was purified by radial chromatography (20% CH_3OH/CH_2Cl_2 as eluent), and the product was redissolved in 250 mL of water. Lyophilization for 48 h afforded 103 mg (91% of a nonhydrated structure) of product as an off-white powder: low-resolution FAB mass spectrum (using dithiothreitol in methanol), m/z 460.8 (100, $MH^+ + H_2 + CH_3OH$ + DTT), 306.8 (93, $MH^+ + H_2 + CH_3OH$), 272.8 (9, MH^+). Recrystallization from water afforded needles: mp 182-184 °C; low-resolution FD mass spectrum, m/z 272 (M^+), 254 ($M^+ - H_2O$); UV λ_{max} nm ($\epsilon \times 10^3$) (H_2O) 265 (12.4), 204 (12.1); (pH 1) 264 (12.3), 208 (11.0); (pH 7) 263 (11.5), 209 (8.6); (pH 11) 264 (10.5), 230 (9.2), 214 (7.4). Analysis of this material revealed that it exists as a 1:10 mixture of structures in $(CD_3)_2SO$ solution, but as a 1:2 mixture of structures in D_2O solution.

A (9% component in $(CD_3)_2SO$): ^1H NMR ($(CD_3)_2SO$) δ 9.85 (s, 1 H, CHO).

D (91% component in $(CD_3)_2SO$): ^1H NMR ($(CD_3)_2SO$) δ 11.38 (s, exchanges with D_2O, 1 H, NH), 7.22 (d, J = 6.3 Hz, exchanges with D_2O, 1 H, hemiacetal-OH), 6.28 (d, J = 4.5 Hz, 1 H, H1'), 5.91 (s, 1 H, H5), 5.80 (d, J = 6.3 Hz, collapses to a singlet upon addition of D_2O, 1 H, hemiacetal-CH), 5.29 (d, J = 6.6 Hz, exchanges with D_2O, 1 H, 2'-OH), 5.06 (d, J = 4.2 Hz, exchanges with D_2O, 1 H, 3'-OH), 4.31 (m, 1 H, H2'), 4.21 (bs, 1 H, H4'), 3.97 (m, 1 H, H3'), 3.85 (s, 2 H, 5'-CH_2); ^{13}C NMR ($(CD_3)_2SO$) δ 162.6 (C4), 153.7 and 151.6 (C2/C6), 100.9 (C5), 94.5 (hemiacetal-CH), 93.1 (C1'), 86.1 (C4'), 77.7 (C2'), 73.5 (C3'), 69.3 (C5').

Long-range correlations observed in a 7.5-Hz-optimized ^1H-^{13}C HETCOR experiment were hemiacetal-CH/5'-CH_2, $C1'/H4'$, $C2'/H4'$, $C3'/H2'$, $C3'/5'$-CH_2 for D.

B (67% component in D_2O): ^1H NMR (D_2O) δ 6.12 (s, 1 H, H5), 5.97 (s, 1 H, $CH(OD)_2$), 5.94 (d, J = 2.7 Hz, 1 H, H1'), 4.75 (m, 1 H, H2'), 4.45 (m, 1 H, H3'), 3.95 (m, 1 H, H4'), 3.87-3.72 (m, 2 H, 5'-CH_2); ^{13}C NMR (D_2O) δ 168.4 (C4), 158.7 and 154.2 (C2/C6), 103.0 (C5), 95.0 (C1'), 88.6 ($CH(OD)_2$), 86.1 (C4'), 74.6 (C2'), 71.9 (C3'), 64.2 (C5').

D (33% component in D_2O): ^1H NMR (D_2O) δ 6.41 (d, J = 4.5 Hz, 1 H, H1'), 6.23 (s, 1 H, H5), 6.10 (s, 1 H, hemiacetal-CH), 4.62 (m, 1 H, H2'), 4.48 (m, 1 H, H4'), 4.30 (m, 1 H, H3'), 4.14-3.99 (m, 2 H, 5'-CH_2); ^{13}C NMR (D_2O) δ 167.9 (C4), 157.1 and 155.1 (C2/C6), 103.8 (C5), 97.2 (hemiacetal-CH), 96.2 (C1'), 89.1 (C4'), 80.4 (C2'), 76.5 (C3'), 57.0 (C5').

Long-range correlations observed in a 10-Hz-optimized ^1H-^{13}C HETCOR experiment were $C2'/H1'$, $C4'/5'$-CH_2, and $C3'/H4'$ for B, and hemiacetal-CH/5'-CH_2 and $C3'/5'$-CH_2 for D.

Acknowledgment. This work was supported by a grant from the Office of Research Development and Administration at Southern Illinois University.

