Registry No. **1**, 833-82-9; **2**, 21213-27-4; **3**, 5296-64-0; **4**, 22456-89-9; **5**, 64732-74-7; **6**, 13640-71-6; **7**, 13307-61-4; **9**, 129315-20-4; **10**, 129315-21-5; **11a-a**, 129389-04-4; **11a-b**, 129389-05-5; **11b**, 129315-22-6; **11c**, 129315-23-7; **11d-a**, 129315-24-8; **11d-b**, 129315-25-9; **12**, 17510-46-2; **13a**, 110874-42-5; **13b**, 129315-26-0; **13c**, 129315-27-1; **13d**, 129315-28-2; **14a**, 110874-43-6; **16a**, 110874-58-3; **16b**, 110874-57-2; **17**, 4551-15-9; **18**, 110874-41-4; **19**, 110874-44-7; **20**, 110874-45-8; **21**, 60253-72-7; **22b**, 2109-22-0; **22c**, 5445-77-2; **22d**, 96-17-3; **24a**, 110874-46-9; **24b**, 110874-47-0; **24c**, 110874-48-1; **24d**, 110903-55-4; **25d**, 110874-50-5; **26a**, 110874-51-6; **26b**, 110874-53-8; **26c**, 110874-55-0; **27c**, 110874-56-1; **28a**, 22456-89-9; **28b**, 129315-29-3; **28c**, 129315-30-6; **29**, 97250-84-5; **30a**, 129315-31-7; **30b**, 129315-32-8; **30c**, 129337-07-1; **31a**, 129315-33-9; **31b**, 129315-34-0; **32a**, 123-72-8; **32b**, 78-84-2; **32c**, 100-52-7; **33a**, 129315-35-1; **33c**, 129315-36-2; **34a**, 129315-37-3; **34c**, 129315-38-4; **35**, 124400-14-2; **36a**, 129315-39-5; **36b**, 129315-41-9; **36c**, 129315-41-9; (*E*)-**37**, 76943-95-8; **39**, 61878-68-0; **40**, 129315-42-0; **41**, 129315-43-1; **42**, 129315-44-2; **43**, 129315-45-3; **44**, 129315-46-4; **45**, 129315-47-5; **46**, 129315-48-6; **47**, 129315-49-7; **48**, 129315-50-0; **49**, 129315-51-1; **50**, 129315-52-2; **51**, 129315-53-3; **52**, 129315-54-4; **53**, 129315-55-5; **54**, 129315-56-6; **55**, 129315-57-7; **56**, 129315-58-8; **57**, 129315-59-9; **58**, 129389-06-6; **59**, 129315-60-2; (*S*)-1, 23430-41-3; (*S*)-2, 4148-81-6; (*S*)-3, 16241-12-6; (*S*)-4, 24010-73-9; (*S*)-5, 16241-13-7; (*S*)-6, 24010-52-4; (*S*)-7, 118-72-9; (*S*)-8, 91638-62-9; (*S*)-9, 129315-61-3; (*S*)-10, 129315-62-4; (*S*)-11, 129315-63-5; (*S*)-12, 1541-10-2; (*S*)-13, 22693-41-0; (*S*)-14, 129315-64-6; CH_2=$CHCH_2SiMe_3$, 762-72-1; PhSH, 108-98-5; $PhSCH_2Ph$, 831-91-4; $PhSCH_2CH(CH_3)_2$, 13307-61-4; 2,4,6-$(Me)_3C_6H_2SCH_2CH(CH_3)_2$, 129315-65-7; 2-phenylpropanal, 93-53-8; benzyl chloride, 100-44-7; isobutyl bromide, 78-77-3; pinacolone trimethylsilyl enol ether derivative, 55638-27-2; 2-phenyl-1-propanol, 1123-85-9; 2,6-dimethylphenol, 576-26-1; dimethylthiocarbamoyl chloride, 16420-13-6; 2,6-diisopropylphenol, 2078-54-8; 2-methyl-2-propanethiol, 75-66-1; 2,4,6-trimethylbenzenesulfonyl chloride, 773-64-8; 2,4,6-triisopropylbenzenesulfonyl chloride, 6553-96-4.

Supplementary Material Available: Full experimental details for the preparation of benzyl phenyl sulfide, 3-methyl-1-propyl phenyl sulfide, **1–7**, **9–10**, 2-phenylpropyl tosylate, phenyl 2-phenyl-1-propyl sulfide, **11a**, *O*-2,6-dimethylphenyl *N,N*-dimethylthiocarbamate, *O*-2,6-diisopropylphenyl *N,N*-dimethylthiocarbamate, *S*-2,6-dimethylphenyl *N,N*-dimethylthiocarbamate, *S*-2,6-diisopropylphenyl *N,N*-dimethylthiocarbamate, 2,6-dimethylthiophenol, 2,6-diisopropylthiophenol, 1-[(2,6-dimethylphenyl)thio]-2-phenylpropane, 1-[(2,6-diisopropylphenyl)thio]-2-phenylpropane, 1-(*tert*-butylthio)-2-phenylpropane, **11c–d**, 2,4,6-trimethylthiophenol, **21**, and **28b,c** and X-ray crystal data for compound **43** (27 pages). Ordering information is given on any current masthead page.

Utilization of Ethyl 2-((Phenylsulfonyl)methyl)acrylate for the Synthesis of α-Methylenevalerolactones[1]

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A two-step sequence is described for conversion of cyclic and acyclic ketone enolates into α-methylenevalerolactones. The first step involves Michael addition to ethyl α-((phenylsulfonyl)methyl)acrylate **1** with concomitant elimination of $PhSO_2$ and formation of unsaturated keto esters **2–7**. In the next sequence chemoselective ketone reduction is usually followed by spontaneous lactonization of acidification. Contrary to the five- and six-membered ring systems, the cis-fused isomer predominates in the seven- and eight-membered ring compounds **12** and **13**. Spiro α-methylenevalerolactones **17a,b** are as well obtainable by a short sequence of steps from 2-oxocyclohexanecarboxylate and **1**.

Introduction

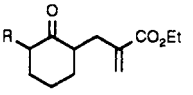
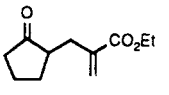
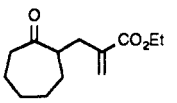
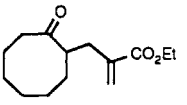
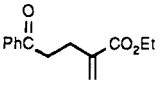
The presence of the α-methylene lactone structural unit in various natural products has been credited as responsible for the biological activity exhibited by a number of these compounds.[2] Preparative activity in this area has been focused mainly on the synthesis of α-methylenebutyrolactones,[3] whereas the development of effective methods leading to α-methylenevalerolactones has received less attention,[4] although the latter lactones can be expected to exhibit similar biological properties due to the possibility of analogous 1,4-conjugate addition reactions involving functions present in peptides and proteins. Interesting biological activity is indeed exhibited by vernolepin,[5] vernomenin,[5] and pentalenolactone E,[6] which contain α-methylenevalerolactone moieties within their molecule.

