(400 MHz, $CDCl_3$): δ (for major diastereomer 8 only) 7.34 (d, J = 8.1 Hz, 1 H), 7.07 (d, J = 8.1 Hz, 1 H), 7.05 (d, J = 8.5 Hz, 1 H), 6.94 (d, J = 7.9 Hz, 1 H), 6.69 (s, 1 H), 6.66 (s, 1 H), 5.08 (s, 1 H), 4.62 (d, J = 16.4 Hz, 1 H), 4.61 (d, J = 16.3 Hz, 1 H), 4.56 (br m, $w_{1/2}$ = 27 Hz, 1 H), 4.42 (s, 2 H), 4.17 (d, J = 16.5 Hz, 1 H), 4.01 (d, J = 16.4 Hz, 1 H), 3.66 (s, 3 H), 3.64 (d, J = 17.8 Hz, 1 H), 3.62 (d, J = 13.7 Hz, 1 H), 3.40 (d, J = 14.0 Hz, 1 H), 3.39 (d, J = 16.5 Hz, 1 H), 2.38–2.1 (m, 2 H), 1.9–0.85 (m), 0.85 (s, 3 H), 0.78 (d, J = 6.3 Hz, 3 H), 0.70 (s, 3 H), 0.46 (q, J = 11.6 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (for both diastereomers) 174.49, 174.43, 170.97, 170.83, 170.70, 146.36, 146.21, 146.17, 146.13, 129.84, 129.79, 128.65, 128.52, 128.49, 128.37, 127.95, 127.69, 127.58, 127.48, 127.08, 125.12, 124.56, 124.48, 124.30, 78.08, 76.38, 74.95, 74.53, 67.81, 67.46, 59.85, 59.68, 59.40, 59.29, 51.46, 48.71, 48.18, 48.01, 47.75, 45.53, 45.07, 42.31, 42.24, 42.09, 41.81, 41.56, 40.18, 35.96, 35.82, 34.92, 34.80, 34.68, 34.59, 34.56, 34.49, 34.43, 32.72, 32.57, 30.95, 30.78, 29.62, 27.59, 27.36, 27.21, 26.43, 26.37, 26.08, 25.74, 25.58, 25.51, 23.73, 23.49, 23.42, 17.57, 17.38, 12.39, 12.12. IR (neat, thin film on NaCl plate): 2944 (m), 1728 (s), 1497 (m), 1437 (w), 1260 (s) cm^{-1}. UV log ε (284 nm) = 3.24 (c 1.58 × 10^{-4} M, 2% $CHCl_3/CH_3OH$).

Tröger's Base Analogue 9. The mixture of diastereomers (8/9, 0.350 g) was dissolved in warm ethanol (20 mL) with the aid of a few drops of dichloromethane. The solution was left at room temperature (ca. 26 °C) for a few days after seeding with a crystal of 9. The colorless needles were collected, washed with cold ethanol, and dried to give 0.045 g of pure 9. Mp: 242–244 °C dec. R_f: 0.2, 25% ethyl acetate/chloroform. ^1H NMR (200 MHz, $CDCl_3$); δ 7.27 (dd, J = 8.3, 1.6 Hz, 1 H), 7.13 (d, J = 8.3 Hz, 1 H), 7.02 (d, J = 8.2 Hz, 1 H), 6.94 (dd, J = 8.2, 1.8 Hz, 1 H), 6.86 (s, 1 H), 6.73 (s, 1 H), 4.95 (s, 1 H), 4.66 (d, J = 16.4 Hz, 1 H), 4.62 (d, J = 16.5 Hz, 1 H), 4.55 (br m, $w_{1/2}$ = 30 Hz, 1 H), 4.39 (s, 2 H), 4.15 (d, J = 16.5 Hz, 1 H), 4.10 (d, J = 16.5 Hz, 1 H), 3.66 (s, 3 H), 3.59 (d, J = 14.2 Hz, 1 H), 3.47 (s, 2 H), 3.43 (d, J = 12.7 Hz, 1 H), 2.38–1.0 (br), 0.87 (s, 3 H), 0.81 (d, J = 5.9 Hz, 3 H), 0.71 (s, 3 H), 0.38 (q, J = 11.8 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.45, 170.97, 170.85, 146.45, 146.31, 129.89, 128.69, 128.62, 128.53, 127.72, 127.55, 127.16, 127.08, 124.61, 124.51, 78.12, 74.57, 67.54, 59.46, 59.35, 51.48, 48.23, 48.07, 45.59, 42.30, 42.15, 41.86, 36.03, 34.85, 34.74, 34.54, 32.79, 30.99, 30.98, 27.65, 27.44, 26.48, 26.42, 25.63, 23.78, 23.54, 17.43, 12.16. FTIR: 2939 (s), 2864 (m), 1722 (s), 1494 (s), 1444 (m), 1331 (w), 1260 (s), 1223 (m), 1205 (m), 1150 (s), 1114 (w), 1097 (w), 1066 (w), 1012 (m). Deconvolution (with 4 cm^{-1} resolution) showed the following carbonyl peaks: 1736, 1724, 1714 cm^{-1}. UV: log ε (283 nm) = 3.23 (c 1.27 × 10^{-4} M, 0.1% $CHCl_3/CH_3OH$). LRMS: 293 (22), 338 (17), 371 (12), 708 (100). HRMS: exact mass calcd for $C_{44}H_{56}N_2O_6$ 708.4139, found 708.4154. $[\alpha]^{25}_D$ = +144.3° (c 0.07, ethanol). CD: $\Delta\epsilon_{286}$ = +1.67 M^{-1} cm^{-1} (c 1.27 × 10^{-4} M, 0.1% $CHCl_3/CH_3OH$). Anal. Calcd for $C_{44}H_{56}N_2O_6$: C, 74.54; H, 7.96; N, 3.95. Found: C, 74.38; H, 8.12; N, 3.58.

