71; H, 8.61.

Ethyl (±)-(2*R,3*S**)-2-(Ethoxycarbonyl)-2,6,6-trimethyl-2*H*-tetrahydropyran-3-acetate (39a):** 172 mg (0.60 mmol, 60%) from **26**; IR (thin film) 1738, 1382, 1369 cm^{-1}; ^1H NMR δ 4.27−4.10 (complex, 4 H), 2.73 (m, 1 H), 2.54 (dd, 1 H, J = 15.3, 5.8 Hz), 2.27 (dd, 1 H, J = 15.3, 9.0 Hz), 1.96 (m, 1 H), 1.59 (m, 1 H), 1.51 (m, 1 H), 1.36 (m, 1 H), 1.30 (t, 3 H, J = 7.1 Hz), 1.29 (s, 3 H), 1.28 (t, 3 H, J = 7.1 Hz), 1.25 (s, 3 H), 1.14 (s, 3 H); ^{13}C NMR δ 175.3, 173.0, 73.4, 61.0, 60.4, 45.0, 34.4, 33.3, 31.8, 31.3, 26.6, 24.4, 22.0, 14.2, 14.0; HRMS *m/z* Calcd for $C_{15}H_{26}O_5$: 286.1780. Found: 286.1782. Anal. Calcd for $C_{15}H_{26}O_5$: C, 62.94; H, 9.09. Found: C, 63.11; H, 9.12.

Ethyl (±)-(2*R,3*R**)-2-(Ethoxycarbonyl)-2,6,6-trimethyl-2*H*-tetrahydropyran-3-acetate (39b):** 43 mg (0.15 mmol, 15%) from **26**; IR (thin film) 1739, 1388, 1374 cm^{-1}; ^1H NMR

(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% $Na_2S_2O_3$, saturated NaCl, dried ($MgSO_4$), and concentrated under vacuum.

δ 4.23−4.06 (complex, 4 H), 2.73 (dd, 1 H, J = 16.5, 9.9 Hz), 2.51 (dd, 1 H, J = 16.5, 2.9 Hz), 1.98 (m, 1 H), 1.84 (m, 1 H), 1.67 (m, 1 H), 1.57 (m, 2 H), 1.41 (s, 3 H), 1.30 (t, 3 H, J = 7.1 Hz), 1.26 (t, 3 H, J = 7.1 Hz), 1.24 (s, 3 H), 1.13 (s, 3 H); ^{13}C NMR δ 174.7, 173.4, 73.7, 60.5, 60.3, 45.0, 41.6, 37.0, 36.7, 32.2, 27.0, 24.3, 23.0, 14.2, 14.0; HRMS *m*/*z* Calcd for $C_{15}H_{26}O_5$: 286.1780. Found: 286.1777. Anal. Calcd for $C_{15}H_{26}O_5$: C, 62.94; H, 9.09. Found: C, 63.02; H, 9.05.

Ethyl (±)-(2*R,3*S**)-2-(Ethoxycarbonyl)-2,5,5-trimethyl-2*H*-tetrahydropyran-3-acetate (40a):** 152 mg (0.55 mmol, 55%) from **27**; IR (thin film) 1738, 1390, 1372 cm^{-1}; ^{1}H NMR δ 4.30−4.06 (complex, 4 H), 3.35 (s, 2 H), 2.68 (m, 1 H), 2.51 (dd, 1 H, J = 15.5, 3.6 Hz), 1.94 (dd, 1 H, J = 15.5, 10.3 Hz), 1.50 (m, 2 H), 1.35 (s, 3 H), 1.31 (t, 3 H, J = 7.1 Hz), 1.25 (t, 3 H, J = 7.1 Hz), 1.10 (s, 3 H), 0.86 (s, 3 H); ^{13}C NMR δ 173.2, 172.0, 78.5, 71.3, 61.4, 60.4, 38.9, 36.7, 33.5, 30.4, 27.1, 24.1, 14.3, 14.1 (2); HRMS *m*/*z* Calcd for $C_{15}H_{26}O_5$: 286.1780. Found 286.1774. Anal. Calcd for $C_{15}H_{26}O_5$: C, 62.94; H, 9.09. Found: C, 63.19; H, 9.13.

The minor 2*R**,3*R** isomer **40b** could not be isolated free of contamination.