In this context, α-(bromomethyl)acrylate has been utilized as an alkylating reagent for strongly activated methylene groups, like those of 1,3-diketones[7] or β-keto esters,[8] to give products which eventually could be used for further conversion to α-methylenevalerolactones.[7] For simple ketones devoid of additional activation, alkylation with the above acrylate reagent was considered to require, however, prior conversion to the corresponding enamines,[9]

(1) Synthetic methods 36. For part 35, see: Fischer, B.; Hassner, A. *J. Org. Chem.* **1990**, *55*, 5225.
(2) See, e.g.: Kupchan, S. M. *Trans. N.Y. Acad. Sci.* **1970**, *32*, 85.
(3) For recent reviews, see: Grieco, P. A. *Synthesis* **1975**, 67. Petragnani, N.; Ferraz, N. M. C.; Silva, G. V. J. *Ibid.* **1986**, 157.
(4) See: (a) Sunitha, K.; Balasubramian, K. K.; Rajagopolan, K. *Tetrahedron Lett.* **1984**, 3125. (b) Grieco, P. A.; Hiroi, K. *Tetrahedron Lett.* **1973**, 1831. (c) Yamada, K.; Kato, M.; Hirata, Y. *Ibid.* **1973**, 2745. Groutas, W. C.; Felker, D.; Magnin, D. *Synth. Commun.* **1980**, *10*, 355. (e) Trost, B. M.; Miller, C. H. *J. Am. Chem. Soc.* **1975**, *97*, 7182. (f) Semmelhack, M. F.; Brickner, J. S. *J. Org. Chem.* **1981**, *46*, 1723.
(5) Kupchan, S. M.; Hemingway, R. J.; Werner, D.; Karim, A.; McPhail, A. T.; Sim, G. A. *J. Am. Chem. Soc.* **1968**, *90*, 3596.
(6) Cane, D. E.; Rossi, T. *Tetrahedron Lett.* **1979**, 2973.
(7) Groutas, W. C.; Felner, D.; Magnin, D.; Meitzner, G.; Gaynor, T. *Synth. Commun.* **1980**, *10*, 1. de Groot, A.; Jansen, B. J. M. *Recl. Trav. Chim. Pays-Bas* **1974**, *93*, 153.
(8) (a) Ameer, F.; Drewes, S. E.; Houston-McMillian, M. W.; Kaye, P. T. *S. Afr. J. Chem.* **1985**, *39*, 57. (b) Stetter, H.; Elfer, K. *Synthesis* **1974**, 36.
(9) See: Nelson, R. P.; Lawton, R. G. *J. Org. Chem.* **1969**, *34*, 1225.

0022-3263/90/1955-5977$02.50/0

Table I. Reactions of Ketones with Ethyl 2-(Phenylsulfonyl)methyl)acrylate

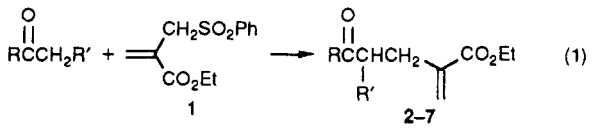
entry	ketone	product	% yield[a]
			
1	R = H	**2**: R = H	93
2	R = CH_3	**3a**: R = CH_3 (cis) **3b**: R = CH_3 (trans)	77[b]
3	 n = 1	 **4**	86
4	n = 3	 **5**	84
5	n = 4	 **6**	85
6	PhC(O)CH_3	 **7**	60

[a] The yields are based on the amount of 1. Use of stoichiometric amounts of cyclohexanone, base, and acrylate 1 or inverse addition resulted in a somewhat lower yield (85%) of **2**. [b] Yields of **3a** + **3b** (1:1). This ratio did not change when an equimolar mixture of 1, ketone, and LDA were used.

and the route to α-methylenevalerolactones consisted of a four-step sequence of variable effectiveness.[10]

Results and Discussion

We describe herein a general and efficient elaboration of α-methylenevalerolactones by a two-step sequence: (a) alkylation of ketones with ethyl 2-((phenylsulfonyl)-methyl)acrylate (1) and (b) selective reduction of the resulting keto esters followed by direct ring closure to α-methylene lactones. Although the sulfone-substituted ester 1 had previously been reported too labile in the presence of base to serve as a nucleophile,[11] we found that under basic conditions it reacts effectively as an electrophile in Michael additions with concomitant elimination of the phenylsulfonyl group (eq 1).

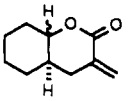
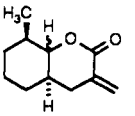
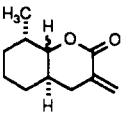
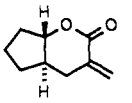
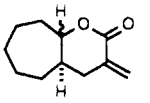
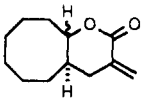
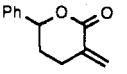


(1)

Various ketones, deprotonated at low temperature (−78 °C) with lithium diisopropylamide (LDA) in THF in the presence of HMPA (~1.5 eqiv), afforded, after addition of sulfone ester 1, the addition–elimination products shown in Table I. Bis Michael adducts were not observed.

It is interesting to note that under the above reaction conditions the yield of conjugate addition of cyclohexanone enolate to methyl methacrylate was very poor (<10% of a diastereomeric mixture), probably because of the reversibility of the reaction. The ready elimination of the phenylsulfonyl group this provides the driving force ensuring the efficiency of the addition. We found that 2-(bromomethyl)acrylate can react as well with cyclohexanone, even without the intermediacy of an enamine, under similar reaction conditions (LDA, −78 °C); however, the yield of **2** was somewhat lower (~70%).[12] Moreover, the handling of the highly stable 1 is advantageous in comparison with the bromo derivative.

Table II. Synthesis of α-Methylenevalerolactones

keto ester	product	trans:cis ratio	% yield
2	 **8a**, trans **8b**, cis	2:1[a] 9:1[b]	75 62
3a	 **9a**, trans + **9b**, cis	1:4	66
3b	 **10a**, trans + **10b**, cis	45:55[a]	60
4	 **11**		81
5	 **12a**, trans + **12b**, cis	1:5[a] 1:3[b]	77 62
6	 **13a**, trans + **13b**, cis	1:2[c]	65
7	 **14**		68

[a] Reduction by $NaBH_4$. [b] Reduction by $LiAlH(t\text{-}BuO)_3$. [c] Reduction by $NaCNBH_3$.

Chemoselective reduction of the ketone function in the above-mentioned keto esters, followed by acidification of the reaction mixture, afforded directly α-methylenevalerolactones in good yield (Table II). As expected, the stereochemistry at the ring fusion in the bicyclic products was influenced by the ring size of the utilized cycloalkanones and by the hydride reagent used for reduction. Treatment of keto ester **2** with $NaBH_4$ in methanol at low temperature (−78 °C) provided, after acidification, chromatographically separable trans- and cis-fused stereoisomers **8a** and **8b** in a 2:1 ratio in 75% yield. The configurational assignments are based on ^1H NMR shifts of the protons at the lactone ring junction: in the trans isomer **8a**, the axial proton next to the lactone oxygen appears at higher field, with a larger coupling constant (δ 3.94, td, J

(10) Marshall, H.; Vogel, F.; Weyerstahl, P. *Chem. Ber.* **1974**, *107*, 2852. Tanaka, A.; Nakata, K. *Agr. Biol. Chem.* **1973**, *37*, 2365.