2,8-Bis(2-acetoxyethyl)-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (10/11). A mixture of diastereomers 8 and 9 (0.074 g, 0.104 mmol) was refluxed with a solution of LAH (0.034 g, 0.896 mmol) in THF (6.8 mL, freshly distilled from LAH) for 23 h. The reaction mixture was cooled, and finely powdered $MgSO_4 \cdot 7H_2O$ was added to quench the excess of LAH. The mixture was stirred, diluted with ethyl acetate (10 mL), and filtered through a bed of Celite. The solvent was removed, and the crude product (0.065 g) was stirred with acetic anhydride (1.08 g, 10.6 mmol) and pyridine (0.99 g, 12.5 mmol) at 27–30 °C under a nitrogen atmosphere for 16 h. Volatiles were removed under high vacuum, and the crude product was first purified by flash chromatography on silica gel using 25% ethyl acetate/chloroform as the eluant. The partially purified product (0.023 g, 62%) was further purified by PTLC (silica gel GF_{254}) using 25% ethyl acetate/chloroform as the developing agent. The product was isolated in 46% yield (0.017 g). ^1H NMR (90 MHz, $CDCl_3$): δ 7.03 (s, 4 H), 6.75 (s, 2 H), 4.68 (d, J = 16.6 Hz, 2 H), 4.28 (s, 2 H), 4.20 (t, J = 7.6 Hz, 4 H), 4.11 (d, J = 16.6 Hz, 2 H), 2.81 (t, J = 7.1 Hz, 4 H), 2.02 (s, 6 H). ^{13}C NMR (22.5 MHz, $CDCl_3$): δ 170.61, 146.34, 133.12, 127.60, 126.95, 124.89, 66.60, 64.54, 58.36, 34.31, 20.66. IR (neat): 2944 (m), 1737 (s), 1668 (m), 1617 (w), 1497 (s), 1440 (m), 1389 (m), 1368 (s), 1332 (m), 1251 (s), 1209 (s), 1164 (w), 1143 (w), 1116 (m), 1098 (m), 1065 (s), 1035 (s) cm^{-1}. UV: log ε (282.5 nm) = 3.23 (c 9.79 × 10^{-5} M, 1.2% $CHCl_3/CH_3OH$). $[\alpha]^{25}_D$ = +83.2° (c 0.84, $CHCl_3$). CD: $\Delta\epsilon_{286}$ = −2.12 M^{-1} cm^{-1} (c 2.12 × 10^{-4} M, 1% $CHCl_3/CH_3OH$). LRMS: 43 (48), 274 (77), 334 (40), 394 (100). HRMS: exact mass calcd for $C_{23}H_{26}N_2O_4$ 394.1893, found 394.1862.

Spectral Data on Authentic 10/11 (Racemic). ^1H NMR (90 MHz, $CDCl_3$): δ 7.04 (s, 4 H), 6.75 (s, 2 H), 4.67 (d, J = 16.6 Hz, 2 H), 4.27 (s, 2 H), 4.18 (t, J = 7.2 Hz, 4 H), 4.10 (d, J = 15.4 Hz, 2 H), 2.79 (t, J = 7.2 Hz, 4 H), 2.00 (s, 6 H). ^{13}C NMR (22.5 MHz, $CDCl_3$): δ 170.61, 146.34, 133.12, 127.60, 126.95, 124.89, 66.60, 64.54, 58.36, 34.31, 20.66. IR (neat): 2944 (m), 1740 (s), 1665 (w), 1617 (w), 1497 (s), 1440 (m), 1389 (m), 1365 (m), 1332 (m), 1242 (s), 1209 (s), 1164 (w), 1143 (w), 1113 (m) cm^{-1}. UV: log ε (283 nm) = 3.24 (c 2.16 × 10^{-4} M, 2% $CHCl_3/CH_3OH$). LRMS: 43 (35), 274 (74), 334 (40), 394 (100). HRMS: exact mass calcd for $C_{23}H_{26}N_2O_4$ 394.1893, found 394.1880.

Spectral Data on Pure Enantiomer 11. ^1H NMR (90 MHz, $CDCl_3$): δ 7.03 (s, 4 H), 6.75 (s, 2 H), 4.67 (d, J = 16.6 Hz, 2 H), 4.27 (s, 2 H), 4.20 (t, J = 7.3 Hz, 4 H), 4.12 (d, J = 16.6 Hz, 2 H), 2.81 (t, J = 7.3 Hz, 4 H), 2.03 (s, 6 H). $[\alpha]^{25}_D$ = −195° (c 0.51, $CHCl_3$). CD: $\Delta\epsilon_{286}$ = +5.62 M^{-1} cm^{-1} at 298 K (c 5.12 × 10^{-5} M, 0.4% $CHCl_3/CH_3OH$). UV: log ε (283 nm) = 3.25 (c 5.12 × 10^{-5} M, 0.4% $CHCl_3/CH_3OH$).

Acknowledgment. Financial assistance from Prof. C. N. R. Rao, Director, Indian Institute of Science, and from the Department of Science and Technology (Grant No. SP/YS/CO7/88) is gratefully acknowledged. We also thank CSIR for the award of a fellowship to B.G.B. The Sophisticated Instruments Facility at IISc is thanked for recording 400-MHz NMR spectra.

Six-Membered Cyclic β-Keto Esters by Tandem Conjugate Addition–Dieckmann Condensation Reactions

Richard A. Bunce* and Christina R. Harris[1]

Department of Chemistry, Oklahoma State University, Stillwater, Oklahoma 74078-0447

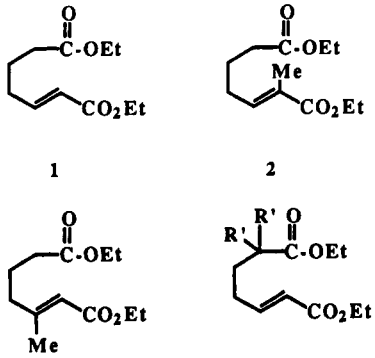
Received June 15, 1992

Carbon functionalization of anions generated by conjugate addition of organocopper reagents to α,β-unsaturated carbonyl compounds has found wide use in organic synthesis.[2-4] One subset of these reactions, cycloacylations, has provided an efficient synthetic route to highly functionalized cyclic compounds. Most notable among these is an account detailing the formation of dimethyl cyclohexanone-2,4-dicarboxylates by addition of lithium dialkylcuprates to methyl crotonate[5] and three reports describing conjugate addition–cycloacylations to form substituted cyclopentenones[6] and cycloalkanones.[7,8] One of these reports[7] has described the preparation of C-5-substituted 2-oxocyclopentanecarboxylate esters by cuprate addition to dimethyl (*E*)-2-hexenedioate and applied this technology to the synthesis (±)-mitsugashiwalactone. Since we required access to 2-oxocyclohexanecarboxylate esters bearing substitution at C-6, we were interested in the possibility of adapting this conjugate addition–Di-

(1) Undergraduate Research Participant, 1991–1992.
(2) Chapdelaine, M. J.; Hulce, M. *Org. React.* **1990**, *38*, 225–653.
(3) Perlmutter, P. *Conjugate Addition Reactions in Organic Synthesis*; Pergamon Press: New York, 1992; pp 218–225, 347–350.
(4) Posner, G. H. *Chem. Rev.* **1986**, *86*, 831–844.
(5) Olsson, T.; Rahman, M. T.; Ullenius, C. *Tetrahedron Lett.* **1977**, 75–78.
(6) Crimmins, M. T.; Mascarella, S. W.; DeLoach, J. A. *J. Org. Chem.* **1984**, *49*, 3033–3035.
(7) (a) Nugent, W. A.; Hobbs, F. W., Jr. *J. Org. Chem.* **1983**, *48*, 5364–5366. (b) Nugent, W. A.; Hobbs, F. W., Jr. *J. Org. Chem.* **1986**, *51*, 3376–3378.
(8) Tada, M.; Takahashi, T. *Chem. Lett.* **1978**, 275–278.

