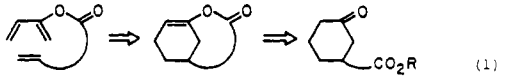
Synthesis of Bridgehead Enol Lactones via Type 2 Intramolecular Diels-Alder Cycloaddition. New Intermediates for Stereocontrolled Organic Synthesis

Kenneth J. Shea,* William M. Fruscella, Robert C. Carr, Lonnie D. Burke, and David K. Cooper

Contribution from the Department of Chemistry, University of California, Irvine, California 92717. *Received December 16, 1985. Revised Manuscript Received April 18, 1986*

Abstract: The type 2 intramolecular Diels-Alder cycloaddition is utilized in a new annulation strategy for achieving complete stereo- and regiochemical control in additions between unsymmetrical dienes and dienophiles. The approach employs cycloaddition of a dienol ester to yield a bridgehead enol lactone, a key intermediate in the annulation strategy. An X-ray crystal structure of bridgehead enol lactone **7** confirms the stereochemistry of the cycloaddition. Cleavage of bridgehead enol lactone **7** yields *trans*-decalone **8** with complete control over the relative configurations of four contiguous asymmetric centers.

The synthetic utility of the Diels-Alder reaction between unsymmetrically substituted dienes and dienophiles is often limited by a lack of control of the stereochemical and regiochemical elements of the cycloaddition. A number of ingenious solutions to this problem, including both catalysis and chelation, have been developed.[1] These methods, however, do not always yield the desired stereoisomer. Intramolecular variants of the Diels-Alder reaction often exhibit stereo- and regioselectivity that is influenced by limiting conformational arrangements of the tether joining diene and dienophile *in addition to* electronic factors originating solely from interaction of diene and dienophile. Despite these additional control elements, intramolecular reactions often exhibit disappointing stereoselection.[2] One variant of this reaction which proves to be a notable exception to this trend is the type 2 intramolecular Diels-Alder reaction. Union of diene and dienophile at the two position of the diene imposes severe constraints on the cycloaddition geometry, the result of which is the selection of a *single regio- and stereoisomeric transition state*. To date, this reaction has been used principally for the construction of strained bridgehead alkenes.[3] In this paper we demonstrate an annulation strategy that utilizes the type 2 intramolecular Diels-Alder cycloaddition for achieving complete stereo- and regiochemical control in additions between unsymmetrical dienes and dienophiles. The approach employs cycloaddition of a dienol ester **1** to yield a bridgehead enol lactone **2**,[4] a key intermediate in the annulation strategy. Subsequent cleavage of the intermediate liberates a functionalized cyclohexanone (**3**). The application of this strategy

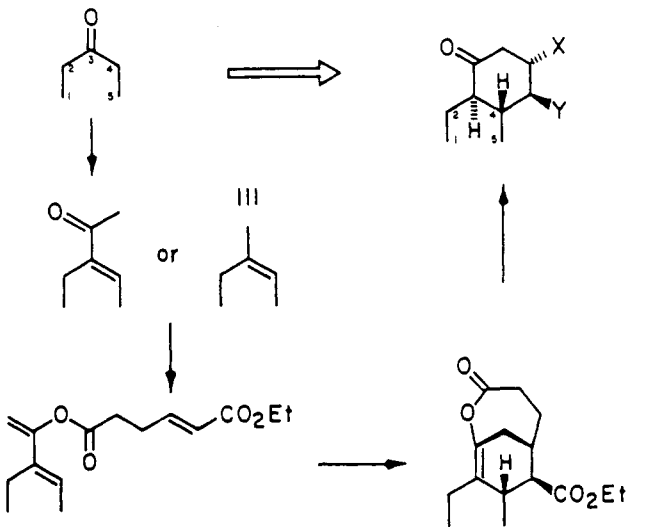


(1)

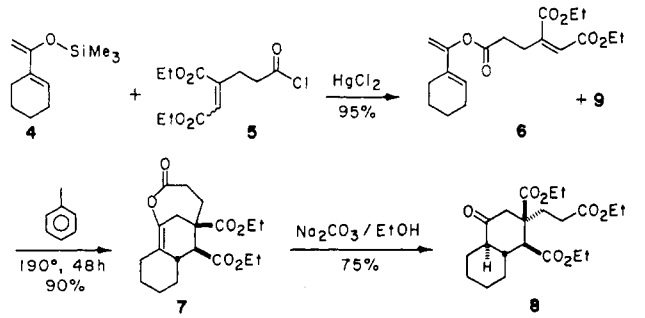
1 2 3

to annulation methodology permits formal annulation of a six-membered ring to a ketone with concomitant 1,2-shift in carbonyl position and control of the relative configuration of up to four contiguous asymmetric centers (Scheme I). As will be shown in a later section, the corresponding bimolecular cycloaddition gives rise to the expected mixture of four stereo- and regioisomers (excluding enantiomers).

Scheme I



Scheme II



Results and Discussion

The Diels-Alder precursors are assembled from diene and dienophile components as outlined for the synthesis of **6** (Scheme II). A key step in the synthesis involves union of dienophile and diene via a dienol ester linkage. This is accomplished by mer-

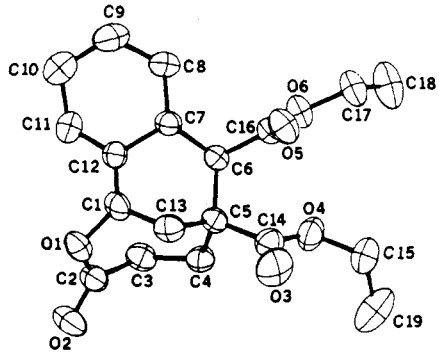
(1) (a) Evans, D. A.; Chapman, K. T.; Bishaha, J. *J. Am. Chem. Soc.* **1984**, *106*, 4261. (b) Oppolzer, W.; Dupuis, D. *Tetrahedron Lett.* **1985**, *26*, 5437. (c) Roush, W. R.; Hall, S. E. *J. Am. Chem. Soc.* **1981**, *103*, 5200. (d) Rousch, H. R.; Gillis, H. R.; Ko, A. I. *J. Am. Chem. Soc.* **1982**, *104*, 2269. (e) Mukaiyama, T.; Iwasawa, N. *Chem. Lett.* **1981**, 29. (f) Paquette, L. A. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 3, 1984; Vol. 3, also references therein.