(11) Tanaka, K.; Yoda, H.; Kaji, A. *Tetrahedron Lett.* **1985**, *26*, 4747. This instability led to utilization of the corresponding propenamides instead of esters as nucleophilic reagents: Tanaka, K.; Horiuchi, H.; Yoda, H. *J. Org. Chem.* **1989**, *54*, 63.

(12) On the basis of previous results (ref 8a), it may be assumed that under aprotic reaction conditions a conjugate addition to bromomethylacrylate is favored over a S_N2 reaction.

= 10.5 and 4.5 Hz) than the analogous equatorial proton in the cis isomer (δ 4.60–4.56 br s). The stereoselectivity during the reduction of the keto ester (preferential axial hydride attack[13,14]) was substantially improved (9:1 ratio for **8a**:**8b**) when the bulkier $LiAlH(t\text{-}BuO)_3$ was used as the reagent instead of $NaBH_4$. The reduction of the cyclopentanone derivative **4** with $NaBH_4$ was even more stereoselective due to ring flattening;[13] the cis-fused isomer being present only in minute amounts (<3%). Unlike for other entries in Table II, direct acidification of the reaction mixture resulting from the reduction of **4** did not lead to lactonization, which was however achieved by refluxing the hydroxy ester in benzene containing p-TsOH.

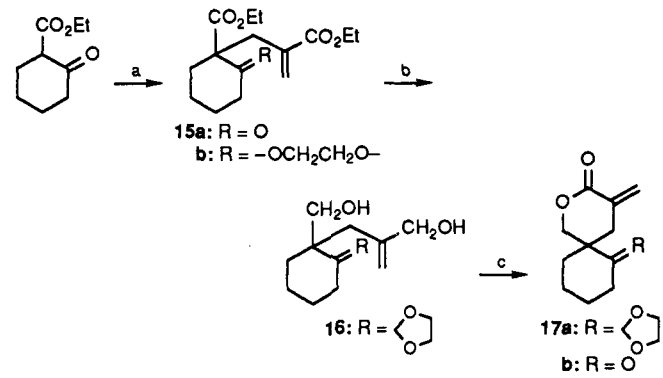
The reaction of 2-methylcyclohexanone with **1** resulted in a 1:1 ratio of cis and trans stereoisomers **3a** and **3b** (Table I). In the first eluted isomer (**3a**, cis) both protons vicinal to the carbonyl function are assumed to be axial because they appear at a relatively higher field (δ 2.62–2.51, m, 1 H, and 2.49–2.34, m, 1 H) with a broader sum of halfwidth couplings (32 and 38 Hz, respectively) than in the trans-disubstituted **3b** (δ 2.76–2.69, m, 1 H, and 2.68–2.57, m, 1 H, sum of couplings 21 and 27 Hz, respectively).[15] Reduction of the cis 2,6-disubstituted cyclohexanone **3a** with $NaBH_4$ gave predominantly the cis-fused lactone **9b** (1:4 ratio of **9a**:**9b** due to the preferential trans hydride attack), while the trans-disubstituted **3b** afforded a 45:55 ratio of **10a** and **10b**.

In the seven-membered ring derivative **5**, $NaBH_4$ reduction gave preferentially the cis-fused lactone (1:5 ratio of **12a**:**12b**), presumably due to equatorial attack on a twist chair[16] cycloheptanone. The use of the bulkier $LiAlH(t\text{-}BuO)_3$ reduced somewhat this preference (1:3 ratio of **12a**:**12b**).

In the cyclooctanone derivative **6**, reduction with $NaBH_4$, with or without $CeCl_3$, at 20 °C was slow and led to partial reduction of the ester and of the conjugated double bond. The use of $LiAlH(t\text{-}BuO)_3$ led to the recovery of **6**. Chemoselective reduction of **6** proceeded cleanly with $NaCNBH_3$ in acid media to give two stereoisomeric lactones (65%) with the cis-fused **13b** as the major stereoisomer (**13a**:**13b** = 1:2).[17]

Next we explored the possibility of utilizing **1** for the preparation of the spiro α-methylenevalerolactone unit which, like other spirolactones, should present biological interest and synthetic versatility.[18] Previous interest in the preparation of spiro α-methylenebutyrolactone-containing molecules was associated with their tumor-inhibitory activity.[19] Such structural moieties had been obtained by a Reformatsky-type reaction between ethyl 2-(bromomethyl)acrylate and a cyclic ketone.[19,20] However, this method is not applicable for the elaboration of six-membered spiro α-methylene lactones. We succeeded in obtaining **17** by using the route indicated in Scheme I, which involves as the first step the conjugate addition of ethyl oxocyclohexane-2-carboxylate to **1** to give the diester

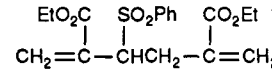
Scheme I[a]



[a] (a) NaH, THF, 1; (b) DIBAL toluene, 0 °C; (c) MnO_2, CH_2Cl_2, room temperature.

15a. Protection of the ketone to **15b**, reduction of both ester groups by Dibal to give the diol **16**, and selective oxidation of the allylic hydroxyl group in the latter by MnO_2 afforded the spiro α-methylenevalerolactone **17a**. Acidification led to deketalization and formation of crystalline **17b**.

In the absence of an activating β-ketone function, the conjugate addition of carbethoxycycloalkanes to **1** is unsuccessful. Instead, proton transfer from the slightly more acidic **1** causes partial self-condensation of the latter, with formation of **18**.



18

Experimental Section

General. All air- and moisture-sensitive reactions were carried out in flame-dried, argon-flushed, two-necked flasks sealed with rubber septa, and the reagents were introduced with a syringe. Tetrahydrofuran (THF) was freshly distilled from sodium/benzophenone. Chromatography was done on Merck silica gel 60 (230–400 mesh), and precoated Merck silica gel plates (60F-254) were used for TLC. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Brucker AC-200 or on a Brucker AM-300 spectrometer. Mass spectra (CI in methane) were recorded at 60–70 eV.

Ethyl 2-((Phenylsulfonyl)methyl)propenoate (1). To a solution of ethyl 2-(bromomethyl)acrylate[21] (1 g, 5.2 mmol) in dry methanol (25 mL) was added sodium phenylsulfinate (855 mg, 5.2 mmol). After 2.5 h of reflux the mixture was concentrated under reduced pressure, the obtained residue was dissolved in CH_2Cl_2 and filtered, and the filtrate was evaporated and purified by chromatography (pentane–ethyl acetate, 2:1) to give **1** as a viscous oil (1.1 g, 84%): ^1H NMR δ 7.89–7.83 (m, 2 H), 7.68–7.61 (m, 1 H), 7.58–7.50 (m, 2 H), 6.51 (d, J = 1 Hz, 1 H), 5.91 (d, J = 1 Hz, 1 H), 4.17 (d, J = 1 Hz, 2 H), 4.01 (q, J =7 Hz, 2 H), 1.18 (t, J = 7 Hz, 3 H); MS m/e 255 (MH^+), 183, 165. Anal. Calcd for $C_{12}H_{14}O_4S$: C,56.69; H, 5.55. Found: C, 56.56; H, 5.61.