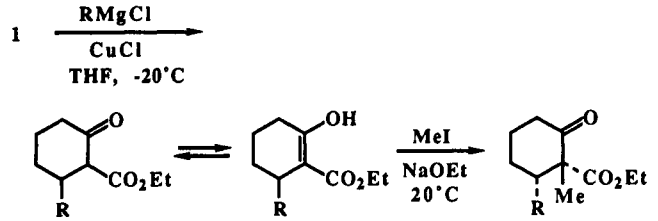
0022-3263/92/1957-6981$03.00/0

Chart I. Cyclization Substrates



1 2 3 4 R',R' = Me 5 R',R' = -(CH$_2$)$_4$-

Table I. Yields of Six-Membered Cyclic β-Keto Esters Prepared from 1 and the Methylation Products



6-10 11-15

R	keto–enol (%)	methylation[a] (%)
Me	6 (84)	11 (70)
Et	7 (86)	12 (68)
Bu	8 (96)	13 (69)
Ph	9 (92)	14 (70)
-CH=CH$_2$	10 (80)	15 (68)

[a] Yield refers to isolated yield of trans alkylation product. The cis product was also formed in ≤7% (GC).

eckmann strategy for the synthesis of these compounds. Furthermore, since six-membered cyclic β-keto esters constitute a useful family of synthetic building blocks, it would be of general interest to further evaluate the influence of steric and electronic factors on the reaction. This paper describes a conjugate addition–Dieckmann condensation sequence for the preparation of these targets.

Results and Discussion

Diethyl (*E*)-2-heptenedioate (1) and diethyl (*E*)-2-methyl-2-heptenedioate (2) were prepared from ethyl 5-hexenoate[9] using a sequence involving (1) ozonolysis and (2) Wittig olefination with (carbethoxymethylidene)triphenylphosphorane or (carbethoxyethylidene)triphenylphosphorane, respectively. Diethyl (*E*)-3-methyl-2-heptenoate (3) was prepared by Wadsworth–Emmons reaction[10] of ethyl 4-acetylbutyrate with triethyl phosphonoacetate. Diethyl (*E*)-6,6-dimethyl-2-heptenedioate (4) and ethyl (*E*)-(4-(ethoxycarbonyl)-3-butenyl)cyclopentanecarboxylate (5) were prepared from ethyl isobutyrate and ethyl cyclopentanecarboxylate, respectively, by (1) alkylation[11] with 4-bromo-1-butene, (2) ozonolysis, and (3) Wittig olefination.

The results of our study of the conjugate addition–Dieckmann cyclization of 1:1 RMgX–CuCl and diethyl (*E*)-2-heptenedioate (1) are given in Table I. Addition

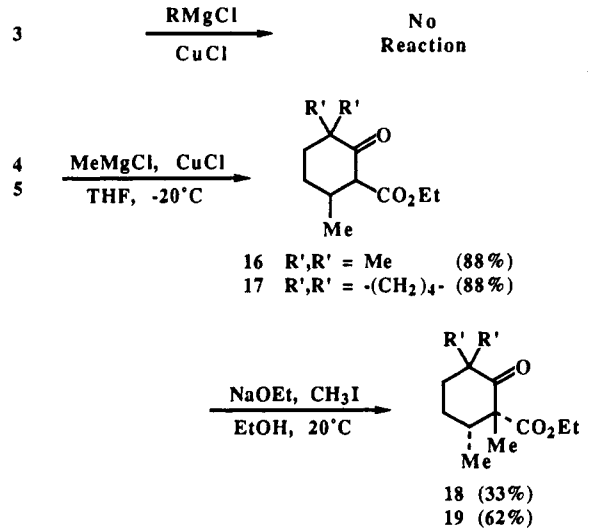
(9) Degenhardt, C. R. *J. Org. Chem.* **1980**, *45*, 2763–2766.
(10) Balsevich, J. *Can. J. Chem.* **1983**, *61*, 1053–1059.
(11) Beckwith, A. L. J.; Lawrence, T. *J. Chem. Soc., Perkin Trans. 2* **1979**, 1535–1539.

Table II. Optimization Studies of the Conjugate Addition–Dieckmann Reaction

condns[a]	yield of 8 (%)
n-BuLi (5.0 equiv), CuI (2.5 equiv), Et$_2$O–hexane	37–50[b]
n-BuLi (2.7 equiv), CuCN (1.5 equiv), Et$_2$O–hexane	45–54[b]
n-BuMgBr (2.5 equiv), CuCl (2.5 equiv), THF	41
n-BuMgBr (5.0 equiv), CuCl (5.0 equiv), THF	64
n-BuMgBr (6.0 equiv), CuCl (6.0 equiv), THF	96

[a] The number of equivalents used is relative to diethyl (*E*)-2-heptenedioate. All reactions were run at −20 °C for 30–60 min. Stoichiometry was similar for other RMgX–CuCl except when R = vinyl, where 12 equiv of the reagent was necessary. [b] More equivalents of these reagents did not significantly improve the yields.

Scheme I. Substitution Effects in the Conjugate Addition–Dieckmann Reaction



16 R',R' = Me (88%)
17 R',R' = -(CH$_2$)$_4$- (88%)
18 (33%)
19 (62%)

of the diester to an excess of the organocopper reagent afforded the six-membered cyclic β-keto esters as keto–enol mixtures.[12] Alkylation of these enolic products subsequently afforded the quaternized keto esters which were more easily characterized.

A summary of reaction optimization studies for R = Bu is given in Table II. The best results were obtained using 6 equiv of the organocopper reagent relative to the diester; attempts to use less of the organometallic agent resulted in dramatically lower yields.[13,14] Other organocopper reagents were also explored but proved less satisfactory. Cuprates generated from *n*-butyllithium and either copper(I) iodide[15] or copper(I) cyanide[16] were difficult to generate reproducibly and yielded varying amounts of the alcohol resulting from 1,2-addition to the ester carbonyl. Consequently, lower yields of the cyclized product were realized.

(12) Studies have shown that the 2-oxocyclohexanecarboxylate esters favor the enolic form more than the five-membered cyclic analogues; see: (a) Rhoads, S. J.; Pryde, C. *J. Org. Chem.* **1965**, *30*, 3212–3214. (b) Rhoads, S. J. *J. Org. Chem.* **1966**, *31*, 171–174. (c) Sterk, H. *Monatsh. Chem.* **1969**, *100*, 1246–1249.
(13) A similar stoichiometric requirement has been reported for a related reaction in: Saito, S. Hirohara, Y.; Narahara, O.; Moriwake, T. *J. Am. Chem. Soc.* **1989**, *111*, 4533–4535.
(14) With the exception of phenylmagnesium bromide, Grignard reagents incorporating a double bond were generally found to require 8–12 equiv of the cuprate for acceptable yields. Additional examples applied to the synthesis of functionalized fused-ring systems will be the subject of a future publication.
(15) (a) House, H. O.; Respess, W. L.; Whitesides, G. M. *J. Org. Chem.* **1966**, *31*, 3128–3141. (b) Posner, G. H. *Org. React.* **1972**, *19*, 1–113.
(16) (a) Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. A.; Parker, D. *J. Org. Chem.* **1984**, *49*, 3928–3938. (b) Lipshutz, B. H. *Tetrahedron Lett.* **1983**, *24*, 127–130.