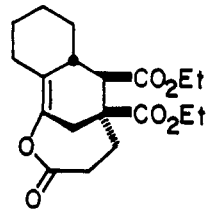
(2) (a) Ciganik, E. *Org. React.* **1984**, *32*, 1. (b) Fallis, A. *Can. J. Chem.* **1984**, *62*, 183. (c) Taber, D. F. *Intramolecular Diels-Alder and Ene Reactions*; Springer-Verlag: Berlin, 1984. (d) Brown, F. K.; Houk, K. N. *Tetrahedron Lett.* **1985**, *26*, 2297. (e) Wu, T.-C.; Houk, K. N. *Tetrahedron Lett.* **1985**, *26*, 2293. (f) Lin, Y.-T.; Houk, K. N. *Tetrahedron Lett.* **1985**, *26*, 2269. (g) Lin, Y.-T.; Houk, K. N. *Tetrahedron Lett.* **1985**, *26*, 2517.

(3) (a) Shea, K. J.; Burke, L. D. *J. Org. Chem.* **1985**, *50*, 725. (b) Shea, K. J.; Burke, L. D.; Doedens, R. J. *Tetrahedron* **1986**, *42*, 1841. (c) Shea, K. J.; Gilman, J. W. *Tetrahedron Lett.* **1983**, 697. (d) Shea, K. J.; Wise, S.; Burke, L. D.; Davis, P. D.; Gilman, J. W.; Greeley, A. C. *J. Am. Chem. Soc.* **1982**, *104*, 5708. (e) Shea, K. J.; Wise, S. *Tetrahedron Lett.* **1979**, 1011. (f) Shea, K. J.; Wise, S. *J. Am. Chem. Soc.* **1978**, *100*, 6519.

(4) Shea, K. J.; Wada, E. *J. Am. Chem. Soc.* **1982**, *104*, 5715.

0002-7863/87/1509-0447$01.50/0



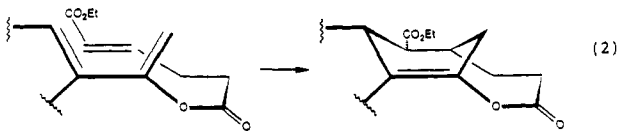


7

Figure 1. ORTEP drawing of bridgehead enol lactone **7** showing the atomic numbering scheme.

cury-catalyzed condensation[5] of trimethylsilyl dienol ether **4** with acid chloride **5** (mixture of *E* and *Z* isomers). *E* dienol ester (**9**, 83%) and the *Z* isomer (**6**, 12%) are readily isolated by column chromatography.

The cycloaddition of **6** is carried out at 190 °C for 48 h in toluene (0.1 M). The cycloadduct, a stable bridgehead enol lactone (**7**), is isolated by crystallization in 90% yield. Importantly the reaction yields a single cycloadduct. An analysis of models of transition-state conformations for the cycloaddition reveals that only one orientation of the diene and dienophile allows for *both* a reasonable overlap of dienophile and diene fragments *and* formation of "plausible" cycloaddition products.[6] Interestingly the allowed cycloaddition geometry, illustrated in eq 2, enforces a near *s-trans* geometry on the ester linkage in the tether joining diene and dienophile. This conformational arrangement has proven detrimental in several type 1 intramolecular Diels–Alder reactions.[7] From our experience we conclude that it would be imprudent to

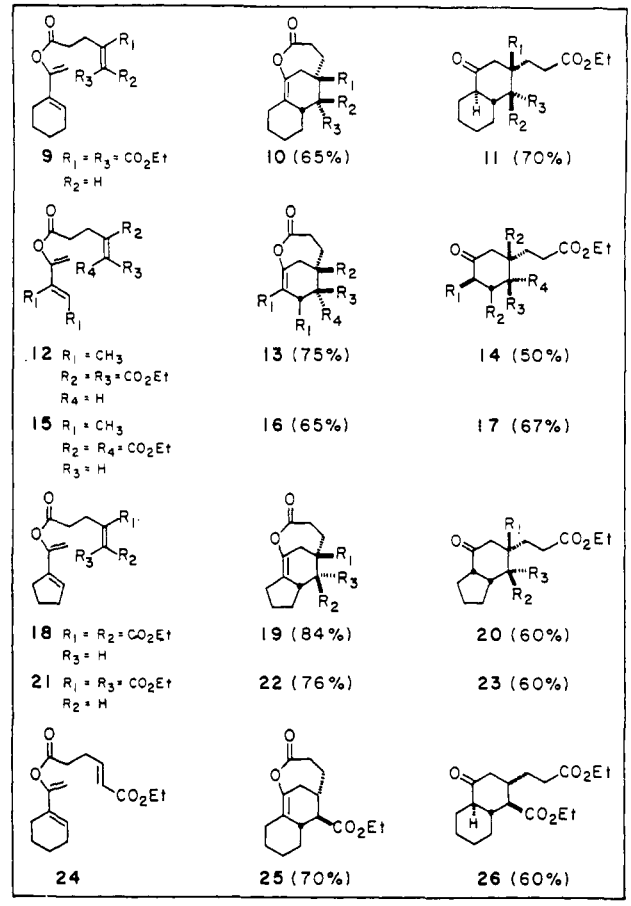


(2)

generalize on the basis of the success or failure of selected examples. The Diels–Alder reaction provides adequate thermodynamic driving force to permit synthesis of even very highly strained cycloadducts,[3] and the success or failure of these reactions is often determined by the onset of competing side reactions which are difficult to anticipate.