General Procedure for the Reaction of Cycloalkanones with Ethyl 2-((Phenylsulfonyl)methyl)propenoate (1). Preparation of Compounds 2–7. To a cooled (-78 °C) solution of the ketone (2.5 mmol, Table I), in dry THF (12 mL) under argon was added lithium diisopropylamide (2 mmol), prepared from BuLi (2 mmol, 1.4 mL of 1.47 M BuLi solution in hexane) and diisopropylamine (0.28 mL, 2 mmol) in THF (1.5 mL). After the mixture was stirred for 30 min at the above temperature, HMPA (0.25 g, 1.4 mmol) and a solution of **1** (0.254 g, 1 mmol) in dry THF (12 mL) were added successively and dropwise. The reaction mixture was stirred for additional 40 min, poured into cold 3 N HCl, and extracted with ether. The ether extracts were washed

(13) See, e.g.: Boone, J. R.; Ashby, E. C. *Top. Stereochem.* **1979**, *11*, 53.
(14) Wigfield, D. C.; Phelps, D. J. *J. Am. Chem. Soc.* **1974**, *96*, 543.
(15) Bhacca, N. S.; Williams, D. H. *Applications of NMR Spectroscopy in Organic Chemistry*; Holden-Day Publishers: San Francisco, 1964; pp 47, 78.
(16) Dale, J. *Stereochemistry and Conformational Analysis*; Verlag Chemie: Weinheim, 1978; p 191.
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successively with aqueous $NaHCO_3$ and water, dried ($MgSO_4$), filtered, and evaporated under reduced pressure. The residue was purified by chromatography (elution with pentane–ethyl acetate, 2:1, unless stated otherwise).

Ethyl 2-methylene-3-(2′-oxocyclohexyl)propanoate (2) was obtained as a colorless liquid (lit.[10]), in 93% yield: ^1H NMR δ 6.19 (d, J = 2 Hz, 1 H), 5.56 (dt, J = 2, 1 Hz, 1 H), 4.2 (q, J = 7 Hz, 2 H), 2.92 (ddd, J = 14, 5, 1 Hz, 1 H), 2.45–2.25 (m, 2 H), 2.17–1.9 (m, 3 H), 1.9–1.79 (m, 1 H), 1.77–1.56 (m, 3 H), 1.29 (t, J = 7 Hz, 3 H), 1.39–1.24 (m, 1 H); ^{13}C NMR δ 211.8 (s), 167.1 (s), 138.7 (s), 126.5 (dd), 60.8 (t), 49.4 (d), 42.1 (t), 33.2 (dd), 32.1 (dd), 28.0 (t), 25.1 (t), 14.2 (q); MS 211 (MH^+), 193, 165.

Ethyl 2-Methylene-3-(3′-methyl-2′-oxocyclohexyl)-propanoate, Cis (3a) and Trans (3) Isomers. The ^1H NMR spectrum of the residue after workup showed a 1:1 ratio of **3a**:**3b** (by integration of the ^1H NMR spectrum). Chromatography purification (elution with pentane–ethyl acetate, 20:1) gave separated isomers (77% total yield); **3a** (eluting first), as an oil: ^1H NMR δ 6.19 (d, J = 2 Hz, 1 H), 5.57 (dd, J = 2, 1 Hz, 1 H), 4.19 (q, J = 7 Hz,2 H), 2.91 (ddd, J = 8, 3, 1 Hz, 1 H), 2.62–2.51 (m, 1 H), 2.49–2.34 (m, 1 H), 2.18–2.02 (m, 3 H), 1.9–1.6 (m, 2 H), 1.44–1.18 (m, 2 H), 1.30 (t, J = 7 Hz, 3 H), 1.01 (d, J = 6.5 Hz, 3 H); ^{13}C NMR δ 213.2 (s), 167.1 (s), 138.7 (s), 126.7 (dd), 60.6 (t), 49.3 (d), 45.7 (d), 37.4, 34.8, 32.1, 25.5 (4 t), 14.5, 14.2 (2 q); MS m/e 225 (MH^+), 179, 178, 167, 150. Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.92; H, 9.29. Isomer **3b** eluted next as an oil: ^1H NMR δ 6.20 (d, J = 2 Hz, 1 H), 5.55 (dd, J = 2, 1 Hz, 1 H), 4.21 (q, J = 7 Hz, 2 H), 2.83 (ddd, J = 13.5, 7, 1 Hz, 1 H), 2.76–2.69 (m, 1 H), 2.68–2.57 (m, 1 H), 2.32 (ddd, J = 13.5, 7, 1 Hz, 1 H), 2.04–1.47 (m, 6 H), 1.30 (t, J = 7 Hz, 3 H), 1.09 (d, J = 7 Hz, 3 H); ^{13}C NMR 215.4 (s), 166.9 (s), 138.4 (s), 126.4 (dd), 60.7 (t), 47.4, 43.2 (2 d), 34.9, 32.8, 32.5, 20.4 (4 t), 15.8, 14.2 (2 q); MS m/e 225 (MH^+). Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: 69.72, H, 8.91.

Ethyl 2-methylene-3-(2′-oxocyclopentyl)propanoate (4) was obtained as a colorless oil (lit.[10]): 86% yield; ^1H NMR δ 6.2 (d, J = 1.5 Hz, 1 H), 5.57 (dt, J = 1.5, 1 Hz, 1 H), 4.21 (q, J = 7 Hz, 2 H), 2.88 (ddd, J = 14.5, 4.5, 1 Hz, 1 H), 2.41–2.28 (m, 2 H), 2.22–2.10 (m, 3 H), 2.08–1.95 (m, 1 H), 1.86–1.7 (m, 1 H), 1.5 (dtd, J = 12.5, 11, 6.5 Hz, 1 H), 1.32 (t, J = 7 Hz, 3 H); ^{13}C NMR δ 219.5 (s), 166.9 (s), 138.9 (s), 126 (dd), 60.7 (t), 48.4 (d), 37.8 (t), 32.1 (t), 29.4 (dd), 20.5 (t), 14.2 (q); MS m/e 197 (MH^+), 151.122.

Ethyl 2-methylene-3-(2′-oxocycloheptyl)propanoate (5) was obtained as a colorless oil in 84% yield: ^1H NMR δ 6.18 (d, J = 1.5 Hz, 1 H), 5.51 (dt, J = 1.5, 1 Hz, 1 H), 4.17 (q, J = 7 Hz, 2 H), 2.88–2.73 (m, 1 H), 2.69 (ddd, J = 6.5, 1.3, 0.5 Hz, 1 H), 2.54–2.37 (m, 2 H), 2.32–2.14 (m, 1 H), 1.93–1.54 (m, 6 H),1.40–1.16 (m, 2 H), 1.28 (t, J = 7 Hz, 3 H); ^{13}C NMR δ 214.8 (s), 167 (s), 138.6 (s), 126.7 (dd), 60.7 (t), 50.5 (d), 43.1 (t), 34.2 (dd), 30.8 (t), 29.2 (t), 28.6 (dd), 24.1 (t), 14.2 (q); MS m/e 225 (MH^+), 178, 150, 122. Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.80; H, 9.12.