Substitution on the diester cyclization substrates was found to be extremely important to the success of the reaction. Methyl substitution on the α or β positions of the acrylate moiety completely suppressed the initial addition reaction, and starting material was recovered. Though additions of organocopper reagents to substituted acrylate esters are known,[15b,16b,17] the current observation must derive in part from a combination of steric and electronic effects. While β-substitution would impede approach of the organometallic reagent to the double bond, both α- and β-substitution would tend to change the electronic character of the double bond making it more electron-rich and less susceptible to attack by the organocopper species. By comparison, when substitution was introduced α to the saturated ester, the reaction was slowed but yields of the cyclization products **16** and **17** were not significantly reduced. These results are summarized in Scheme I.

Methylation of the purified keto–enol products (1.5 equiv of NaOEt, 5.0 equiv of MeI, EtOH, 20 °C, 12 h) gave a preponderance (>90%) of the alkylation product having the methyl group trans to the C-6 R group.[18] The 93:7:trace mixture of trans–cis–polyalkylated products obtained in the methylation of **6** is markedly better than the 80.5:12:7.5 mixture reported previously[18e] though this earlier report utilized more vigorous conditions (1 equiv of NaH, 2 equiv of MeI, DMF, 60 °C, 72 h). β-Keto esters bearing no C-3 substituents were generally alkylated in ca. 70% yield while the more hindered 3,3-dimethyl and spirocyclopentyl cyclization products (**16** and **17**) afforded 33% of **18** and 62% of **19**, respectively. The latter result clearly illustrates the reduced steric demand (cyclohexane 1,3-diaxial interaction) of the spiro five-membered ring relative to a geminal dimethyl substituent.

The current synthetic approach to the title compounds compares quite favorably with methods reported previously. Dieckmann condensation of diethyl 3-methylheptanedioate is known to give a mixture of products favoring the 4-methyl over the 6-methyl keto ester.[19] Cyclocondensation of ethyl acetoacetate and ethyl crotonate, conversion of the resulting dione to the enol chloride, and hydrogenation have afforded **6** on a large scale but in only 19% overall yield.[20] More recently, β-addition of various organocopper reagents to 2-(methoxycarbonyl)-2-cyclohexen-1-one has provided a number of C-6-substituted keto esters in 43–61% yield.[21] Similarly, copper(I)-catalyzed addition of an alkylmagnesium iodide to 4,4-dimethyl-2-cyclohexen-1-one followed by quenching with methyl chloroformate has also furnished a keto ester derivative in 60% yield.[22] Our procedure, while somewhat limited in scale, provides a versatile route to six-membered cyclic β-keto esters in ≥80% yield from **1**.

In summary, we have developed and optimized a tandem conjugate addition–Dieckmann condensation reaction for the preparation of six-membered cyclic β-keto esters from 1:1 RMgX–CuCl reagents and (*E*)-2-heptenedioate esters. Though the initial β-addition is highly sensitive to substitution on the unsaturated ester, the process allows for the efficient preparation of an important class of synthetic building blocks bearing an ethoxycarbonyl group on the more hindered α-carbon of a C-3-substituted cyclohexanone. Applications of this reaction to the synthesis of ring structures indigenous to a number of natural products are currently underway.

Experimental Section

THF was distilled from $LiAlH_4$ prior to use; all other solvents and reagents were used as received from the vendors. Temperature conditions were achieved using dry ice–solvent baths: CCl_4 (−20 °C), acetone (−78 °C). All reactions were run under dry N_2. Unless otherwise indicated, the 0.5–1 M HCl, NH_4Cl, $NaHCO_3$, $Na_2S_2O_3$, and NaCl 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 no. 21521) with 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 chromatographic separations were performed using one of the following methods: (1) PTLC on 20-cm × 20-cm silica gel GF (2000 μm thickness) plates (Analtech no. 02015) or (2) flash vacuum chromatography[23] on silica gel (Grace, grade 62, 60–200 mesh) mixed with Sylvania 2282 phosphor and slurry packed into Vycor columns. Band elution, in all cases, 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. MS (EI/DP) and HRMS (EI/DP) were obtained at 70 eV.

(Carbethoxymethylidene)triphenylphosphorane,[24] (carbethoxyethylidene)triphenylphosphorane,[25] ethyl 5-hexenoate,[9] ethyl 2,2-dimethyl-5-hexenoate,[11] and ethyl 1-(3-butenyl)cyclopentanecarboxylate[11] were prepared and purified by literature methods or adaptations thereof. The physical and spectral data for ethyl 1-(3-butenyl)cyclopentanecarboxylate follow: bp 92–94 °C (2 mmHg); IR (thin film) 3060, 1722, 1639, 1381, 1175, 990, 905 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.79 (ddt, 1 H, J = 17.1, 10.3, 7.1 Hz), 4.98 (d, 1 H, J = 17.1 Hz), 4.92 (d, 1 H, J = 10.3 Hz), 4.12 (q, 2 H, J = 7.2 Hz), 2.13 (m, 2 H), 1.96 (m, 2 H), 1.70 (m, 2 H), 1.63 (m, 4 H), 1.48 (m, 2 H), 1.25 (t, 3 H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 177.6, 138.5, 114.3, 60.2, 53.8, 38.4, 36.0, 30.3, 24.9, 14.2; HRMS m/e for $C_{12}H_{20}O_2$ calcd 196.1463, found 196.1461.

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.46; H, 10.20. Found: C, 73.44; H, 10.22.

Representative Ozonolysis–Wittig Procedure. Diethyl (*E*)-2-Heptenedioate (1). A 500-mL CH_2Cl_2 solution of 14.2 g (100 mmol) of ethyl 5-hexenoate was cooled to −78 °C and treated with ozone until the solution turned a light blue color. The reaction was quenched at −78 °C with 8.46 g (10.0 mL, 136 mmol) of dimethyl sulfide, warmed to rt, stirred for 3 h, and concentrated in vacuo. To the resulting light yellow oil was added 250 mL of benzene and 40.0 g (115 mmol) of (carbethoxymethylidene)triphenylphosphorane. The solution was refluxed for 12 h and then cooled and concentrated in vacuo to afford a tan semisolid mass. The residue was placed on top of a 10-cm × 10-cm plug of silica gel in a sintered glass frit, and 2 L of 15% ether in hexane was poured through under aspirator vacuum.[23] Concentration of the filtrate afforded the crude diester as a light yellow oil. This crude product was diluted with ether, washed with $NaHCO_3$, NaCl, dried

(17) See for example: (a) Beckwith, A. L. J.; Easton, C. J.; Lawrence, T.; Serelis, A. K. Aust. *J. Chem.* **1983**, *36*, 545–556. (b) Eliel, E. L.; Hitchins, R. O.; Knoeber, M. *Organic Syntheses*; Noland, W. E., Ed.; Wiley: New York, 1988; Collect. Vol. VI, pp 442–445.