The stereochemical analysis of the transition-state conformations was confirmed by a single-crystal X-ray structure of cycloadduct **7**.[8] Figure 1 shows an ORTEP plot of the bridgehead enol lactone.

Table I



The relative stereochemistry at carbons 5–6–7, carboethoxy groups syn to the hydrogen at C-7, is consistent with the transition-state analysis (eq 2). The seven-membered lactone ring contains an ester linkage in the *s-trans* conformation. Two bond angles in the ring, C(1)–O(1)–C(2) (117.0°) and C(3)–C(4)–C(5) (118.1°), experience distortions greater than 10° from ϵ-caprolactone.[9] In addition, the oxygen atom of the bridgehead enol lactone group (O(1)) is distorted 17° from the plane defined by atoms C(7)–C(12)–C(1)–C(13).[10]

Treatment of cycloadduct **7** with EtOH/Na_2CO_3 (30 min, RT) results in lactone cleavage affording keto ester **8** in 75% yield. The cleavage produces a single product which does not undergo epimerization upon prolonged exposure to the reaction conditions. On the basis of both chemical and spectroscopic data, the structure of the cleavage product is assigned as *trans*-decalone **8**.

The utility of the preceding series of transformations is emphasized upon comparison with the bimolecular Diels–Alder cycloaddition of diene **5** and dienophile **30**. Capillary gas chro-

(5) Lutsenko, I. F.; Lomonosov, M. V.; Kramarova, E. N.; Baukov, I. N.; Yu, I. *Zh. Obsch. Khim.* **1973**, *43*, 1843.

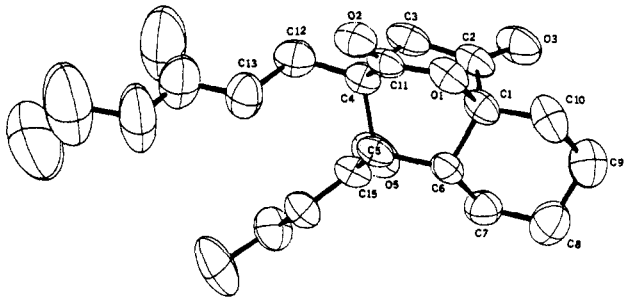
(6) Two of the four possible cycloadducts have an "inverted" configuration at a bridgehead carbon. The third possibility corresponds to the para cycloadduct. For medium length tethers this skeleton corresponds to a significantly higher energy configuration.

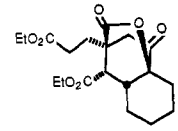
(7) (a) Boeckman, R. K.; Flann, C. J. *Tetrahedron Lett.* **1983**, *24*, 5035. (b) Boeckman, R. K., Jr.; Demko, D. M. *J. Org. Chem.* **1982**, *47*, 1789.

(8) Single crystals of bridgehead enol lactone **7** suitable for X-ray diffraction analysis were obtained by slow evaporation from 1:1 CH_2Cl_2 pentanes. X-ray crystal structure data: $C_{18}H_{26}O_6$, monoclinic, space group $P2_1/n$, a = 9.180 (2) Å, b = 9.816 (2) Å, c = 20.197 (4) Å^3, β = 91.78 (2) Å, U = 1819 (1) Å^3, Z = 4. Intensity measurements were made on a Syntex $P2_1$ diffractometer, Mo Kα radiation λ = 0.71073 Å, graphite monochromator. A total of 4704 reflections were collected to $2\theta \leq 55°$ among which 2922 had intensities $I > 3\sigma(I)$. No absorption correction was made. The structure was solved by direct methods (MULTAN 80) and refined by full-matrix least-squares calculations to R = 0.060 and R_w = 0.084 (anisotropic thermal parameters for carbon and oxygen, hydrogen in calculated position). Tables of positional parameters, anisotropic temperature factors, bond angles, and interatomic distances are included as supplemental information.

(9) Allinger, N. L. *Tetrahedron* **1982**, *54*, 2515.

(10) The non-coplanarity of the enol lactone linkage can result in a significant modification of the chemical properties of this functional group. Studies directed toward an exploration of this behavior are currently underway.

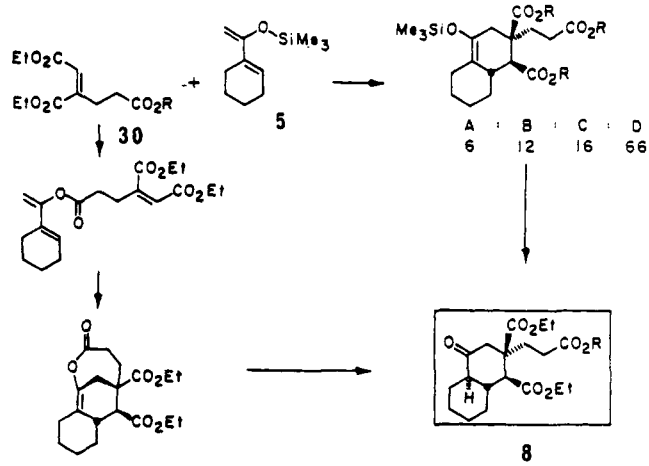




29

Figure 2. ORTEP drawing of keto lactone **29** showing the atomic numbering scheme.