Ethyl 2-methylene-3-(2′-oxocyclooctyl)propanoate (6) was obtained as a colorless oil in 85% yield: ^1H NMR δ 6.15 (d, J = 2 Hz, 1 H), 5.52 (dd, J = 2, 1 Hz, 1 H), 4.21 (q, J = 7 Hz, 2 H), 3.03–2.86 (m, 1 H), 2.64 (ddd, J = 14, 8, 1 Hz, 1 H), 2.46–2.24 (m, 3 H), 2.13–1.12 (m, 10 H), 1.31 (t, J = 7 Hz, 3 H); ^{13}C NMR δ 218.8 (s), 166.9 (s), 138.4 (s), 126.8 (dd), 60.7 (t), 48.7 (d), 42.9 (t), 34.6 (t), 32.9 (t), 27.7 (t), 25.3 (t), 24.8 (2 t), 14.16 (q); MS m/e 239, 193, 164, 134. Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.55; H, 9.3. Found: C, 70.25; H, 9.54.

Ethyl 2-methylene-5-oxo-5-phenylpentanoate (7) was obtained in 60% yield (elution with pentane–ethyl acetate, 10:1): ^1H NMR δ 8.01–7.93 (m, 2 H), 7.6–7.52 (m, 1 H), 7.5–7.41 (m, 2 H), 6.21 (d, J = 1.5 Hz, 1 H), 5.64 (q, J = 1.5 Hz, 1 H), 4.23 (q, J = 7 Hz, 2 H), 3.19 (t, J = 7.5 Hz, 2 H), 2.76 (td, J = 7.5, 1.5 Hz, 2 H), 1.31 (t, J = 7 Hz, 3H); ^{13}C NMR δ 199 (s), 166.8 (s), 139.6 (s), 136.6 (s), 133 (d), 128.6 (d), 128 (d), 125.8 (dd), 60.7 (t), 37.7 (t), 27 (t), 14.2 (q); MS m/e 233, 204, 186, 158. Anal. Calcd for $C_{14}H_{16}O_3$: C 72.39; H, 6.94. Found: C, 72.25; H, 7.23.

2-Methylene-3-(2′-hydroxycyclohexyl)propanoic Acid, δ-Lactone, Trans (8a) and Cis (8b) Isomers. To a cold (−78 °C) stirred solution of **2** (210 mg, 1 mmol) in methanol (10 mL) under anhydrous conditions was added $NaBH_4$ (38 mg, 1 mmol) in methanol (5 mL). After 4 h the solution was warmed to 0 °C, acidified with 3 N HCl (10 mL), stirred for an additional 2 h at room temperature, and then neutralized with aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The organic layer was washed with brine, dried ($MgSO_4$), filtered, and evaporated under reduced pressure. The residue (by ^1H NMR integration of >C*H*O protons) showed a 2:1 ratio of **8a**:**8b**; chromotagraphic purification (125 mg, 75% total yield) resulted in separation of isomers (elution with pentane–ethyl acetate, 2:1) to give first **8a**: mp 33–35 °C (lit.[4f] mp 34–36 °C); ^1H NMR δ 6.43 (td, J = 3, 1 Hz, 1 H), 5.54 (td, J = 3, 1 Hz, 1 H), 3.94 (td, J = 10.5, 4.5 Hz, 1 H), 2.64 (ddt, J = 16, 4, 1 Hz, 1 H), 2.27 (ddt, J = 16, 13, 3 Hz, 1 H), 1.96–1.59 (m, 4 H), 1.55–1.19 (m, 4 H), 1.17–0.99, (m, 1 H); ^{13}C NMR δ 165.8 (s), 134.3 (s), 128 (dd), 83.2 (d), 38.9 (d), 35.1 (t), 32.1, 30.8, 24.9, 24 (4 t); MS m/e 167 (MH^+), 149, 121. Cis isomer **8b**: mp 61–63 °C (lit.[4f] mp 63.5–67 °C); ^1H NMR δ 6.44 (td, J = 3, 1 Hz, 1 H), 5.54 (td, J = 3, 1 Hz, 1 H), 4.60–4.56 (br s, 1 H), 2.72 (ddt, J = 16.5, 5.5, 3 Hz, 1 H), 2.48 (ddt, J = 16.5, 3.5, 0.5 Hz, 1 H), 2.1–1.9 (m, 2 H), 1.79–1.64 (m, 1 H), 1.64–1.2 (m, 6 H); ^{13}C NMR δ 165.6 (s), 132.4 (s), 127.7 (dd), 78.5 (d), 33.6 (d), 33.4 (t), 30.5, 25.5, 24.2, 19.5 (4 t); MS m/e 167 (MH^+), 121.

Reduction of 2 with LiAlH(t-BuO)$_3$. To a cooled (−78 °C) solution of **2** (210 mg, 1 mmol) in dry THF (10 mL) was added $LiAlH(t\text{-}BuO)_3$ (380 mg, 1.5 mmol) in THF (5 mL), and the reaction mixture was stirred at the above temperature for 4 h. Acidification, workup, and purification as shown above gave 103 mg (62%) of **8a** and **8b** in a 9:1 ratio.

2-Methylene-3-(2′-hydroxycyclopentyl)propanoic Acid, δ-Lactone, Trans Isomer (11). Keto ester **4** was reduced with $NaBH_4$ by the procedure described for **2**. The reaction mixture, on treatment with 3 N HCl, even on heating, did not show lactonization (TLC). Workup as described before gave a polar compound (*trans*-hydroxy ester) as an oil in 90% yield: ^1H NMR δ 6.19 (d, J = 2 Hz, 1 H), 5.58 (dt, J = 2, 1 Hz, 1 H), 4.21 (q, J = 7 Hz, 2 H), 3.80 (q, J = 6 Hz, 1 H), 2.48 (ddd, J = 14, 6, 1 Hz, 1 H), 2.25 (ddd, J = 14, 8, 1 Hz, 1 H), 2.18–2.02 (br s, 1 H),2.01–1.48 (m, 6 H), 1.31 (t, J = 7 Hz, 3 H), 1.30–1.14 (m, 1 H). A signal at δ 4.01 (br s, C*H*O) indicated the presence of a small amount (<3%) of the *cis*-hydroxy ester. The obtained compound (198 mg, 1 mmol) was dissolved in benzene (25 mL) and refluxed in the presence of *p*-toluenesulfonic acid (17 mg, 0.1 mmol), using a Dean-Stark water collector. After 1.5 h the mixture was cooled, diluted with ether, worked up, and chromatographically purified as shown for **8a–b**, to give **11**: 138 mg (90%, 81% from **4**); mp 44 °C (from cold pentane) (lit.[10] mp 45–46 °C); ^1H NMR δ 6.49 (dt, J = 3, 1.5 Hz, 1 H), 5.61 (dt, J = 3, 1.5 Hz, 1 H), 4.07 (td, J = 10, 8 Hz, 1 H), 2.87 (ddt, J = 16, 4, 1 Hz, 1 H), 2.34 (ddt, J = 16, 13, 3 Hz, 1 H), 2.21–2.04 (m, 1 H), 2.03–1.52 (m, 5 H), 1.38–1.14 (m, 1 H); ^{13}C NMR δ 166.6 (s), 133.5 (s), 129.7 (dd), 84.2 (d), 40 (d), 33 (t), 29.1 (t), 26.6 (dd), 19.9 (t); MS m/e 153 (MH^+), 124, 135, 109.