Supplementary Material Available: ^1H and ^{13}C NMR spectral data for 1 and 2 in $CDCl_3$ and for 4 in $CDCl_3$; long-range HETCOR NMR spectral data for 1 and 2 in $CDCl_3$; and COSY and short- and long-range HETCOR NMR spectral plots of 1, 2, 3, and 4 in $(CD_3)_2SO$ solution and for uridine-6-carboxaldehyde in both D_2O and $(CD_3)_2SO$ solution (20 pages). Ordering information is given on any current masthead page.

Ene Reactions of Dialkyl Dioxosuccinate Esters

Peter Beak,* Zhiguo Song, and James E. Resek

Department of Chemistry, University of Illinois, Urbana, Illinois 61801

Received August 6, 1991

The ene reactions of dimethyl dioxosuccinate (1) and of diethyl dioxosuccinate (2) with olefins give the expected addition products. The reactions of 1 with vinyl ethers or an eneamine provide the cyclopentenones 15 and 16 in a sequence which is consistent with an ene reaction followed by a cyclization. The tin tetrachloride catalyzed conversion of 6 to 17 provides an example of a formal type II ene reaction to give a cyclopentyl ring. However, the stereochemistry of 17 suggests the reaction involves a stepwise ionic process.

The ene reaction, once considered a novel process, has been developed into a reaction of considerable synthetic value with catalyzed and intramolecular carbon-carbon bond formations receiving serious attention in recent years.[1] Our interest in the mechanism of the ene reaction led us to study dimethyl dioxosuccinate, a previously uninvestigated eneophile.[2] In this paper, we report that dialkyl dioxosuccinate esters undergo the ene reaction with a variety of olefins, and that five-membered carbocycles can be obtained from the initial products in certain cases.[3,4]

Preparation of Dialkyl Dioxosuccinate Esters. The syntheses of dimethyl and diethyl dioxosuccinate (1 and 2, respectively) were achieved by the acid-catalyzed dehydration and esterification of readily available dihydroxy tartaric acid disodium salt with the appropriate alcohol following the procedures of Fox and of Boger.[5] Although these orange-yellow diketo diesters form viscous oils or

(1) (a) Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 556. (b) Oppolzer, W.; Snieckus, V. *Ibid.* **1978**, *17*, 476. (c) Snider, B. B. *Acc. Chem. Res.* **1980**, *13*, 426. (d) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 876. (e) Whitsell, J. K. *Ibid.* **1985**, *18*, 280. (f) Dubac, J.; Laporterie, A. *Chem. Rev.* **1987**, *87*, 319. (g) Stephenson, L. M.; Grdina, M. J.; Orfanopoulos, M. *Acc. Chem. Res.* **1980**, *13*, 419. (h) Taber, D. F. *Intramolecular Diels-Alder and Ene Reactions*; Springer-Verlage: Berlin, 1984. (i) Mikami, K.; Terada, M.; Shimizo, M.; Nakai, T. *J. Synth. Org. chem. Jpn.* **1990**, *48*, 292.

(2) Song, Z.; Beak, P. *J. Am. Chem. Soc.* **1990**, *112*, 8126.

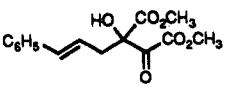
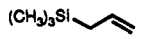
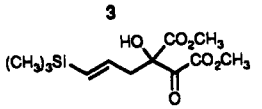
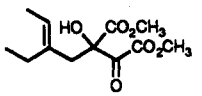
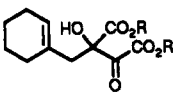
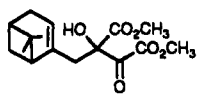
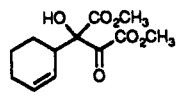
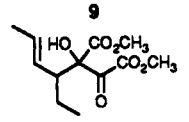
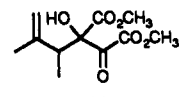
(3) For representative cases of type II ene reactions see: (a) Snider, B. B.; Karas, M.; Price, R. T.; Rodini, D. J. *J. Org. Chem.* **1982**, *47*, 4538. (b) Snider, B. B.; Deutsch, E. A. *Ibid.* **1983**, *48*, 1822. (c) Snider, B. B.; Cartya-Marin, C. P. *J. Org. Chem.* **1984**, *49*, 153. (d) Andersen, N. H.; Hadley, S. W.; Kelly, J. D.; Bacon, E. R. *Ibid.* **1985**, *50*, 4144. (e) Aubert, C.; Bergne, J. D. *Tetrahedron Lett.* **1986**, *29*, 1011. (f) Johnston, M. I.; Kwass, J. A.; Beal, R. B.; Snider, B. B. *Ibid.* **1987**, *52*, 5419. (g) Maruoka, K.; Ooi, J.; Yamamoto, A. *J. Am. Chem. Soc.* **1990**, *112*, 9011 and references cited therein.