(18) (a) Zimmerman, H. E. *J. Org. Chem.* **1955**, *20*, 549–557. (b) Zimmerman, H. E. *J. Am. Chem. Soc.* **1956**, *78*, 1168–1173. (c) Corey, E. J.; Sneen, R. A. *J. Am. Chem. Soc.* **1956**, *78*, 6269–6278. (d) Boeckman, R. K., Jr. *J. Org. Chem.* **1973**, *38*, 4450–4452. (e) Paquette, L. A.; Wiedeman, P. E.; Bulman-Page, P. C. *J. Org. Chem.* **1988**, *53*, 1441–1450. (f) Piers, E.; Llinas-Brunet, M. *J. Org. Chem.* **1989**, *54*, 1483–1484.

(19) (a) Einhorn, A.; Klages, L. *Chem. Ber.* **1901**, *34*, 3793–3798. (b) Chakravarti, R. N. *J. Ind. Chem. Soc.* **1944**, *21*, 322–330.

(20) Mukherjee, S. *J. Ind. Chem. Soc.* **1962**, *39*, 347–352.

(21) (a) Bruhn, J.; Heimgartner, H.; Schmid, H. *Helv. Chim. Acta* **1979**, *62*, 2630–2654. (b) Piers, E.; Tse, H. L. A. *Tetrahedron Lett.* **1984**, *25*, 3155–3158. (c) Majetich, G.; Song, J.-S.; Ringold, C.; Nemeth, G. A.; Newton, M. G. *J. Org. Chem.* **1991**, *56*, 3973–3988.

(22) Jackson, W. P.; Ley, S. V. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1516–1519. Intermolecular capture of the organocopper enolate by methyl cyanoformate has been reported in the preparation of a 2-oxocyclopentanecarboxylate derivative; see: Hashimoto, S.; Kase, S.; Shinoda, T.; Ikegami, S. *Chem. Lett.* **1989**, 1063–1066.

(23) Leopold, E. J. *J. Org. Chem.* **1982**, *47*, 4592–4593.

(24) (a) Maercker, A. *Org. React.* **1965**, *14*, 270–490. (b) Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*, Wiley: New York, 1967; Vol. 1, pp 112–114.

(25) Isler, O.; Gutmann, H.; Montavon, M.; Rüegg, R.; Ryser, G.; Zeller, P. *Helv. Chim. Acta* **1957**, *40*, 1242–1249.

($MgSO_4$), concentrated in vacuo, and fractionated through a 15-cm Vigreux column (1.5-cm i.d.) at reduced pressure to afford 1 as a colorless oil: 15.1 g (71 mmol, 71%); bp 80–85 °C (0.5 mmHg); 92:8 *E*:*Z*; IR (thin film) 1740, 1720, 1658, 1370 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.90 (dt, 1 H, J = 15.7, 7.4 Hz), 5.81 (dt, 1 H, J = 15.7, 1.5 Hz), 4.15 (q, 2 H, J = 7.2 Hz), 4.07 (q, 2 H, J = 7.2 Hz), 2.30 (t, 2 H, J = 7.4 Hz), 2.22 (dq, 2 H, J = 7.4, 1.5 Hz), 1.76 (quintet, 2 H, J = 7.4 Hz), 1.25 (t, 3 H, J = 7.2 Hz), 1.22 (t, 3 H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 173.0, 166.4, 147.7, 122.1, 60.3, 60.1, 33.4, 31.3, 23.2, 14.2, 14.1; HRMS m/e for $C_{11}H_{18}O_4$ calcd 214.1205, found 214.1202.

Anal. Calcd for $C_{11}H_{18}O_4$: C, 61.68; H, 8.41. Found: C, 61.57; H, 8.40.

Diethyl (*E*)-2-methyl-2-heptenedioate (2): 9.42 g (41 mmol, 41%); 95:5 *E*:*Z*; bp 92–94 °C (0.5 mmHg); IR (thin film) 1738, 1712, 1650, 1370 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.73 (t, 1 H, J = 7.3 Hz), 4.18 (q, 2 H, J = 7.1 Hz), 4.13 (q, 2 H, J = 7.1 Hz), 2.33 (t, 2 H, J = 7.3 Hz), 2.23 (q, 2 H, J = 7.3 Hz), 1.83 (s, 3 H), 1.79 (m, 2 H), 1.29 (t, 3 H, J = 7.1 Hz), 1.26 (t, 3 H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 173.1, 167.9, 140.6, 128.6, 60.4, 60.2, 33.6, 27.8, 23.7, 14.2, 14.1, 12.3; HRMS m/e for $C_{12}H_{20}O_4$ calcd 228.1361, found 228.1356.

Anal. Calcd for $C_{12}H_{20}O_4$: C, 63.16; H, 8.77. Found: C, 63.08; H, 8.74.

Diethyl (*E*)-6,6-dimethyl-2-heptenedioate (4): 12.6 g (52 mmol, 52%); 93:7 *E*:*Z*; bp 127–128 °C (0.8 mmHg); IR (thin film) 1720, 1652, 1385, 1365 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.94 (dt, 1 H, J = 15.7, 6.8 Hz), 5.81 (d, 1 H, J = 15.7 Hz), 4.16 (q, 2 H, J = 7.1 Hz), 4.12 (q, 2 H, J = 7.1 Hz), 2.14 (m, 2 H), 1.68 (m, 2 H), 1.26 (m, 6 H), 1.19 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 177.2, 166.5, 148.5, 121.3, 60.3, 60.1, 41.8, 38.6, 27.8, 25.0, 14.2, 14.1; HRMS m/e for $C_{13}H_{22}O_4$ calcd 242.1518, found 242.1512.

Anal. Calcd for $C_{13}H_{22}O_4$: C, 64.46; H, 9.09. Found: C, 64.26; H, 9.12.

Ethyl (*E*)-(4-(ethoxycarbonyl)-3-butenyl)cyclopentanecarboxylate (5): 11.3 g (42 mmol, 42%); 93:7 *E*:*Z*; bp 98–99 °C (0.1 mmHg); IR (thin film) 1720, 1652, 1380, 1372 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.93 (dt, 1 H, J = 15.7, 6.9 Hz), 5.80 (d, 1 H, J = 15.7 Hz), 4.17 (q, 2 H, J = 7.1 Hz), 4.13 (q, 2 H, J = 7.1 Hz), 2.13 (m, 4 H), 1.76 (m, 2 H), 1.64 (m, 4 H), 1.47 (m, 2 H), 1.28 (t, 3 H, J = 7.1 Hz), 1.25 (t, 3 H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 172.2, 166.5, 148.5, 121.3, 60.3, 60.1, 53.6, 37.2, 36.0, 28.8, 24.9, 14.2; HRMS m/e for $C_{15}H_{24}O_4$ calcd 268.1674, found 268.1668.

Anal. Calcd for $C_{15}H_{24}O_4$: C, 67.16; H, 8.96. Found: C, 67.08; H, 8.99.