2-Methylene-3-(2′-hydroxycycloheptyl)propanoic Acid, δ-Lactone, Trans (12a) and Cis (12b) Isomers. The keto ester **5** (1 mmol) was treated as shown for **2** with $NaBH_4$ (2 mmol) at −78 °C. After 3 h the cooling was discontinued, the reaction was allowed to proceed for 12 h at room temperature, and then the mixture was acidified with aqueous 3 N HCl and refluxed for 2 h. After cooling and workup the ratio of isomers was determined by ^1H NMR integration of >CHO protons (1:5 for **12a**:**12b**). Chromatographic purification (138 mg, 77% total yield) gave first an inseparable mixture of **12a** and **12b** (90 mg) and then gave **12b** (cis isomer, 48 mg): mp 38 °C (from cold pentane); ^1H NMR δ 6.37 (dd, J = 2.5, 1 Hz, 1 H), 5.53 (dt, J = 2.5, 1 Hz, 1 H), 4.69 (td, J = 6, 4 Hz, 1 H), 2.73 (ddt, J = 15.5, 2.5 Hz, 1 H), 2.49 (ddt, J = 15.5, 4.5, 1 Hz, 1 H), 2.16–2.04 (m, 1 H), 2.0–1.34 (m, 10 H); ^{13}C NMR δ 165.9 (s), 133 (s), 127.5 (dd), 82.7 (d), 37.7 (d), 36.3 (t), 32.8, 28.3, 27.6, 26.2, 21 (5 t); MS m/e 181 (MH^+) 163, 135. Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.29; H, 8.95. Found: C, 73.49; H, 9.15. The trans isomer (**12a**, within the isomeric mixture) had ^1H NMR δ 6.39 (td, J = 3, 1.5 Hz, 1 H), 5.55 (J = 3, 1.5 Hz, 1 H),4.03 (ddd, J = 10, 9, 4, 1 H), 2.64 (ddt, J = 16, 4.5, 1.5 Hz, 1 H), 2.35 (ddt, J = 16, 13, 3 Hz, 1 H), 2.21–1.99 (m, 1 H), 1.98–1.10 (m, 10 H); ^{13}C NMR δ 166.1 (s), 134.3 (s), 127.3 (dd), 86.3 (d), 41.1 (d), 36.6 (t), 33.9, 29.9, 27.1, 25.6, 21.6 (5 t).

Reduction of **5** with $LiAlH(t\text{-}BuO)_3$ as shown for **2** (12 h at −78 °C) gave, after acidification (2 h reflux) and workup, a residue which by ^1H NMR spectroscopy was a 1:3 mixture of **12a**:**12b** (62% after purification).

2-Methylene-3-(2′-hydroxycyclooctyl)propanoic Acid, δ-Lactone, Trans (13a) and Cis (13b) Isomers. To a solution of keto ester **6** (238 mg, 1 mmol) in dry MeOH (15 mL) at 0 °C was added $NaCNBH_3$ (126 mg, 2 mmol) and then, dropwise, a 3 N HCl solution (to pH 3). The reaction mixture was stirred for 9 h at room temperature (TLC), more 3 N HCl was added (to pH 1), and stirring was continued for 16 h at room temperature. Workup as described for **8** and chromatographic purification gave 126 mg (65% yield) of inseparable **13a** and **13b**. The ratio 1:2 for **13a**:**13b** was determined by ^1H NMR signals for C*H*O in **13a**: δ 4.2 (ddd, J = 9.5, 5.5, 4 Hz). In **13b**: 4.61 (td, J = 7, 3 Hz) (most of other signals overlap). ^{13}C NMR of the mixture: δ 166.3 (s), 165.7 (s), 134.5 (s), 132.8 (s), 127.3 (dd), 128.2 (dd), 85.5 (d), 83.1 (d), 36.6 (t), 36.5 (d), 36.4 (t), 34.1 (d), 31.4, 29.8, 27.2, 26.9, 26.7, 25.9, 25.1, 25.0, 22.4, 22 (12 t). MS m/e: 195 (MH^+), 177, 167, 149. Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found (**13a** + **13b**): C, 74.48; H, 9.13.

Reduction of 3a. Formation of δ-Lactones 9a and 9b. The reduction of **3a** (1 mmol) with $NaBH_4$ (see **8**), required 6 h at room temperature. The reaction mixture was acidified with aqueous 3 N HCl, refluxed for 2 h, and then worked up as shown before to give a residue which showed in the ^1H NMR spectrum a 1:4 ratio of **9a**:**9b** by integration of the >C*H*O signals. **9a**: δ 3.58 (t, J = 10 Hz), **9b**: δ 4.36 (br s) (other proton signals overlap). Chromatographic purification gave 111 mg (66% yield) of two inseparable isomers: ^{13}C NMR of **9a** δ 166 (s), 134.3 (s), 127.7 (dd), 88.3 (d), 38.2 (d), 37.4 (d), 34.1 (t), 33.2 (t), 31.1 (t), 24.6 (t), 18.1 (q); ^{13}C NMR of **9b** δ 166.2 (s), 132.8 (s), 128.7 (dd), 82.2 (d), 36.2 (d), 34.5 (d), 34.2 (t), 26.9 (t), 24.9 (t), 24.6 (t), 17.9 (q); MS of **9a** + **9b**: m/e 181 (MH^+), 163, 135.

Reduction of 3b. Formation of δ-Lactones 10a and 10b. The reduction as above (6 h, room temperature) was followed by acidification with aqueous 3 N HCl (ambient temperature, overnight). Workup as shown before gave a residue which showed a 45:55 ratio of **10a**:**10b** (60% total yield): ^1H NMR of **10a** δ 4.05 (>C*H*O, dd, J = 10.5, 5 Hz); **10b** δ 4.11 (>C*H*O, dd, J = 6.5, 4 Hz); ^{13}C NMR of **10a** + **10b** δ 165.8, 165.5, 134.2, 133.1, 128.3, 127.5, 85.6, 84.7, 35.5, 32.9, 32.9, 32.1, 31.8, 31.5, 31.3, 30.6, 29.1, 27.1, 19.3, 19, 16.9, 11.4; MS 181 (MH^+), 163. Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found (**10a** + **10b**): C, 73.15; H, 9.10.