(4) Efforts to make cyclopentenes by type II ene reactions usually have led to products in which the ring is formed but nucleophilic substitutions or rearrangements occur. This can be taken to suggest the reactions are not ene processes.[3a,c-e] Precedent for the conversion of 6 to 17 and 18 is provided by the work of Andersen et al.[3d]

(5) (a) Fox, H. H. *J. Org. Chem.* **1947**, *22*, 535. (b) Boger, D. L.; Panek, J. S.; Yasuda, M. *Org. Synth.* **1987**, *66*, 142.

0022-3263/92/1957-0944$03.00/0

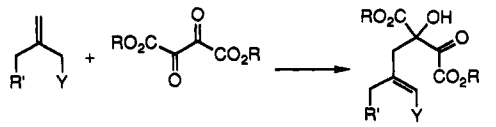
Table I. Thermal Ene Reactions of Dimethyl Dioxosuccinate (1) and Diethyl Dioxosuccinate (2)

olefin	eneophile	product	yield (%)	isomer(s)
	1	 3	84	*E*
	1	 4	95	*E*/*Z* = 50/50
	1	 5	89	*E*/*Z* = 60/40
	1,2	 6, R = CH_3; 7, R = C_2H_5	97, 89	
	1	 8	84	two diastereomers = 50/50
	1[a]	 9	56	two diastereomers = 50/50
	1[a]	 10	90	four isomers
	1[a]	 11	56	two diastereomers = 82/18

[a] Reaction at 150 °C.

solid hydrates on standing or on exposure to the atmosphere, they can be obtained and used as pure compounds with some care.

Thermal Ene Reactions. The thermal ene reactions between 1 or 2 and a number of olefins were carried out in toluene at 120 °C in sealed tubes to give the products 3–11 as summarized in Table I. The structures of the products were assigned on the basis of ^1H and ^{13}C NMR, IR, MS, and elemental analytical data. The *E*/*Z* ratios of the olefins were based on analysis by ^1H NMR coupling and capillary GLPC.



1, R = CH_3
2, R = C_2H_5

The data in Table I are consistent with previous experience for related reactions.[1] The *E* selectivity observed for allylbenzene is similar to that reported by Salomon for the ene reactions of allylbenzene with 2-oxomalonate.[6] The 1,1-disubstituted olefins are more reactive than the 1,2-disubstituted olefins as judged by the higher temperatures required for the latter reactions. The major isomer from the reaction of 2-ethyl-1-butene is assigned as *E* because the major isomer shows a NOE of 2.7% between the vinyl hydrogen and the methylene of the ethyl group as opposed to a 7.8% NOE for these groups in the minor isomer.[7,8] The stereochemistry of these reactions and the results in Table I are consistent with a concerted reaction mechanism as suggested by the inter- and intramolecular isotope effects previously reported for an ene reaction of 1.[1,2,7]

The thermal ene reactions of 1 with the vinyl ethers 12 and 13 and the enamine 14 were found to provide the cyclopentenones 15 and 16 in modest yields. The ratio of diastereomers of 16 is ca. 50:50. When 1 and 14 were mixed at room temperature, a rapid reaction occurred to give a mixture which was converted to 16 by heating at 100 °C for 24 h. Attempted dehydration of 15 and 16 to give the corresponding cyclopentadieneones as transient, trappable species was not successful.[9] The formations of 15 and 16 may be considered to proceed via a formal ene reaction to give an intermediate which cyclizes under the acidic reaction conditions.

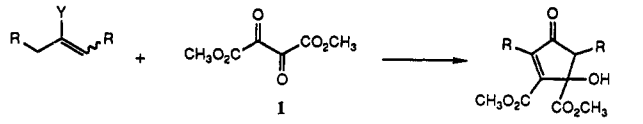
Cyclopentene Ring Formation by a Type II Intramolecular Ene Reaction. The products of the ene re-

(6) Salomon, M. F.; Pardo, S. N.; Salomon, R. G. *J. Org. Chem.* 1984, *49*, 2446.

(7) For a similar case see: Antechis, M.; DeBruyn, A.; DePooter, H.; Verbegge, G. *Bull. Soc. Chim. Belg.* 1968, *77*, 371.

(8) Of the many attempts we made to catalyze this reaction with $SnCl_4$, $TiCl_4$, and $ZnBr_2$, only the latter was successful and provided the expected product from 2-ethyl-1-butene and 1 in 33% yield. In other cases intractable mixtures were produced.

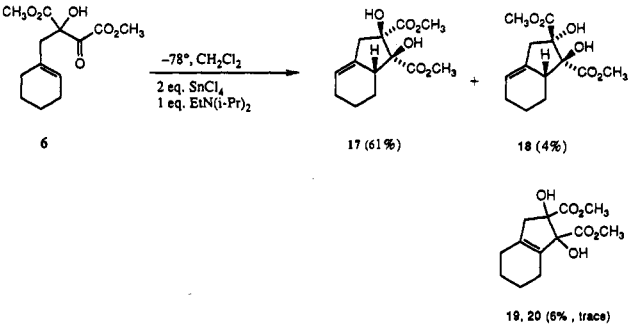
(9) For a review of cyclopentadienones see: Schore, N. E. *Chem. Rev.* 1988, *88*, 1081.