Diethyl (*E*)-3-Methyl-2-heptenedioate (3). The general procedure of Balsevich[10] was used. NaH (3.92 g of a 60% mineral oil dispersion, 98.0 mmol) was washed with pentane (3×), dried under vacuum, and suspended in 150 mL of dry THF. The mixture was cooled to 0 °C, and a solution of 22.2 g (99.0 mmol) of triethyl phosphonoacetate in 30 mL of dry DMSO was added dropwise during 20 min. The mixture was stirred at 0 °C for 30 min, and 13.7 g (86.8 mmol) of ethyl 4-acetylbutyrate in 20 mL of dry THF was added during 20 min. The reaction was warmed to 20 °C and stirred for 20 h and then diluted with 200 mL of pentane and washed with $NaHCO_3$ (5×). The combined aqueous layer was back-extracted with 100 mL of pentane (1×). The combined organic phase was dried (Na_2SO_4), the solvent was removed in vacuo, and the residue was vacuum distilled (0.5 mmHg) through a 30-cm jacketed Vigreux column (1.5-cm i.d.) to afford the following: fraction 1, bp 66–70 °C, 2.24 g of a 1:2 *E*:*Z* mixture containing an unidentified impurity; fraction 2, bp 71–72 °C, 1.06 g of a 1:1 *E*:*Z* mixture; fraction 3, bp 74–75 °C, 1.85 g of a 2:1 *E*:*Z* mixture; fraction 4, bp 75–77 °C, 8.66 g (38 mmol, 44%) of a 95:5 *E*:*Z* mixture of 5. The *E* isomer gave the following spectral data: IR (thin film) 1738, 1715, 1648, 1370 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.66 (s, 1 H), 4.14 (m, 4 H), 2.30 (t, 2 H, J = 7.4 Hz), 2.17 (t, 2 H, J = 7.4 Hz), 2.16 (s, 3 H), 1.82 (quintet, 2 H, J = 7.4 Hz), 1.28 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 172.9, 166.4, 158.4, 116.1, 60.2, 59.3, 39.9, 33.3, 22.4, 18.4, 14.1 (2); HRMS m/e for $C_{12}H_{20}O_4$ calcd 228.1361, found 228.1362.

Anal. Calcd for $C_{12}H_{20}O_4$: C, 63.16; H, 8.77. Found: C, 63.12; H, 8.75.

Representative Procedure for the Preparation of Six-Membered Cyclic β-Keto Esters. Ethyl 6-Methyl-2-oxocyclohexanecarboxylate (6). To a flame-dried 250-mL three-necked round-bottomed flask equipped with magnetic stirring, an addition of funnel, and a septum was added 10 mL of 3 M methylmagnesium chloride in THF (30.0 mmol). This was diluted with 40 mL of dry THF, and the flask was cooled to −20 °C. To this solution was added 3.17 g (32.0 mmol) of anhydrous CuCl, and the resulting mixture was stirred at −20 °C for 1 h. A 10-mL THF solution of 1.07 g (5.00 mmol) of 1 was then added dropwise during 15 min. The reaction was stirred at −20 °C until TLC indicated the complete consumption of starting material. The reaction mixture was transferred by cannula to a vigorously stirred solution of NH_4Cl at 0 °C and stirred until a bright blue color appeared. The mixture was extracted with ether (3×), and the combined ether layers were washed with NaCl (1×), dried ($MgSO_4$), and concentrated in vacuo to yield a light yellow oil. The crude product was purified on two 20-cm × 20-cm PTLC plates eluted with increasing concentrations of ether in hexane: 0.77 g (4.20 mmol, 84%); 3:2 keto–enol; IR, ^1H NMR, and MS matched those reported[26] previously.

Ethyl 6-ethyl-2-oxocyclohexanecarboxylate (7): 0.85 g (4.30 mmol, 86%); 7:3 keto–enol; IR (thin film) 1750, 1718, 1648, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 12.37 (s, 0.3 H), 4.20 (m, 2 H), 3.10 (d, 0.7 H, J = 11.5 Hz), 2.52–1.93 (complex, 5 H), 1.69 (m, 2 H), 1.42 (m, 2 H), 1.28 and 1.25 (2 t, 3 H, J = 6.8 Hz), 0.91 and 0.87 (2 t, 3 H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 206.4, 172.9, 172.3, 169.9, 103.0, 63.4, 60.8, 60.0, 42.4, 41.1, 33.2, 29.1, 28.3, 27.5, 27.1, 24.8, 24.6, 17.1, 14.2 (2), 12.4, 10.8; HRMS m/e for $C_{11}H_{18}O_3$ calcd 198.1256, found 198.1249.

Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.67; H, 9.09. Found: C, 66.46; H, 9.13.

Ethyl 6-butyl-2-oxocyclohexanecarboxylate (8): 1.09 g (4.80 mmol, 96%); 1:1 keto–enol; IR (thin film) 1750, 1720, 1652, 1618 cm^{-1}; ^1H NMR ($CDCl_3$) δ 12.39 (s, 0.5 H), 4.22 (m, 2 H), 3.11 (d, 0.5 H, J = 11.4 Hz), 2.48 (m, 1 H), 2.36–2.12 (complex, 2 H), 2.03 (m, 1 H), 1.69 (m, 2 H), 1.56–1.18 (complex, 10 H), 0.90 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 206.4, 172.8, 172.2, 169.9, 103.1, 63.7, 60.8, 60.0, 41.1, 40.9, 34.4, 33.9, 31.3, 30.0, 29.1, 28.9, 28.6, 25.3, 24.7, 22.6 (2), 17.1, 14.2 (2), 14.1, 13.9; HRMS m/e for $C_{13}H_{22}O_3$ (M^+ + 1) calcd 227.1647, found 227.1649.

Anal. Calcd for $C_{13}H_{22}O_3$: C, 69.03; H, 9.73. Found: C, 68.79; H, 9.71.

Ethyl 2-oxo-6-phenylcyclohexanecarboxylate (9): 1.13 g (4.60 mmol, 92%); mp 39–41 °C; 7:3 keto–enol; IR (thin film) 3090, 3070, 3035, 1750, 1720, 1652, 1625, 755, 705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 12.57 (s, 0.3 H), 7.44–7.10 (complex, 5 H), 4.02 (m, 2.7 H), 3.38 (m, 0.3 H), 3.66 (d, 0.3 H, J = 12.0 Hz), 3.38 (dt, 0.7 H, J = 12.0, 3.9 Hz), 2.57 (dm, 0.7 H, J = 15.6 Hz), 2.32–1.50 (complex, 7 H), 1.04 and 0.93 (2 t, 3 H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 205.4, 173.6, 172.4, 168.7, 146.4, 142.2, 128.6, 127.9, 127.5, 127.0 (2), 125.6, 100.1, 63.7, 60.7, 60.0, 47.6, 41.1, 38.7, 33.0, 31.6, 29.2, 25.4, 17.2, 13.9, 13.8; HRMS m/e for $C_{15}H_{18}O_3$ calcd 246.1256, found 246.1251.

Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.17; H, 7.32. Found: C, 73.14; H, 7.35.

Ethyl 6-ethenyl-2-oxocyclohexanecarboxylate (10). [Note: the reaction sequence run with vinylmagnesium bromide required 12 equiv of RMgX–CuCl[14]]: 0.78 g (4.00 mmol, 80%); 3:2 keto–enol; IR, ^1H NMR, ^{13}C NMR, and MS matched those reported[21a] previously.