3-Methylene-6-phenyltetrahydropyran-2-one (14). To a solution of **7** (232 mg, 1 mmol) in dry MeOH (10 mL) at 0 °C was added $NaBH_4$ (38 mg, 1 mmol), in 5 mL of MeOH, and the stirred reaction mixture was allowed to warm to room temperature. After 2.5 h (TLC monitoring) 5 mL of an aqueous solution (10%) of NaOH was added, and after stirring for an additional hour 20 mL of 3 N HCl was added. After stirring for 3 h the mixture was worked up as described before. Chromatographic purification (pentane–ethyl acetate, 2:1) gave pure **14** (128 mg 68%): mp 87 °C; ^1H NMR δ 7.37 (m, 5 H), 6.51 (dd, J = 2, 1 Hz, 1 H), 5.63 (dd, J = 2, 2 Hz, 1 H), 5.41 (dd, J = 10, 3 Hz, 1 H), 2.81–2.66 (m, 2 H), 2.31–1.89 (m, 2 H); ^{13}C NMR δ 165.4 (s), 139.4 (s), 133.6 (s), 128.6 (d, 2 CH), 128.32 (dd), 128.27 (d), 125.7 (2 d), 81.6 (d), 30.9 (t), 27.2 (t); MS m/e 189 (MH^+), 171, 160, 143. Anal. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.27; H, 6.18.

Ethyl 3-(Ethoxycarbonyl)-3-(2′-oxocyclohexyl)propanoate (15a). To a suspension of NaH (113 mg, 4.7 mmol) in THF (20 mL) at 0 °C under argon was added dropwise a solution of ethyl 2-oxocyclohexanecarboxylate (885 mg, 5.2 mmol) in THF (25 mL). After stirring at room temperature for 30 min, the reaction mixture was cooled (−78 °C) and a solution of **1** (1 g, 3.93 mmol) in THF (30 mL) was added. Stirring was continued for 1.5 h at −78 °C and for 30 min at 0 °C, a saturated aqueous solution of NH_4Cl was added, and the aqueous phase was extracted thrice with ether. The combined ether extracts were washed with brine, dried ($MgSO_4$), and evaporated under reduced pressure. Chromatographic purification of the residue (pentane–ethyl acetate, 5:1) gave 877 mg (80%) of **15a**: white crystals; mp 33 °C; ^1H NMR δ 6.24 (d, J = 2 Hz, 1 H), 5.56–5.52 (m, 1 H), 4.28–4.04 (m, 4 H), 3.06 (dd, J = 14, 1 Hz, 1 H), 2.62 (dd, J = 14, 1 Hz, 1 H), 2.53–2.38 (m, 3 H), 2.09–1.93 (m, 1 H), 1.81–1.52 (m, 3 H), 1.51–1.34 (m, 1 H), 1.30 (t, J = 7 Hz, 3 H), 1.27 (t, J = Hz, 3 H); ^{13}C NMR δ 206.7 (s), 170.9 (s), 167.1 (s), 136.6 (s), 128.2 (dd), 61.3 (t), 60.8 (t), 41.1 (t), 35.7 (s), 35.7 (t), 35.5 (t), 27.5 (t), 22.5 (t), 14.2 (q), 14 (q); MS m/e 283 (MH^+), 237. Anal. Calcd for $C_{15}H_{22}O_5$: C, 63.81; H, 7.85. Found: C, 63.51; H, 8.05.

Preparation of Ketal 15b. To a solution of diester **15a** (350 mg, 1.24 mmol) in dry benzene (25 mL) were added ethylene glycol (230 mg, 3.7 mmol) and *p*-TsOH (20 mg), and the mixture was refluxed in the presence of a Dean-Stark trap. After 4 h the mixture was cooled, diluted with ether, washed with brine, dried ($MgSO_4$), and filtered, and the filtrate was evaporated under reduced pressure. Chromatographic purification gave **15b** (372 mg, 92%) as an oil: ^1H NMR δ 6.15 (d, J = 2 Hz, 1 H), 5.56–5.49 (m, 1 H), 4.24–4.01 (m, 4 H), 4.01–3.92 (m, 4 H), 3.01 (dd, J = 14, 1 Hz, 1 H), 2.77 (dd, J = 14, 1 Hz, 1 H), 2.09–1.91 (m, 1 H), 1.75–1.34 (m, 7 H), 1.26 (q, J = 7 Hz, 6 H); ^{13}C NMR δ 173 (s), 167.6 (s), 137.8 (s), 127.1 (dd), 110.8 (s), 65 (t), 64.4 (t), 60.7 (t), 60.2 (t), 55.5 (s), 32.5 (t), 32.1 (t), 30.5 (t), 23.1 (t), 21.3 (t), 14.2 (q), 14.1 (q); MS m/e 327 (MH^+), 281. Anal. Calcd for $C_{17}H_{26}O_6$: C, 62.55; H, 8.03. Found: C, 62.29; H, 8.15.

Reduction of 15b to 16. To a solution of **15b** (500 mg, 1.53 mmol) in dry toluene (6 mL) at 0 °C under argon was added a 1 M solution of diisobutylaluminum hydride in hexane (6.7 mL, 6.7 mmol). After the mixture was stirred at 0 °C for 4 h, an aqueous saturated solution of sodium potassium tartrate (20 mL) was added, and the mixture was further stirred at room temperature until the organic phase became clear (~2 h) and then was extracted with ethyl acetate (× 3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Chromatographic purification of the residue (pentane–ethyl acetate, 1:1) gave the diol **16** (262 mg, 71%) as an oil: ^1H NMR δ 5.18–5.13 (m, 1 H), 4.96–4.91 (m, 1 H), 4.16 (dd, J = 6, 2 Hz, 2 H), 4.09–3.91 (m, 6 H), 3.31 (d, J = 12 Hz, 1 H), 2.61 (d, J = 14 Hz, 1 H), 2.26 (d, J = 14 Hz, 1 H), 1.76–1.29 (m, 9 H); ^{13}C NMR δ 145.4 (s), 114.4 (dd), 113.2 (s), 67.2 (t), 64.9 (t), 64.6 (t), 63.8 (t), 44.9 (s), 31.1 (t), 30.4 (t), 30.1 (t), 23.0 (t), 20.2 (t); MS m/e 243 (MH^+), 225, 181. Anal. Calcd for $C_{13}H_{22}O_4$: C, 64.43; H, 9.15. Found: C, 64.21; H, 9.32.

Oxidation of 16. Formation of 2-Methylene-3-[1′-(hydroxymethyl)-2′,2′-bis(methylenedioxy)cyclohexyl]propanoic Acid Lactone (17a). To a solution of the diol **16** (0.168 g, 0.7 mmol) in CH_2Cl_2 was added freshly prepared MnO_2[22] (1.096 g, 12.6 mmol) in small portions, during 33 h. The mixture was then filtered, and the solid was thoroughly washed with warm $CHCl_3$. Evaporation of the filtrate under reduced pressure gave **17a** (123 mg, 74%) as an oil: ^1H NMR δ 6.32–6.26 (m, 1 H), 5.49–5.43 (m, 1 H), 4.36 (d, J = 11 Hz, 1 H), 4.09 (dd, J = 11, 2 Hz, 1 H), 3.96–3.79 (m, 4 H), 2.83 (dt, J = 16, 2 Hz, 1 H), 2.46 (dq, J = 18, 2 Hz, 1 H), 1.68–1.32 (m, 8 H); ^{13}C NMR δ 165.6 (s), 133.1 (s), 127.5 (dd), 110.4 (dd), 72.6 (t), 64.9 (t), 64.5 (t), 40.8 (s), 33.9 (t), 31.3 (t), 30.8 (t), 23 (t), 20.1 (t); MS m/e 239 (MH^+), 213, 195. Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.29; H, 7.80.