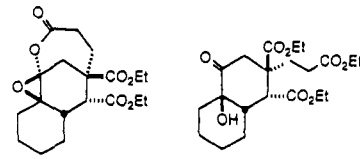
matography reveals the formation of four cycloaddition products in a ratio of 6:12:16:66. Hydrolysis of this reaction mixture affords a complex mixture of isomeric keto triesters. The GC retention time of a *minor* component (<12%) of this reaction mixture corresponds to *trans*-2-decalone **8**. This result suggests the exo transition state for **30** is of minor importance in the bimolcular cycloaddition.



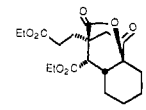
8

Further examples, representative of this methodology, are summarized in Table I. The overall transformation achieves the annulation outlined in Scheme I. In all cases a single product was obtained which corresponds to a ring junction stereochemistry that is established under the thermodynamic conditions of the lactone cleavage. For the decalone ring system this corresponds to the trans-ring junction.

Elaboration of bridgehead enol lactones permits enhancement of the utility of this annulation methodology. For example, reagents add to bridgehead double bonds with complete exo-facial selectivity.[11] Addition of reagents to the bridgehead double bond of bicyclic bridgehead enol lactones therefore can be utilized for stereocontrolled synthesis of polysubstituted cis-fused rings. The following example illustrates this point. Treatment of bridgehead enol lactone **10** with *m*-chloroperbenzoic acid (1.1 equiv) in CH_2Cl_2 affords epoxy lactone **27** as a stable crystalline solid (85%). Upon exposure of **27** to $EtOH/K_2CO_3$ (25 °C, 1 h) the epoxy lactone is converted to *cis*-hydroxy ketone triester **28** which undergoes subsequent cyclization to lactone **29** in 70% overall yield. This approach allows stereospecific functionalization of C-2 with

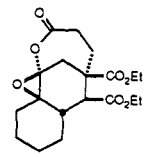


27 28



29

formation of cis-ring junction stereochemistry. The cis-ring junction and relative configuration of the four asymmetric centers was unambiguously established by X-ray structural analysis of lactone **29** (Figure 2).[12] By a similar procedure bridgehead **31** was also prepared.



31

The cycloaddition–cleavage sequence enables the stereo- and regiocontrolled synthesis of highly functionalized cyclohexanones including decalones and hydrindanones. Importantly it introduces a control element in Diels–Alder chemistry that permits utilization of highly substituted dienes and dienophiles in organic synthesis. The application of this methodology to natural product synthesis, including adrenal corticoid steroids, is currently in progress.

Experimental Section

Preparation of Silyl Enol Ethers. The following procedure illustrates the general method:

(1-(1-Cyclohexen-1-yl)ethenyloxy)trimethylsilane.[13] Into an oven-dried 1000-mL three-necked flask, fitted with internal thermometer, stir bar, addition funnel, and N_2 inlet, are transferred, via cannula, freshly distilled (from Na, benzophenone) THF (200 mL), and freshly distilled (from CaH_2) diisopropylamine (45.0 g, 445 mmol). The flask is cooled to −78 °C (dry ice:acetone bath) under a positive N_2 pressure while *n*-butyllithium (314 mL, 1.4 M, 439.6 mmol) in hexanes is added dropwise. After the addition is complete, the yellow solution is stirred at −78 °C for 30 min. Redistilled acetylcyclohexene (50.0 g, 402.6 mmol) in dry THF (50 mL) is added dropwise over 30 min. After the addition is complete freshly distilled trimethylsilyl chloride (from CaH_2) (87.3 g, 804 mmol) is added in a slow stream. The reaction is stirred at −78 °C for another 30 min and then allowed to warm slowly to room temperature. The yellow reaction mixture is poured into petroleum ether (500 mL) and ice-cold saturated $NaHCO_3$ (1000 mL). The organic layer is washed with $NaHCO_3$ solution (1000 mL) and dried ($MgSO_4$). Filtration and evaporation affords a yellow oil which was fractionated at reduced pressure to afford the silyl enol ether as a colorless liquid (bp 112–113 °C (17 mmHg) [lit.[13] bp 111–118 °C (18 mmHg)]. The yield was 61.0 g (77.2%).

(1-(Cyclopenten-1-yl)ethenyloxy)trimethylsilane. The title compound was prepared in a manner analogous to that described for the preceding silyl enol ether. Workup and distillation yields 5.75 g (60%) of silyl diene as a colorless liquid (bp 80–82 °C (17 mmHg)). IR ($CHCl_3$) 2961, 2231, 1371, 1311, 1261 (s), 1091, 1021 (s) cm^{-1}; ^1H NMR (250 MHz,

(11) Shea, K. J. *Tetrahedron* **1980**, *36*, 1683.

(12) Crystal structure of the decalone lactone: Single crystals of the decalone lactone (**29**) suitable for X-ray diffraction studies were obtained by slow evaporation from a 1:1 benzene:isooctane solution. A clear, transparent crystal of dimensions 0.2 × 0.2 × 0.3 mm was selected for intensity measurements. Intensity measurements were made on a Syntex $P2_1$ diffractometer, Mo Kα radiation λ(Kα) = 0.7107 Å, graphite monochromator. X-ray crystal structure data: $C_{19}H_{26}O_7$, monoclinic, space group $P2_1/n$, a = 13.698 (5) Å, b = 6.561 (3) Å, c = 21.496 (8) Å, β = 94.51 (3)°, U = 1926 (1) Å^3, Z = 4. A total of 3018 reflections were collected to 2θ = 45°, among which 1523 had intensities $I > 3\sigma(I)$. No absorption correction was made. The structure was solved by MITHRIL and refined by full-matrix least-squares refinement to R = 0.067 and R_w = 0.085. Tables of positional parameters, anisotropic temperature factors, bond angles, and interatomic distances are included as supplemental information.