Ethyl 3,3,6-trimethyl-2-oxocyclohexanecarboxylate (16): 0.93 g (4.39 mmol, 88%); 7:3 keto–enol; IR (thin film) 1738, 1700, 1635, 1600, 1365 cm^{-1}; ^1H NMR ($CDCl_3$) δ 12.65 (s, 0.3 H), 4.23 (m, 2 H), 3.26 (d, 0.7 H, J = 12.2 Hz), 2.69 (m, 0.3 H), 2.22 (m, 0.7 H), 1.80–1.57 (complex, 3 H), 1.39 (m, 1 H), 1.29 (m, 3 H), 1.19 (s, 3 H), 1.18 and 1.07 (2 s, 3 H), 1.07 and 1.03 (2 d, 3 H, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 210.3, 178.4, 173.4, 170.2, 101.5, 61.3, 60.7, 60.1, 44.4, 39.2, 37.1, 35.8, 33.3, 28.8, 27.4, 27.3, 26.7, 26.1, 25.1, 24.8, 21.0, 14.2 (2); HRMS m/e for $C_{12}H_{20}O_3$ calcd 212.1412, found 212.1419.

Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.92; H, 9.43. Found: C, 67.65; H, 9.54.

Ethyl 8-methyl-6-oxospiro[4.5]decane-7-carboxylate (17): 1.05 g (4.41 mmol, 88%); 4:1 keto–enol; IR (thin film) 1735, 1700, 1635, 1600, 1365 cm^{-1}; ^1H NMR ($CDCl_3$) δ 12.67 (s, 0.2 H), 4.23

(26) Fráter, G.; Günther, W.; Müller, U. *Helv. Chim. Acta* **1989**, *72*, 1846–1851.

(m, 2 H), 3.19 (d, 0.8 H, J = 12.2 Hz), 2.69 (m, 0.2 H), 2.42 (dt, 0.8 H, J = 12.9, 4.9 Hz), 1.90–1.46 (complex, 11 H), 1.31 and 1.29 (2 t, 3 H, J = 7.2 Hz), 1.07 and 1.01 (2 d, 3 H, J = 6.6 Hz); ^{13}C NMR ($CDCl_3$) δ 208.8, 178.3, 170.2, 121.3, 102.1, 62.4, 60.8, 60.1, 55.8, 38.5, 38.4, 38.0, 36.7, 36.5, 34.0, 30.2, 27.3, 26.9, 25.8, 25.4, 24.9, 21.0, 14.2; HRMS m/e for $C_{14}H_{22}O_3$ calcd 238.1569, found 238.1577.

Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.59; H, 9.24. Found: C, 70.82; H, 9.39.

Representative Procedure for Methylation of the 6-Membered Cyclic β-Keto Ester Derivatives. (1*R,6*R**)-Ethyl 1,6-Dimethyl-2-oxocyclohexanecarboxylate (11).** Ethanolic sodium ethoxide was prepared by dissolving 0.104 g (4.50 g-atom) of sodium metal in 5 mL of absolute EtOH. The solution was cooled to 20 °C, a 2-mL absolute EtOH solution of 0.55 g (3.00 mmol) of **6** was added dropwise, and the mixture was stirred for 30 min. To the resulting yellow solution was added 2.13 g (15.0 mmol) of methyl iodide, and the reaction was stirred at 20 °C for 12 h. The crude reaction mixture was concentrated in vacuo, diluted with 0.5 M HCl, and extracted (2×) with ether. The combined ether extracts were washed with water, $Na_2S_2O_3$, water, and NaCl, dried ($MgSO_4$), and concentrated under vacuum. The crude product, containing a 93:7 mixture of trans–cis alkylation products (GC analysis), was separated on one 20-cm × 20-cm PTLC plate eluted with increasing concentrations of ether in hexane to give the pure trans isomer: 0.42 g (2.10 mmol, 70%); IR, ^{1}H NMR, ^{13}C NMR, and HRMS matched those reported[18e] previously.

(1*R,6*R**)-Ethyl 6-ethyl-1-methyl-2-oxocyclohexanecarboxylate (12)**: isolated from a 93:7 trans–cis mixture; 0.43 g (2.04 mmol, 68%); IR (thin film) 1740, 1718, 1380 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.14 (q, 2 H, J = 7.1 Hz), 2.75 (dt, 1 H, J = 14.0, 7.4 Hz), 2.45 (dm, 1 H, J = 14.0 Hz), 2.07 (m, 1 H), 1.92 (m, 1 H), 1.80–1.50 (complex, 2 H), 1.50–1.20 (complex, 2 H), 1.35 (s, 3 H), 1.25 (t, 3 H, J = 7.1 Hz), 0.94 (t, 3 H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 208.5, 171.3, 61.0, 60.9, 51.0, 40.0, 26.2, 25.3, 23.8, 18.7, 14.1, 13.2; HRMS m/e for $C_{12}H_{20}O_3$ calcd 212.1412, found 212.1415.

Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.92; H, 9.43. Found: C, 68.18; H, 9.61.

(1*R,6*R**)-Ethyl 6-butyl-1-methyl-2-oxocyclohexanecarboxylate (13)**: isolated from a 95:5 trans–cis mixture; 0.50 g (2.07 mmol, 69%); IR (thin film) 1741, 1720, 1380 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.13 (q, 2 H, J = 7.2 Hz), 2.71 (dt, 1 H, J = 14.1, 7.3 Hz), 2.42 (dm, 1 H, J = 14.1 Hz), 2.04 (m, 1 H), 1.88 (m, 1 H), 1.80–1.50 (complex, 3 H), 1.45–1.08 (complex, 6 H), 1.33 (s, 3 H), 1.24 (t, 3 H, J = 7.2 Hz), 0.89 (t, 3 H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 208.5, 171.4, 61.0, 60.9, 49.1, 40.1, 30.9, 30.7, 27.0, 25.4, 22.8, 18.8, 14.1, 14.0; HRMS m/e for $C_{14}H_{24}O_3$ calcd 240.1725, found 240.1724.

Anal. Calcd for $C_{14}H_{24}O_3$: C, 70.00; H, 10.00. Found: C, 69.95; H, 10.13.

(1*R,6*S**)-Ethyl 1-methyl-2-oxo-6-phenylcyclohexanecarboxylate (14)**: isolated from a 99:1 trans–cis mixture; 0.55 g (2.10 mmol, 70%); mp 51–52 °C; IR (thin film) 3090, 3070, 3035, 1741, 1715, 1602, 1498, 1380 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.36–7.16 (complex, 5 H), 4.04 (m, 2 H), 3.07 (dt, 1 H, J = 14.1, 7.5 Hz), 2.73 (m, 2 H), 2.54 (dm, 1 H, J = 14.1 Hz), 2.19 (m, 1 H), 1.94–1.68 (complex, 2 H), 1.24 (s, 3 H), 1.12 (t, 3 H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 207.9, 170.6, 140.4, 128.9, 128.0, 127.2, 61.7, 61.1, 55.3, 39.8, 28.0, 25.4, 19.1, 13.9; HRMS m/e for $C_{16}H_{20}O_3$ calcd 260.1412, found 260.1410.

Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.85; H, 7.69. Found: C, 73.85; H, 7.66.