Formation of 2-Methylene-3-[1′-(hydroxymethyl)-2′-oxocyclohexyl]propanoic Acid Lactone (17b) by Hydrolysis of 17a. A mixture containing **17a** (70 mg, 0.29 mmol), aqueous HCl (5%, 3 mL), and THF (3 mL) was stirred for 18 h at room temperature, diluted with brine, and extracted with ether. The organic layer was washed with 10% aqueous $NaHCO_3$ and brine, dried ($MgSO_4$), and evaporated. Chromatographic purification gave 40 mg (71%): mp 47–49 °C (from cold pentane); ^1H NMR δ 6.45–6.42 (m, 1 H), 5.65–5.61 (m, 1 H), 4.59 (dd, J = 11, 2 Hz, 1 H), 4.19 (dd, J = 11, 2 Hz, 1 H), 2.98 (dq, J = 16, 2, 1 H), 2.59 (dq, J = 16, 2 Hz, 1 H), 2.49–2.42 (m, 2 H), 1.97–1.87 (m, 1 H), 1.84–1.77 (m, 4 H); ^{13}C NMR δ 210.5 (s), 164.6 (s), 131.6 (s), 129.3 (dd), 72.9 (t), 48.0 (s), 38.7 (t), 35.7 (t), 34.1 (t), 27.1 (t), 20.6 (t); MS m/e 195 (MH^+), 177. Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: 67.65; H, 7.28.

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Registry No. **1**, 89295-32-9; **2**, 54312-36-6; **3a**, 128243-06-1; **3b**, 128243-07-2; **4**, 54312-35-5; **4** *trans*-hydroxy ester derivative, 128243-08-3; **5**, 128243-09-4; **6**, 128243-10-7; **7**, 128243-11-8; **8a**, 51043-42-6; **8b**, 51043-43-7; **9a**, 128243-12-9; **9b**, 128243-13-0; **10a**, 128243-14-1; **10b**, 128243-15-2; **11**, 54312-52-6; **12a**, 86312-08-5; **12b**, 128243-16-3; **13a**, 128243-17-4; **13h**, 128243-18-5; **14**,

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51043-40-4; **15a**, 128243-19-6; **15b**, 128243-20-9; **16**, 128243-21-0; **17a**, 128243-22-1; **17b**, 128243-23-2; $PhCOCH_3$, 98-86-2; cyclohexanone, 108-94-1; 2-methylcyclohexanone, 583-60-8; cyclopentanone, 120-92-3; cycloheptanone, 502-42-1; cyclooctanone, 502-49-8; ethyl 2-oxocyclohexanecarboxylate, 1655-07-8; ethyl 2-(bromomethyl)acrylate, 17435-72-2.

Supplementary Material Available: ^1H and ^{13}C NMR spectra for **12a-b** and **9a/b** mixture (4 pages). Ordering information is given on any current masthead page.

An Efficient Synthesis of Some Substituted Vinylic Chloroformates: Reaction Scope and Limitations

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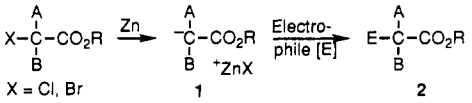
2,2-Dichlorovinyl chloroformate is isolated in 50% distilled yield when chloral is treated with phosgene and zinc dust in 2:1 methyl acetate/ether. The reaction has been extended to other α-chloro and α-bromo aldehydes and ketones in which both other α-positions are occupied by either halo and/or alkyl groups. The reaction fails with hydrogen in an α-position. Examples include the synthesis of $Cl_2C{=}C(Me)OC(=O)Cl$ in 23% yield, $MeC(Cl){=}CHOC(=O)Cl$ (56%, *E*:*Z* = 1:1.1), $Cl_2C{=}C(C_6H_5)OC(=O)Cl$ (66%), and 2-methyl-1-cyclohexenyl chloroformate (68%). Similar treatment of α-halo esters gives only the C-acylated products expected from a Reformatsky type reaction, while ketenes are the well-known products from α-halo acid chlorides. However, acyl cyanides and acyl phosphonates, with leaving groups intermediate between fluoride and alkoxide, are converted to chloroformates; e.g., $Me_2C{=}C(CN)OC(=O)Cl$ in 67% yield and $Me_2C{=}C[P(O)(OMe)_2]OC(=O)Cl$ in 83% yield. Carbonates and urethans from these chloroformates are of interest as monomers, pesticides, and chemical intermediates.

Since Reformatsky first treated α-bromo esters with zinc in 1887,[2] the ester zinc enolates **1** thus generated have become widely useful in synthetic chemistry. Part of the value of these ambident anions may be attributed to their exclusive reactivity at carbon. Whether the added electrophile is an aldehyde or a ketone (the Reformatsky reaction), an acid chloride or an anhydride, carbon dioxide, or an alkylating agent, no O-product is obtained.[2] Even reagents with strong affinities for oxygen such as TMS-Cl afford only C-silylated products.[3] The chemistry is the same whether the α-carbon substituents of **1** are H, alkyl, aryl, or halogen. For example, the products from reaction of trichloroethyl acetate with zinc and (a) aldehydes or ketones, (b) acetic anhydride, or (c) active alkylating agents all have structure **2** (A = B = Cl).[2]



Treatment of α-chloro or α-bromo ketones with zinc is widely used to reduce these reactants to the parent ketones.[4] Sometimes, however, the intermediate zinc enolates have been intercepted by other electrophiles, including active alkylating agents, aldehydes and ketones, acid halides and sulfenyl chlorides, and Michael acceptors.[4] Again in all of these processes, the electrophile is attached to the carbon originally bearing the halogen. The only apparent exception is the reaction with TMS-Cl, which yields O-silylated enol ethers.[5] Even this may not be real, since C-silylated ketones readily undergo Lewis acid catalyzed isomerization to their *O*-silyl tautomers.[6]

While a long bibliography on the zinc plus α-halo ester reaction can be compiled and the literature on the chemistry of α-halo ketones with zinc is substantial, references to the treatment of α-halo aldehydes with zinc are virtually nonexistent.[7] This would be anticipated, given the expected tar-forming side reactions involving the highly reactive aldehyde carbonyl as a nucleophile acceptor.

Recently we reported[8] a simple synthesis of the previously unknown 2,2-dihalovinyl chloroformates **4** and **5** by a zinc-induced Boord elimination from the readily available tetrahaloethyl precursors **3**.[9] The process is significant because of the expected pesticidal activity of derived 2,2-dihalovinyl carbonates and carbamates.[10,11] Also, Chevalier at SNPE has found that 2,2-dichlorovinyl carbonates are too hindered to self-polymerize but do give alternating 1:1 copolymers with vinyl acetate with an unusual head to head structure.[12]

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