12, R = H, Y = OCH_3
13, R = CH_3, Y = $OSi(CH_3)_3$
14, R = CH_3, Y = $N(CH_2)_4$

15, R = H (41%)
16, R = CH_3(46%)

actions of 1 have an olefin and a keto carbonyl group that are appropriately positioned for cyclopentane ring formation by an intramolecular type II ene reaction. The possibilities of activation of the keto carbonyl by an adjacent ester and by Lewis acid catalysis, along with the potential for development of a general cyclopentene synthesis by a sequential two-carbon bridging of olefins, prompted investigation of the cyclization of **6**. In the most successful reaction, treatment of **6** with $SnCl_4/EtN(i\text{-}Pr)_2$ (2/1) gives **17** in 61% yield, accompanied by 4% of the diastereoisomer, **18**. The two cis/trans isomers of **19** and **20** are also produced; **19** in 6% yield and **20** in trace amounts. The stereochemistry of these isomers was not resolved. The structures initially assigned to **17** and **18** by spectroscopic and elemental analytical data were subsequently established by X-ray crystallography. The structures of **19** and **20** are based on spectral and elemental analytical data. With 1 equiv of tin tetrachloride **17** is formed in 19% yield, **18** in 21% yield, **19** in 22% yield, and **20** in 2% yield from **6**. Since **19** is stable to treatment with 3 equiv of tin tetrachloride in CH_2Cl_2 at −78 °C for 2 h, it appears that the cyclopentyl products are not interconverted under the reaction conditions. Efforts to increase the yield and selectivity of the reaction under a variety of conditions or by the use of $Ti(O\text{-}i\text{-}Pr)_4$, $TiCl_4$, $MgBr_2$, $ZnCl_2$, and $FeCl_3$ were not successful. Attempted induction of a radical cyclization of **6** with use of SmI_2, following the precedent of Molander, did not provide **17**–**20**.[10] Efforts to extend the cyclization to other systems, e.g. **4**, were not successful.

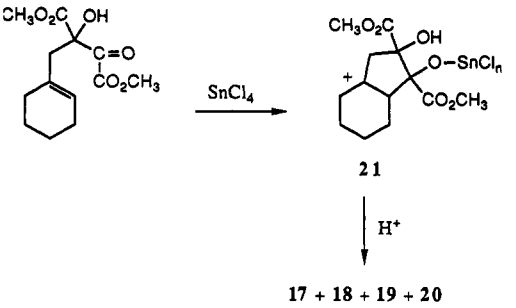


6 17 (61%) 18 (4%)

19, 20 (6%, trace)

The stereochemistry of **17** suggests that the mechanism of the reaction is not that of a concerted ene reaction in which the enophile participates in hydrogen transfer. If that were the case, in order for the oxygen of the eneophile to reach to the hydrogen being removed in the transition state a trans geometry would be expected between the alcohol and the hydrogen at the adjacent ring juncture.[11] Since the alcohol and hydrogen are cis in **17**, a mechanism in which initial complexation of **6** by $SnCl_4$ gives **21** which can lead to the observed products by loss of a proton to an external base seems most reasonable and consistent with precedent.[3d]

The present work establishes that dialkyl dioxosuccinates can be effective as eneophiles and the formation



21

17 + 18 + 19 + 20

of cyclopentene rings from the ene adducts is possible in certain cases.

Experimental Section

Thermal Ene Reactions of 2,3-Dioxobutanedioate Esters with Olefins. General Procedure. The olefins were distilled before use. A Carius tube was charged with equimolar amounts of diketo diester and the olefin dissolved in 1.0 mL of toluene. The tube was flame-sealed at −78 °C under vacuum, and the reaction was heated to 120 °C in a oil bath usually until the orange color of the diketo diester faded.

Methyl (E)-3-Carbomethoxy-3-hydroxy-2-oxo-6-phenyl-5-hexenoate (3). Allylbenzene (65 mg, 0.55 mmol) was allowed to react with **1** (96 mg, 0.55 mmol) for 45 h. The product was distilled (160 °C (1 mmHg)) to give 136 mg (84%) of **3** as a colorless oil: ^1H NMR (300 MHz) δ 2.90 (m, 2 H, CH_2), 3.80 (s, 3 H, OMe), 3.87 (s, 3 H, OMe), 6.10 (m, 1 H), ArC=C*H*), 6.50 (d, J = 15.7 Hz, ArC*H*=C), 7.1–7.6 (m, 5 H, ArH); ^{13}C NMR (75 MHz) δ 37.9, 53.2, 80.5, 121.2, 126.2, 126.3, 128.5, 135.0, 136.7, 161.6, 170.0, 187.8. Anal. Calcd for $C_{15}H_{16}O_6$: C, 61.64; H, 5.52. Found: C, 61.80; H, 5.68.