(13) Rubottom, G. M.; Gruber, J. M. *J. Org. Chem.* **1976**, *42*, 1051.

$CDCl_3$) δ 5.96 (br s, 1 H, =C(H)), 4.28 (s, 2 H, -C(H)(H)), 2.43 (t, 4 H, J = 7.39 Hz (ring CH_2)), 1.95 (quintet, 2 H, J = 7.45 Hz (ring allylic $-CH_2-$)), 0.20 (s, 9 H, $SiC(CH_3)_3$); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 154.03, 141.40, 128.96, 93.06, 33.06, 23.27, 0.25; mass spectrum EI, 70 eV (*m/e*, relative percent) 182.00 (M^+, 39), 167.00 (35), 91.00 (10), 75.00 (23), 73.00 (33); high-resolution mass spectrum calcd for $C_{10}H_{18}OSi$ 182.1127, found 182.1125.

(*E*)-3-Methyl-2-(trimethylsilyloxy)-1,3-pentadiene. Reaction as before followed by distillation affords 15.2 g of silyl enol ether as a colorless mobile liquid (bp 68–70 °C (15 mmHg)) in 57% yield. IR (film) 2960 (s), 1310 (s), 1270 (s), 1000 (br) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 6.05 (q, 1 H, J = 6.85 Hz, =C(H)), 4.40 (s, 1 H, =C(H)), 4.24 (s, 1 H, =C(H)), 1.74 (m, 6 H, 2 CH_3), 0.21 (s, 9 H, $Si(CH_3)_3$); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 157.43, 131.85, 122.75, 90.82, 13.87, 12.88, 0.14; mass spectrum (CI, isobutane, relative percent) *m/e* 171 (MH^+, 7), 89 (100).

Preparation of Triene Esters. The following procedure illustrates the general method.

(*E*)- and (*Z*)-1-Ethyl 6-(1-Cyclohexen-1-yl)ethenyl 3-Carboethoxyhex-2-enedioate (6 and 9). In a 25-mL round-bottomed flask are placed ((1-(1-cyclohexen-1-yl)ethenyl)oxy)trimethylsilane (2.30 g, 13.5 mmol), acid chloride **5** (mixture of *E* and *Z* isomers) (2.50 g, 9.5 mmol), and anhydrous $HgCl_2$ (100 mg, 0.360 mmol). The reaction was stirred and heated to 50 °C in a preheated oil bath for 45 min and then poured into hexanes (100 mL), and the organic phase was washed with saturated ice cold $NaHCO_3$ (100 mL) and H_2O (1 × 100 mL) and dried (Na_2SO_4). The hexanes were removed by rotary evaporation, producing an oil which was then purified by flash column chromatography on SiO_2 with use of 3:1 hexanes:ether. The fractions having R_f 0.44 (UV, I_2 active) were collected. Evaporation of the solvents produced 2.75 g (83%) of the pure (*E*) ester **9** as colorless crystals (mp 56–57 °C). A second set of fractions having R_f 0.24 (UV, I_2 active) were collected as the pure (*Z*) ester **6** in the form of a transparent oil, net 400 mg (12%). Pure (*E*) ester **6** IR (CCl_4): 3005, 2928, 778, 1735 (br, vs), 1680, 1660, 1450, 1390, 1370, 1260–1140 (br vs), 1095, 1038 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 6.33 (s, 1 H, diene H), 5.92 (s br, 1 H), 4.95 (s, 1 H), 4.71 (s, 1 H), 4.23 (quintet, 4 H, J = 7.5 Hz, $2XH_3CCH_2O$), 3.13 (t, 2 H, J = 10.3 Hz, CCH_2), 2.67 (t, 2 H, J = 9.6 Hz, CH_2), 2.25–2.05 (m, 4 H, ring CH_2CH_2), 1.70–1.48 (br m, 4 H, ring CH_2CH_2), 1.28 (m, 6 H, 2 XH_3CCH_2O); ^{13}C NMR ($CDCl_3$) δ 170.45, 166.34, 165.33, 153.74, 145.59, 130.28, 128.07, 125.80, 99.84, 61.68, 60.86, 33.14, 25.34, 24.69, 23.36, 22.33, 21.34, 14.11; mass spectrum, *m/e* (CI, isobutane, relative percent) 351 (MH^+, 7), 245 (15), 228 ($M^+ - C_8H_{12}O$, 100), 124 (37). Anal. Calcd for $C_{19}H_{26}O_6$: C, 65.13; H, 7.48. Found: C, 64.95; H, 7.60. Pure (*E*) ester **9**: IR (CCl_4) 3070, 2965, 1730 (br vs), 1640, 1440, 1370, 1270–1170 (br vs), 1020 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 5.90 (app m, 2 H), 4.96 (s, 1 H, =C(H)), 4.71 (s, 1 H, =C(H)), 4.29 (q, 2 H, J = 7.2 Hz, OCH_2CH_3), 4.18 (q, 2 H, J = 7.2 Hz, OCH_2CH_3), 2.74 (app s, 4 H, CH_2CH_2), 3.23–3.07 (br m, 4 H), 1.78–1.52 (m, 4 H, ring $-CH_2CH_2-$), 1.31 (quintet, 6 H, J = 7.2 Hz, 2 H_3CCH_2O); ^{13}C NMR ($CDCl_3$) δ 169.78, 167.81, 164.49, 153.57, 146.96, 130.04, 125.78, 121.31, 99.79, 61.31, 60.59, 31.48, 29.07, 25.15, 24.51, 22.13, 21.63, 13.92, 13.80; mass spectrum, *m/e* (CI, isobutane, *m/e*, relative percent) 351 (MH^+, 3), 227 ($M^+ - C_8H_{12}O$, 100), 125 (37); high-resolution mass spectrum calcd for MH^+ of $C_{19}H_{26}O_6$ 351.1807, found 351.1805.