Ethyl (±)-(*E*)-6-(1-(Ethoxycarbonyl)ethoxy)-4,4-dimethyl-2-hexenoate (41): 172 mg (0.60 mmol, 60%) from **28**; IR (thin film) 1748, 1730, 1641, 1385, 1372 cm^{-1}; ^{1}H NMR δ 5.96 (d, 1 H, J = 13.1 Hz), 5.69 (d, 1 H, J = 13.1 Hz), 4.23−4.13 (complex, 4 H), 3.92 (q, 1 H, J = 6.9 Hz), 3.63 (m, 1 H), 3.40 (m, 1 H), 1.87 (m, 2 H), 1.38 (d, 3 H, J = 6.9 Hz), 1.29 (2 t, 6 H, J = 7.2 Hz), 1.20 (s, 6 H); ^{13}C NMR δ 173.5, 166.7, 153.0, 119.4, 75.0, 67.4, 60.7, 60.2, 42.0, 36.0, 27.6, 27.5, 18.7, 14.2, 14.1; HRMS *m*/*z* Calcd for $C_{15}H_{26}O_5$: 286.1780. Found: 286.1774. Anal. Calcd for $C_{15}H_{26}O_5$: C, 62.94; H, 9.09. Found: C, 63.16; H, 9.14.

Ethyl (±)-(2*R,3*R**)-2-(Ethoxycarbonyl)-2,3-dihydro-2-methylbenzofuran-3-acetate (42a):** 205 mg (0.70 mmol, 70%) from **31**; IR (thin film) 1734, 1595, 1488, 1373, 752 cm^{-1}; ^{1}H NMR δ 7.19−7.11 (complex, 2 H), 6.88 (m, 2 H), 4.27−4.17 (complex, 5 H), 2.77 (dd, 1 H, J = 16.2, 6.6 Hz), 2.59 (dd, 1 H, J = 16.2, 8.5 Hz), 1.56 (s, 3 H), 1.29 (t, 3 H, J = 7.1 Hz), 1.27 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 173.1, 171.6, 157.9, 128.9, 128.6, 124.5, 121.3, 110.0, 89.0, 61.7, 60.8, 44.3, 35.6, 18.6, 14.0, 13.9; HRMS *m*/*z* Calcd for $C_{16}H_{20}O_5$: 292.1310. Found: 292.1311. Anal. Calcd for $C_{16}H_{20}O_5$: C, 65.75; H, 6.85. Found: C, 65.91; H, 6.87.

Ethyl (±)-(2*R,3*S**)-2-(Ethoxycarbonyl)-2,3-dihydro-2-methylbenzofuran-3-acetate (42b):** 40 mg (0.14 mmol, 14%) from **31**; IR (thin film) 1740, 1602, 1488, 1381, 755 cm^{-1}; ^{1}H NMR δ 7.18 (t, 1 H, J = 8.0 Hz), 7.10 (d, 1 H, J = 7.6 Hz), 6.88 (m, 2 H), 4.31−4.15 (complex, 4 H), 3.85 (t, 1 H, J = 7.4 Hz), 2.61 (dd, 1 H, J = 16.6, 7.1 Hz), 2.59 (dd, 1 H, J = 16.6, 8.1 Hz), 1.71 (s, 3 H), 1.29 (t, 3 H, J = 7.1 Hz), 1.28 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 171.4, 171.3, 158.2, 129.1, 128.3, 124.5, 121.1, 110.1, 89.9, 61.6, 60.8, 47.8, 36.6, 24.6, 14.0 (2); HRMS *m*/*z* Calcd for $C_{16}H_{20}O_5$: 292.1310. Found: 292.1307. Anal. Calcd for $C_{16}H_{20}O_5$: C, 65.75; H, 6.85. Found: C, 65.84; H, 6.88.

Ethyl (±)-(2*R,3*S**)-2-(Ethoxycarbonyl)-3,4-dihydro-2-methyl-2*H*-1-benzopyran-3-acetate (43a):** 176 mg (0.58 mmol, 58%) from **34**; IR (thin film) 1735, 1594, 1490, 1375, 751 cm^{-1}; ^{1}H NMR δ 7.12 (t, 1 H, J = 6.9 Hz), 6.98 (d, 1 H, J = 7.1 Hz), 6.88 (m, 2 H), 4.16 (m, 4 H), 2.91 (m, 2 H), 2.59 (d, 2 H, J = 17.5 Hz), 2.15 (dd, 1 H, J = 16.3, 9.5 Hz), 1.55 (s, 3 H), 1.25 (t, 3 H, J = 7.1 Hz), 1.20 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 173.0, 172.5, 153.2, 129.9, 127.6, 120.9, 118.7, 116.5, 79.9, 61.5, 60.7, 33.3, 33.1, 28.5, 21.9, 14.2, 14.0; HRMS *m*/*z* Calcd for $C_{17}H_{22}O_5$: 306.1468. Found: 306.1463. Anal. Calcd for $C_{17}H_{22}O_5$: C, 66.67; H, 7.19. Found: C, 66.47; H, 7.17.

The minor 2*R**,3*R** isomer **43b** could not be isolated free of contamination.

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Supporting Information Available: Procedures for the preparation of the starting (ω-alkenyloxy)acetic acids and compounds **1**−**3** and **13**−**16**. High resolution ^{1}H and ^{13}C NMR spectra for the (ω-alkenyloxy)acetic acids and compounds **1**−**9**, **13**−**24**, **30**, and **33** (64 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.

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