Methyl 3-Carbomethoxy-3-hydroxy-2-oxo-6-(trimethylsilyl)-5-hexenoate (4). Allyltrimethylsilane (35 mg, 0.31 mmol) was allowed to react with **1** (52 mg, 0.30 mmol) for 72 h. The product was distilled (100 °C (1 mmHg)) to give 85 mg (97%) of **4**, colorless oil, as a mixture of diastereomers: ^1H NMR (300 MHz) δ 6.25–6.10 (m, 0.6 H, (*E*)-SiCH=C*H*), 5.86 (t, J = 5.9 Hz, 0.4 H, (*Z*)-SiCH=C*H*), 5.82 (s, 0.4 H, (*Z*)-SiCH), 5.73 (d, J = 14 Hz, 0.6 H, (*E*)-SiCH), 3.89 (s, 1 H, OH, exchange with D_2O), 3.88 (s, 3 H, OMe), 3.83 (s, 1.6 H, OMe), 3.80 (s, 1.4 H, OMe), 2.7–2.95 (m, 2 H, CH=CHC*H*$_2$), 0.12 (s, 6 H, (*E*)-$SiMe_3$), 0.03 (s, 4 H, (*Z*)-$SiMe_3$); ^{13}C NMR (75 MHz) major *E* isomer δ 0.0, 37.2, 79.8, 135.1, 138.4, 161.6, 170.1, 187.5; minor *Z* isomer δ −1.5, 41.4, 80.5, 137.3, 137.5, 161.6, 169.9, 187.9. Only three signals for the four methoxy groups were observed, 53.2, 53.6, 53.8. Anal. Calcd for $C_{12}H_{20}O_6Si$: C, 49.98; H, 6.99. Found C, 49.98, H, 7.03.

Methyl 3-Carbomethoxy-5-ethyl-3-hydroxy-2-oxo-5-heptenoate (5). 2-Ethyl-2-butene (79 mg, 0.94 mmol) was allowed to react with **1** (165 mg, 0.94 mmol) for 72 H. The product was distilled (100 °C (1 mmHg)) to give 217 mg (89%) of **5**, a colorless oil, as a mixture of diastereomers: ^1H NMR (300 MHz) δ 5.42 (q, J = 6.7 Hz, 0.4 H, =CH, *Z* isomer), 5.23 (q, J = 6.7 Hz, 0.6 H, =CH, *E* isomer), 3.77 (s, 3 H, OCH_3), 3.84 (s, 3 H, OCH_3), 3.6–4.0 (br s, 1 H, OH), 2.97, 2.67 (AB, J = 14.3 Hz, 0.8 H, HOCC*H*$_2$, *Z* isomer), 2.70, 2.66 (AB, J = 14.3 Hz, 1.2 H, HOCC*H*$_2$, *E* isomer), 1.9–2.2 (m, 2 H, C*H*$_2$$CH_3$), 1.54 (d, J = 6.7 Hz, 3 H, CH_3C=C), 0.91 (q, J = 7.8 Hz, 3 H, CH_2C*H*$_3$). Irradiation of the signal at 1.9–2.2 ppm resulted in an NOE of 7.8% for the signal at 5.42 ppm and 2.7% for the signal at 5.23 ppm: ^{13}C NMR (75 MHz) *E* isomer δ 188.5, 170.1, 162.0, 135.4, 124.5, 81.3, 53.4, 53.0, 39.8, 23.3, 13.2, 12.4; *Z* isomer δ 188.1, 170.3, 161.9, 134.6, 123.5, 80.6, 53.4, 53.0, 33.1, 30.4, 13.6, 12.7. Anal. Calcd for $C_{12}H_{18}O_6$: C, 55.81; H, 7.02. Found: C, 55.69; H, 7.06.

Ethyl 3-Carbethoxy-4-(1-cyclohexenyl)-3-hydroxy-2-oxo-2-butanoate (7). Methylenecyclohexane (425 mg, 4.42 mmol) was allowed to react with **2** (709 mg, 3.51 mmol) for 24 h. The product was distilled (100–110 °C (1 mmHg)) to give 929.8 mg (89%) of **7** as a colorless oil: ^1H NMR (300 MHz) δ 1.24 (t, 3 H, CH_2C*H*$_3$), 1.31 (t, 3 H, CH_2C*H*$_3$), 1.49 (m, 4 H, CH_2), 1.93 (m, 4 H, CH_2), 2.70, 2.51 (AB, J = 5.7 Hz, 2 H); 3.89 (s, 1 H, OH), 4.23 (q, 2 H, C*H*$_2$$CH_3$), 4.29 (q, 2 H, C*H*$_2$$CH_3$), 5.49 (s, 1 H, =CH); ^{13}C NMR (75 MHz) δ 13.6, 13.7, 21.7, 22.6, 25.2, 29.4, 41.9, 62.5, 62.7, 80.9, 127.0, 131.4, 161.3, 169.4, 188.6. Anal. Calcd for

(10) Molander, G. A.; Kenny, G. *J. Am. Chem. Soc.* **1989**, *111*, 8236.
(11) The requisite trans disposition of these groups is observed by Snider et al. for a Lewis acid catalyzed type II intramolecular ene reaction which provides a six-membered ring.[1d]

$C_{15}H_{22}O_6$: C, 60.39; H, 7.43. Found: C, 60.14; H, 7.35.