(*E*)- and (*Z*)-1-Ethyl 6-(1-Cyclopenten-1-yl)ethenyl 3-Carboethoxyhex-2-enedioate (18, 21). Reaction conducted as described for the synthesis of triene ester **9**. The crude yellow oil was purified by flash chromatography over SiO_2 with use of 3:1 hexanes:ether as the eluent. The fractions R_f 0.32 (UV, I_2) were collected and identified as pure *E* triene **21** (colorless oil, 56%). The fractions R_f 0.15 (UV, I_2) were collected and identified as pure *Z* triene **18** (colorless oil, 15%). Overall yield is 71%. *E* isomer **21**: IR ($CHCl_3$) 2980, 1750, 1720, 1260–1150 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 6.83 (s, 1 H, $=C(H)CO_2Et$), 5.80 (=C(H)), 4.89 (s, 1 H, =C(H)), 4.83 (s, br, 1 H, =C(H)), 4.25 (quintet, 4 H, J = 7.41 Hz, 2 $-OCH_2-$), 3.15 (t, 2 H, J = 8.39 Hz, $COCH_2$), 2.74 (t, 2 H, J = 8.39 Hz, $-CH_2-$), 2.49 (br m, 4 H, 2 CH_2C=), 1.97 (quintet, 2 H, J = 7.44 Hz, $-CH_2-$), 1.33 (m, 6 H, 2 CH_2CH_3); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 170.49, 166.49, 165.46, 150.87, 145.66, 137.61, 129.49, 128.20, 102.59, 61.80, 60.98, 33.33, 32.13, 23.50, 23.40, 14.21; mass spectrum (CI, isobutane, relative percent), *m/e* 337 (MH^+, 2), 228 (14), 227 (100, $M^+ - C_7H_{10}O$), 111 (26); high-resolution mass spectrum calcd for $C_{18}H_{24}O_6$ 336.1573, found 336.1578. *Z* isomer (**18**): IR ($CHCl_3$) 2980, 1750, 1720, 1260–1150 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 5.90 (s, 1 H, $=C(H)CO_2Et$), 5.75 (s, 1 H, =C(H)—), 4.88 (S, 1 H, =C(H)), 4.80 (S, 1 H, =C(H)), 4.20 (2 partially resolved quartets, 4 H, J = 7.16 Hz, 2 OCH_2CH_3), 2.75–2.35 (m, 9 H, contains chain and ring CH_2CH_2), 1.95 (quintet, 2 H, J = 7.40 Hz, ring-CH_2-allylic), 1.27 (m, 6 H, 2 OCH_2CH_3); ^{13}C NMR (26.9 HMz, $CDCl_3$) δ 170.03, 168.11, 164.86, 150.89, 147.03, 137.48, 129.69, 121.78, 102.75, 61.88, 61.81, 61.68, 61.12, 60.97, 34.38, 33.24, 32.18, 31.91, 29.41, 29.22, 23.59, 23.39, 22.95, 22.86; mass spectrum (CI, isobutane, relative percent), *m/e* 337 (13, MH^+), 228 (15), 227 (100, $M^+ - C_7H_{10}O$), 111 (14); high-resolution mass spectrum calcd for $C_{18}H_{24}O_6$ 336.1573, found 336.1549.

Preparation of (*E*)- and (*Z*)-1-Ethyl 6-(3,4-Dimethyl-1,3-butadienyl)ethenyl 3-Carboethoxyhex-2-enedioate. Reaction conducted in a manner identical with that described for triene ester **9**. Workup as before affords a liquid which was purified by flash column chromatography over SiO_2 with use of 3:1 hexanes:ether as the eluent. The pure *E* triene **15** had R_f 0.29 (UV, I_2) and was obtained as a colorless liquid in 50% yield; the pure *Z* triene **12** had R_f 0.155 (UV, I_2) and was obtained as a colorless oil in 13% yield. *E* triene **15**: IR ($CHCl_3$) 3000, 1770, 1730, 1650, 1450, 1370, 1270–1130, 1100, 1030 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 6.83 (s, 1 H, $=C(H)CO_2Et$), 5.73 (br quartet, 1 H, J = 7.03 Hz, $=C(H)CH_3$), 4.99 (s, 1 H, =C(H)), 4.74 (s, 1 H, =C(H)), 4.25 (quintet, 4 H, J = 7.17 Hz, 2 OCH_2CH_3), 3.13 (t, 2 H, J = 7.92 Hz, allylic CH_2), 2.72 (t, J = 7.94 Hz, $COCH_2$), 1.80 (s, 3 H, $=C(CH_3)$), 1.70 (br d, 3 H, $=C(CH_3)H$), 1.30 (m, 6 H, 2 CH_2CH_3); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 170.24, 166.12, 165.12, 154.22, 145.43, 128.84, 127.87, 122.89, 100.50, 61.49, 60.67, 32.95, 23.16, 13.91, 13.57, 12.56; mass spectrum (CI, isobutane, relative percent *m/e*) 325 (MH^+, 3.11), 227 ($M^+ - C_6H_{10}O$, 100), 153 (15), 95 (11), 91 (36), 85 (58), 83 (47), 81 (73), 77 (16), 71 (84); high-resolution mass spectrum calcd for $C_{17}H_{24}O_6$ 324.1573, found 324.1554.