(1*R,6*S**)-Ethyl 6-ethenyl-1-methyl-2-oxocyclohexanecarboxylate (15)**: isolated from a 93:7 trans–cis mixture; 0.43 g (2.04 mmol, 68%); IR (thin film) 3060, 1730, 1709, 1632, 1368, 995, 911 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.09 (m, 1 H), 5.07 (d, 1 H, J = 10.1 Hz), 5.03 (d, 1 H, J = 16.1 Hz), 4.16 (q, 2 H, J = 7.1 Hz), 2.68 (dt, 1 H, J = 13.7, 6.1 Hz), 2.45 (dm, 1 H, J = 13.7 Hz), 2.09 (m, 3 H), 1.70 (m, 2 H), 1.29 (s, 3 H), 1.28 (t, 3 H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 207.2, 171.2, 137.8, 116.6, 61.0, 60.0, 54.0, 39.9, 28.4, 25.5, 19.1, 14.0; HRMS m/e for $C_{12}H_{18}O_3$ calcd 210.1256, found 210.1257.

Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.57; H, 8.57. Found: C, 68.48; H, 8.59.

(1*R,6*R**)-Ethyl 1,3,3,6-tetramethyl-2-oxocyclohexanecarboxylate (18)**: isolated from a 90:10 trans–cis mixture; 0.23 g (1.00 mmol, 33%); IR (thin film) 1738, 1705, 1380, 1370 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.03 (m, 2 H), 2.00 (m, 1 H), 1.70 (m, 1 H), 1.54 (m, 3 H), 1.28 (s, 3 H), 1.16 (t, 3 H, J = 7.1 Hz), 1.11 (d, 3 H, J = 6.8 Hz), 1.06 (s, 3 H), 1.04 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 212.4, 171.5, 60.6, 58.8, 45.0, 41.6, 38.5, 27.8, 26.6 (2), 21.3, 16.8, 14.0; HRMS m/e for $C_{13}H_{22}O_3$ calcd 226.1569, found 226.1576.

Anal. Calcd for $C_{13}H_{22}O_3$: C, 69.02; H, 9.73. Found: C, 68.92; H, 9.88.

(7*R,8*R**)-Ethyl 7,8-dimethyl-6-oxospiro[4.5]decane-7-carboxylate (19)**: isolated from a 91:9 trans–cis mixture; 0.47 g (1.86 mmol, 62%); IR (thin film) 1740, 1705, 1372 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.09 (m, 2 H), 2.20 (m, 1 H), 2.03 (m, 1 H), 1.83 (m, 1 H), 1.79–1.55 (complex, 10 H), 1.36 (s, 3 H), 1.23 (t, 3 H, J = 7.1 Hz), 1.15 (d, 3 H, J = 6.7 Hz); ^{13}C NMR ($CDCl_3$) δ 212.1, 171.4, 60.6, 59.2, 56.3, 41.0, 37.8, 37.7, 36.1, 27.3, 25.2, 24.8, 21.2, 16.8, 14.0; HRMS m/e for $C_{15}H_{24}O_3$ calcd 252.1725, found 252.1716.

Anal. Calcd for $C_{15}H_{24}O_3$: C, 71.43; H, 9.52. Found: C, 71.45; H, 9.69.

Acknowledgment. The authors thank the Oklahoma Center for the Advancement of Science and Technology (HR1-035) for support of this work. Finally, partial support by NSF grant DMB-8603864 and OCAST grant 1506 for the upgrade of our 300-MHz NMR and NSF grant BSS-8704089 for our mass spectrometry facility is acknowledged with gratitude.

Registry No. 1, 126761-20-4; (*Z*)-1, 144192-19-8; 2, 144192-20-1; (*Z*)-2, 144192-21-2; 3, 103621-29-0; (*Z*)-3, 103621-30-3; 4, 144192-22-3; (*Z*)-4, 144192-23-4; 5, 144192-24-5; (*Z*)-5, 144192-25-6; 6, 58019-68-4; 6 enol, 144192-26-7; 7, 144192-27-8; 7 enol, 144192-28-9; 8, 144192-29-0; 8 enol, 144192-30-3; 9, 144192-31-4; 9 enol, 144192-32-5; 10, 73392-80-0; 10 enol, 144192-33-6; 11, 144192-34-7; *cis*-11, 144192-35-8; 12, 144192-36-9; *cis*-12, 144192-37-0; 13, 144192-38-1; *cis*-13, 144192-40-5; 14, 144192-39-2; 15, 144192-41-6; *cis*-15, 144192-42-7; 16, 144192-43-8; 16 enol, 144192-44-9; 17, 144192-45-0; 17 enol, 144192-46-1; 18, 144192-47-2; *trans*-18, 144192-48-3; 19, 144192-49-4; *trans*-19, 144192-50-7; $EtO_2C(CH_2)_3CH{=}CH_2$, 54653-25-7; $EtO_2C(CH_2)_3CHO$, 22668-36-6; $Ph_3P{=}CHCO_2Et$, 1099-45-2; $Ph_3P{=}C(Me)CO_2Et$, 5717-37-3; $EtO_2C(CH_2)_3COCH_3$, 13984-57-1; $EtO_2CCH_2P(O)(OEt)_2$, 867-13-0; $EtO_2CCH(CH_3)_2$, 97-62-1; $Br(CH_2)_3CH{=}CH_2$, 5162-44-7; MeMgCl, 676-58-4; EtMgCl, 2386-64-3; *n*-BuMgCl, 693-04-9; PhMgCl, 100-59-4; $CH_2{=}CHMgCl$, 3536-96-7; $CH_2{=}CHMgBr$, 1826-67-1; *n*-BuLi, 109-72-8; *n*-BuMgBr, 693-03-8; CuCl, 7758-89-6; CuI, 7681-65-4; CuCN, 544-92-3; ethyl cyclopentanecarboxylate, 5453-85-0.

Synthesis of Thiiranecarboxylic Esters from Cysteine and Cystine Esters

Terence C. Owen* and Joseph K. Leone

Department of Chemistry, University of South Florida, Tampa, Florida 33620

Received July 14, 1992

For many years it was thought that thiiranecarboxylic esters (thioglycidic esters, α,β-epithioesters, **1**) were unstable. Attempts to prepare them[1] had produced instead a variety of isomeric mercaptoacrylates, dithianes, low polymers, and desulfurization products. In 1967 it was

(1) (a) Culvenor, C. C. J.; Davies, W.; Heath, N. S. *J. Chem. Soc.* **1949**, 278. (b) Culvenor, C. C. J.; Davies, W.; Maclaren, J. A.; Nelson, P. F.; Savige, W. E. *J. Chem. Soc.* **1949**, 2573. (c) Owen, T. C.; Gladys, C. L.; Field, L. *J. Chem. Soc.* **1962**, 501. (d) Owen, T. C.; Gladys, C. L.; Field, L. *J. Chem. Soc.* **1962**, 656. (e) Tung, C. C.; Speziale, A. J. *J. Org. Chem.* **1964**, *29*, 1577. Mueller, W. H. *J. Org. Chem.* **1969**, *34*, 2955.

0022-3263/92/1957-6985$03.00/0