Methyl 3-Carbomethoxy-3-(α-pinyl)-3-hydroxy-2-oxopropanoate (8). (1S)-(−)-β-pinene (143 mg, 1.04 mmol) was allowed to react with 1 (187 mg, 1.07 mmol) for 24 h. The crude product was dissolved in ether, washed with brine, and the solution was dried ($MgSO_4$). The product was distilled (130 °C (1 mmHg)) to give 282 mg (87%) of an oil. Purification of 90 mg of this product by reversed-phase HPLC (95% methanol–water) gave 60 mg (58%) of 8 as mixture of diatereomers: ^{1}H NMR (300 MHz) δ 0.77, 0.78 (s, 3 H, Me), 1.04, 1.08 (d, J = 8.7 Hz; d, J = 8.7 Hz; total 1 H), 1.22 (s, 3 H, CH_3), 1.94–2.15 (m, 2 H, CH_2), 2.18 (s, 2 H, CH_2), 2.71 (s, 1.2 H, CH_2C-O, major isomer), 2.79, 2.55 (AB, 0.8 H, J = 14.2 Hz, minor isomer), 3.80 (s, 3 H, OMe), 3.85 (s, 3 H, OMe), 3.8–4.0 (br s, 1 H, OH), 5.3–5.4 (m, 1 H, =CH); ^{13}C NMR (75 MHz) There are two sets of signals, and one set is ca. 1.5 times stronger than that other, δ 21.1, 20.9, 26.19, 26.1, 31.5, 31.5, 31.6, 37.9, 37.7, 40.2, 40.2, 41.4, 41.2, 46.8, 46.6, 53.0, 53.4, 53.5, 80.5, 80.4, 123.4, 122.7, 140.9, 141.5, 161.7, 162.0, 170.0, 188.8, 188.3. Anal. Calcd for $C_{16}H_{22}O_6$: C, 61.92; H, 7.14. Found: C, 61.65; H, 7.00.

Methyl 3-Carbomethoxy-3-(2-cyclohexenyl)-3-hydroxy-2-oxopropanoate (9). Cyclohexene (165 mg, 0.94 mmol) was allowed to react with 1 (81 mg, 0.98 mmol) at 150 °C for 72 h. The crude product was distilled (120 °C (1 mmHg)) to give 132 mg (54%) of 9, a colorless oil, as a mixture of diastereomers: ^{1}H NMR (300 MHz) δ 5.8–5.9 (m, 1 H, =CH), 5.2–5.4 (m, 1 H, =CH), 3.88 (s, 1 H, OH), 3.83 (s, 6 H, $2OCH_3$), 3.1–3.2 (m, 1 H, C=CCH), 1.95 (m, 2 H, allyl CH_2), 1.77 (m, 2 H, CH_2), 1.4–1.6 (m, 2 H, CH_2); ^{13}C NMR (75 MHz) There are two sets of signals with about equal intensities, δ 190.1, 190.0, 170.0, 169.7, 162.9, 162.8; 132.1, 132.1; 124.3, 123.7; 83.6, 83.2; 53.9, 53.9, 52.9, 52.8; 40.5, 24.6, 24.4; 22.8, 22.7; 21.3, 21.2. Anal. Calcd for $C_{12}H_{16}O_6$: C, 56.25; H, 6.29. Found: C, 55.94; H, 6.30.

Methyl 3-Carbomethoxy-4-ethyl-3-hydroxy-2-oxo-5-heptenoate (10). (E)-3-hexene (118 mg, 1.40 mol) was allowed to react with 1 (244 mg, 1.40 mmol) at 150 °C for 72 h. The crude product was distilled (120 °C (1 mmHg)) to give 324 mg (90%) of 10, a colorless oil, as a mixture of diastereomers: ^{1}H NMR (300 MHz) 0.77 (m, 3 H, CH_3), 1.2–1.4 (m, 2 H, CH_2), 1.58–1.61 (m, 3 H, allyl CH_3), 2.70–2.85 (m, 1 H, C=CCH), 3.7–3.8 (m, 6 H, $2OCH_3$), 3.92 (s, 1 H, OH), 5.0–5.2 (m, 1 H, =CH), 5.4–5.7 (m, 1 H, =CH); ^{13}C NMR (75 MNz) A total of 39 signals were observed out of 48 expected. The 8 vinyl carbon signals were well resolved, δ 11.2, 11.6, 11.9, 13.0, 13.4, 17.9, 21.5, 21.8, 21.9, 22.2, 42.6, 42.9, 49.0, 49.5, 52.7, 53.6, 53.7, 53.7, 53.8, 84.3, 84.5, 84.9, 126.3, 126.7, 127.0, 127.4, 128.1, 128.7, 129.7, 130.9, 162.6, 162.7, 163.3, 169.8, 190.2, 190.5, 191.0, 191.1. Anal. Calcd for $C_{12}H_{18}O_6$: C, 55.81; H, 7.02. Found: C, 55.65; H, 7.06.