Z isomer 12: IR ($CHCl_3$) 3000, 1770–1720, 1650, 1390, 1250–1100, 1030 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 5.90 (s, 1 H, $=C(H)CO_2Et$), 5.70 (br quartet, 1 H, J = 7.00 Hz, $=C(H)CH_3$), 4.99 (s, 1 H, =C(H)), 4.70 (s, 1 H, =C(H)), 4.29 (q, 2 H, J = 7.16 Hz, OCH_2), 4.15 (q, 2 H, J = 7.11 Hz, OCH_2), 2.72 (s, 4 H, $-CH_2CH_2-$), 1.78 (s, 3 H, $=C(CH_3)$), 1.68 (d, 3 H, J = 7.02 Hz, $C(CH_3)H$), 1.28 (s, 6 H, 2 OCH_2CH_3); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 169.80, 167.84, 164.51, 154.24, 146.93, 128.73, 123.11, 121.32, 100.67, 61.34, 60.62, 31.48, 29.07, 13.81, 13.58, 12.61; mass spectrum (CI, isobutane, relative percent *m/e* 325 (MH^+, 97), 227 ($M^+ - C_6H_{10}O$, 85), 153 (14), 95 (14), 93 (18), 91 (44), 85 (70), 83 (57), 81 (85), 79 (95); high-resolution mass spectrum calcd for $C_{17}H_{24}O_6$ 324.1573, found 324.1576.

Preparation of Bridgehead Enol Lactones. The following illustrates the general procedure:

***trans*-6,7-Dicarboethoxy-2-oxatricyclo[$8^{8,13}$.4.1]tetradec-1(13)-en-3-one (10).** Into a base-washed Carius tube were placed triene ester **9** (200 mg, 0.617 mmol) and dry (from sodium–benzophenone) toluene (60 mL). The tube was degassed by 3 freeze–pump–thaw cycles and then heated in an oil bath at 190 °C for 72 h. The toluene was removed by rotary evaporation, producing a viscous yellow oil. This crude oil was purified by flash chromatography on SiO_2 with use of 2:1 hexanes:ether as the eluent. The spot R_f 0.21 (UV and I_2 active) was collected. Evaporation produces a waxy crystalline solid (mp 58–60 °C); one recrystallization (2:1 hexanes:ether) yields white needles (mp 60–64 °C). The yield was 134 mg (67%). IR (CCl_4) 2930, 1780, 1740, 1700, 1450, 1380, 1360, 1230, 1180, 1160, 1120, 1010 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.18 (app septet, 4 H, J = 7.0 Hz, 2 $-O-CH_2-$), 3.43 (d, 1 H, J = 7.5 Hz, $C(H)CO_2Et$), 3.10 (ddd, J = 10.4, 3.6 Hz, CCH), 2.68–2.33 (m, 4 H, contains CCH and $=CCH$), 2.28–2.05 (m, 3 H, contains $=CCH$ and $COCH_2CH$), 1.85–1.35 (m, 7 H), 1.25 (m, 6 H, 2 CH_3); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 174.80, 173.68, 172.18, 128.40, 61.44, 60.53, 53.88, 51.09, 37.81, 32.86, 32.60, 23.46, 21.54, 20.80, 20.01, 14.30, 14.06; mass spectrum, *m/e* (CI), isobutane, relative percent 351 (MH^+, 100), 323 (33), 305 ($M^+ - CH_3CH_2OH$, 22), 277 (38). Anal. Calcd for $C_{19}H_{26}O_6$: C, 65.13; H, 7.48. Found: C, 65.35; H, 7.55.

***cis*-6,7-Dicarboethoxy-2-oxatricyclo[$8^{8,13}$.4.1]tetradec-1(13)-en-3-one (7).** The reaction was conducted as described for enol lactone **6**. Upon removal of the toluene and recrystallization of the yellow solid (2:1) hexanes:ether) the pure enol lactone **7** was subsequently obtained in 90% yield as clear, transparent needles (mp 104–106 °C). IR ($CHCl_3$) 2918, 1725, 1270, 1180, 1150 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.15 (m, 4 H, $-OCH_2-$), 2.85 (br d, 1 H, J = 14.0 Hz, C=CCH), 2.67–2.41 (complex m, 4 H, contains $COCH_2$), 2.38–2.21 (two partially overlapping doublets, 2 H, J = 14.0 Hz, $C=CCH$, J = 9.59 Hz, $C(H)CO_2Et$)8 2.20–2.05 (br m, 1 H), 1.97 (distorted t, 2 H, $COCH_2CH_2$), 1.90–1.37 (complex m, 5 H, contains ring aliphatic CH_2), 1.23 (q, 6 H, 2 CH_3); ^{13}C NMR ($CDCl_3$) δ 174.10, 173.93, 171.82, 142.51, 126.88, 61.40, 60.93, 55.17, 51.63, 40.15, 36.67, 35.73, 31.95, 25.49, 20.54, 20.31, 19.84, 14.21, 14.05; mass spectrum, *m/e* (CI, isobutane, relative percent) 351 (MH^+, 100), 305 ($M^+ - CH_3CH_2OH$, 84), 277 (19). Anal. Calcd for $C_{19}H_{26}O_6$: C, 65.13; H, 7.48. Found: C, 65.18; H, 7.49.