Methyl 3-Carbomethoxy-5-ethyl-3-hydroxy-4-methyl-2-oxo-5-hexenoate (11). 3-Methyl-2-butene (62 mg, 0.88 mmol) was allowed to react with 1 (156 mg, 0.89 mmol) at 120 °C for 72 h. The crude product was distilled (100 °C (1 mmHg)) to give 135 mg (56%) of 11, a colorless oil, as a mixture of diastereomers: ^{1}H NMR (300 MHz) δ 4.80–4.90 (m, 2 H, $=CH_2$), 4.00 (s, 1 H, OH), 3.83 (s, 6 H, 2 OCH_3), 3.23 (m, 1 H, CH), 1.69 (s, 3 H, $C=CH_3$), 1.06 (d, J = 7.1 Hz, 3 H, Me); ^{13}C NMR (75 MHz) A total of 19 signals out of the 22 expected were observed, δ 190.7, 169.7, 170.0, 162.7, 144.7, 145.0, 114.8, 114.1, 84.7, 84.7, 54.0, 53.8, 52.8, 44.2, 44.8, 21.5, 20.0, 13.9, 13.2. Anal. Calcd for $C_{11}H_{16}O_6$: C, 54.09; H, 6.60. Found: C, 53.60; H, 6.66.

3,4-Bis(carboxymethyl)-4-hydroxy-2-cyclopentenone (15). In a sealed Carius tube, 2-methoxypropene (117 mg, 1.6 mmol) was allowed to react with 1 (286 mg, 1.6 mmol) in 1.0 mL of toluene at 100 °C for 24 h. The crude product was dissolved in methylene chloride and washed with 1 N HCl. The aqueous layer was then extracted with methylene chloride, and the combined organic solution was dried ($MgSO_4$). Distillation (140 °C (1 mmHg)) of the product followed by recrystallization ($CHCl_3$) gave 140 mg (41%) of 15 as colorless crystals: mp 96.5–99.0 °C; ^{1}H NMR (200 MHz) δ 6.81 (s, 1 H, =CH), 3.88 (s, 3 H, OMe), 3.9–4.1 (br s, 1 H, OH), 2.93, 2.75 (AB, J = 18.8 Hz, 2 H); ^{13}C NMR (50 MHz) 203.2, 172.8, 163.1, 159.9, 138.5, 77.6, 53.8, 52.9, 48.7. Anal. Calcd for $C_9H_{10}H_6$: C, 50.47; H, 4.71. Found: C, 50.43; H. 4.47.

3,4-Bis(carboxymethyl)-4-hydroxy-2,5-dimethyl-2-cyclopentenone (16). Method A. In a sealed Carius tube, 3-(trimethylsiloxy)pentene (13, 204 mg, 1.3 mmol) was allowed to react with 1 (244 mg, 1.4 mmol) at 140 °C for 48 h. The crude product was distilled (140 °C (1 mmHg)), purified by MPLC (30% EtOAc–hexane), and the redistilled to give 145 mg (46%) of 16 as a colorless oil.

Method B. To a solution of 3-pyrolidino-2-pentene (14, 117 mg, 0.83 mmol) in 10 mL of anhydrous THF was added 1 (162 mg, 0.92 mmol). The mixture was stirred at room temperature for 2 h followed by extractive workup with 10% HCl and ether. The product was purified by MPLC (30% EtOAc/hexane) to give 56 mg (27%) of 16, a colorless oil, as a mixture of diastereomers.

16: ^{1}H NMR (300 MHz) δ 1.04 (d, J = 7.3, 3 H, CH_3), 1.08 (d, J = 7.5 Hz, 3 H, CH_3), 2.03 (s, 6 H, allyl CH_3), 2.6–2.7 (m, 2 H, CH), 3.68 (s, 3 H, OCH_3), 3.73 (s, 3 H, OCH_3), 3.78, 3.79 (s, s, 6 H, $2OCH_3$), 3.82 (s, 1 H, OH), 4.11 (s, 1 H, OH); ^{13}C NMR (75 MHz) δ 8.5, 9.6, 9.9, 10.0, 49.3, 52.3, 52.7, 53.1, 53.4, 78.2, 81.6, 147.9, 148.5, 150.0, 150.7, 164.2, 172.3, 174.2, 204.9, 208.0. Anal. Calcd for $C_{11}H_{14}O_6$: C, 54.72; H, 5.81. Found: C, 54.54; H, 5.83.

Cyclization of 6 Promoted by Tin Tetrachloride. To a solution of 6 (70.0 mg, 0.26 mmol) and ethyl diisopropylamine (33 mg, 45 μL, 0.26 mmol) in 10 mL of CH_2Cl_2 at −78 °C was added $SnCl_4$ (1.0 M, 0.26 mL, 0.26 mmol). The solution was stirred at −78 °C for 1 h, and additional $SnCl_4$ (1.0 M, 0.30 mL, 0.30 mmol) was added. The cold solution was poured into 0.1 M HCl; this was extracted with ether (4 × 10 mL). The residue after solvent removal was separated by MPLC (40% EtOAc–hexane) and HPLC (30% EtOAc–hexane) to give 4 products: 3 mg (4%) of 18, 42 mg (61%) of 17, 4 mg (5.6%) of 19, <1 mg of 20.

17: colorless crystals, 42 mg (61%), mp (methanol) 86–88 °C. A sample crystallized from methanol was analyzed by X-ray crystallography: ^{1}H NMR (300 MHz) δ 0.9–1.05 (m, 1 H), 1.4–1.6 (m, 1 H), 1.75–2.2 (m, 4 H), 2.70 (d, J = 17.6 Hz, 1 H), 2.85–2.95 (m, 2 H), 3.0–3.15 (m, 2 H), 3.69 (s, 3 H, OMe), 3.73 (s, 3 H, OMe), 3.6–3.8 (br, 2 H, 2OH); ^{13}C NMR (75 MHz) δ 21.7, 22.8, 24.8, 39.2, 47.0, 52.5, 82.3, 86.5, 120.2, 135.1, 172.5, 173.0. Anal. Calcd for $C_{13}H_{18}O_6$: C, 57.77; H, 6.71. Found: C, 57.58; H, 6.39.

18: colorless crystals, 3 mg (4%), mp (methanol) 98–99 °C. A sample obtained by crystallization from methanol was analyzed by X-ray crystallography: ^{1}H NMR (300 MHz) δ 0.94–1.05 (m, 1 H), 1.8–1.9 (m, 2 H), 2.0–2.2 (m, 2 H), 2.6–2.7 (m, 2 H), 2.9–3.1 (m, 2 H), 3.80 (s, 3 H, OMe), 3.85 (s, 3 H, OMe), 3.84–3.86 (s, 1 H, 20 H), 5.43 (m, 1 H); ^{13}C NMR (75 MHz) δ 21.7, 23.5, 24.8, 39.6, 47.6, 52.8, 53.3, 84.5, 89.9, 119.4, 136.1, 174.8. Anal. Calcd for $C_{13}H_{18}O_6$: C, 57.77; H, 6.71. Found: C, 57.51; H, 6.52.

19: colorless crystals, 4 mg (6%), mp (methanol) 95–97 °C; ^{1}H NMR (500 MHz) δ 4.05 (s, 1 H, OH), 3.80 (s, 1 H, OH), 3.73 (s, 3 H, OMe), 3.73 (s, 3 H, OMe), 3.06 (d, J = 16.3 Hz, 1 H), 2.49 (d, J = 16.3 Hz), 2.0–2.15 (m, 3 H), 1.50–1.75 (m, 5 H); ^{13}C NMR (125 MHz) δ 173.8, 172.7, 140.1, 131.5, 88.7, 82.8, 53.2, 52.4, 44.1, 25.8, 22.3, 22.2, 22.1, 22.1. Anal. Calcd for $C_{13}H_{18}O_6$: C, 57.77; H, 6.71. Found: C, 57.67; H, 6.55.

20: colorless crystals, <1 mg; ^{1}H NMR (500 MHz) δ 3.79 (s, 3 H, OMe), 3.82 (s, 3 H, OMe), 3.76 (s, 1 H, OH), 3.76 (s, 1 H, OH), 2.79 (d, J = 16.0 Hz, 1 H), 2.55 (d, J = 16.0 Hz, 1 H), 2.0–2.15 (m, 3 H), 1.4–1.8 (m, 5 H); ^{13}C NMR (125 MHz) δ 174.5, 173.7, 140.8, 132.4, 92.3, 86.8, 57.9, 53.3, 53.2, 44.1, 25.8, 22.3, 22.2, 21.4.

Acknowledgment. We are grateful to the national Institutes of Health and the National Science Foundation for support of this work.

Supplementary Material Available: X-ray crystal data for 17 and 18 including bond lengths and angles, as well as positional and thermal parameters; experimental procedures for previously reported compounds 1, 2, 6, 13, 14, and GC, IR and EIMS data for 3–11 and 14–20 (16 pages). Ordering information is given on any current masthead page.