***trans*-6,7-Dicarboethoxy-2-oxatricyclo[$8^{8,12}$.3.1]tridec-1(12)-en-3-one (22).** Conducting the cycloaddition as described before with precursor **21** and purification of the residue by flash column chromatography over SiO_2 with use of 2:1 hexanes:ether produces the bridgehead enol lactone

(R_f 0.55, UV, I_2 active) as a white crystalline solid (mp 73–74 °C) in 76% yield. IR ($CHCl_3$) 2990, 1760–1700, 1480–1420, 1380 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$ δ 3.49 (d, 1 H, J = 9.84 Hz, C(H)CO_2Et), 3.08–2.85 (m, 2 H), 2.63 (dddd, 1 H, J = 15.79, 7.83, 3.03 Hz, C(O)C*H*), 2.53–2.28 (m, 4 H), 2.18–1.87 (complex m, 1 H), 1.57–1.40 (complex, m, 1 H), 1.28 (two superimposed triplets, 6 H, J = 7.11 Hz, CH_2CH_3); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 174.90, 174.25, 172.04, 139.16, 134.01, 61.36, 51.57, 41.60, 38.66, 33.42, 31.37, 30.09, 27.43, 26.07, 14.25, 14.05; mass spectrum (CI, isobutane, relative percent), m/e 337 (MH^+, 100), 291 (39), 89 (16). Anal. Calcd for $C_{18}H_{24}O_6$: C, 64.25; H, 7.19. Found: C, 64.23; H, 7.24.

***cis*-6,7-Dicarboethoxy-2-oxatricyclo[$8^{8,12}$.3.1]tridec-1(12)-en-3-one (19).** The cycloaddition was conducted as described above with precursor **18**. After 36 h the reaction mixture was concentrated, and the crude yellow solid recrystallized from 2:1 hexanes:ether to give the bridgehead enol lactone **19** as colorless needles (mp 83 °C) in 84% yield. IR ($CHCl_3$) 2990, 1770–1720, 1560, 1270–1250, 1160, 1130 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.15 (m, 4 H, 2 O$CH_2$$CH_3$), 2.80 (m, 2 H), 2.52 (distorted t, 2 H), 2.48–1.98 (complex m, 7 H), 1.98–1.58 (br m, 3 H), 1.25 (m, 6 H, CH_2CH_3); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 174.16, 173.86, 171.91, 140.17, 133.51, 61.42, 61.06, 54.86, 51.80, 45.24, 37.34, 36.54, 31.70, 31.60, 28.10, 25.63, 14.22, 14.05; mass spectrum (CI, isobutane, relative percent), m/e 337 (MH^+, 100), 291 (39), 89 (16); high-resolution mass spectrum calcd for $C_{18}H_{24}O_6$ 336.1573, found 336.1588.

***trans*-6,7-Dicarboethoxy-8,9-dimethyl-2-oxabicyclodec-1(9)-en-3-one (16)** was prepared from **15** in an identical manner as described for enol lactone **10**. Evaporation of the solvent and purification of the residue by flash column chromatography on SiO_2 (2:1 hexanes:ether) (R_f 0.58, I_2, UV active) affords pure **16** as a colorless oil in 65% yield. IR ($CHCl_3$) 2980, 1760–1710, 1680, 1240, 1200, 1020 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.18 (m, 4 H, O$CH_2$$CH_3$), 3.38 (d, 1 H, J = 6.72 Hz, C(*H*)CO_2Et), 3.00 (ddd, J = 18.7, 3.5 Hz, COC*H*), 2.70–2.50 (br m, 2 H, contains =CC*H* and $H_3CC(H)$), 2.36 (dddd, J = 12.85, 8.68, 2.13 Hz, COC*H*), 2.20 (d, 1 H, J = 13.96 Hz, =CC*H*), 2.19–2.05 (m, 1 H, $COCH_2CH$), 1.81 (s, 3 H, CH_3), 1.80–1.68 (m, 1 H, $COCH_2CH$), 1.23 (m, 9 H, 2 CH_2CH_3 and CH_3CH); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 174.89, 173.90, 171.89, 143.04, 127.46, 61.62, 60.64, 55.48, 51.15, 37.98, 35.10, 32.71, 32.45, 14.39, 14.19, 13.19, 11.17; mass spectrum (CI, isobutane, relative percent), m/e (325 (MH^+, 100), 295 (86), 278 (34), 251 (75), 221 (33), 195 (17), 177 (21), 155 (11), 149 (10), 123 (10), 115 (11), 83 (53), 81 (15), 71 (13); high-resolution mass spectrum calcd for $C_{17}H_{24}O_6$ 324.1573, found 324.1567.

***cis*-6,7-Dicarboethoxy-8,9-dimethyl-2-oxabicyclodec-1(9)-en-3-one (13)** was prepared from **12** as described above. After 36 h the toluene was removed and the crude solid recrystallized from 2:1 hexanes:ether to afford the bridgehead enol lactone **13** as clear, transparent needles (mp 99 °C) in 75% yield. IR ($CHCl_3$) 2990, 2250, 1770–1730 (br vs), 1460, 1440, 1370, 1250, 1180, 1040 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.11 (m, 4 H, 2 O$CH_2$$CH_3$), 2.82 (br d, 1 H, J = 13.7 Hz, =C(O)C*H*), 2.68 (br m, 1 H, =CC*H*), 2.49 (m, 2 H, C(O)CH_2), 2.29 (d, 1 H, J = 14.28 Hz, C=CC*H*), 2.13 (d, 1 *H*, J = 10.27 Hz, C(H)CO_2Et), 1.96 (m, 2 H, CH_2CH_2), 1.70 (s, 3 H, =C(CH_3)), 1.20 (m, 9 H, contains 2 O$CH_2$$CH_3$ and C(H)(CH_3)); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 174.01, 173.87, 171.93, 144.05, 125.73, 61.39, 60.89, 56.85, 51.66, 38.07, 38.64, 35.74, 31.63, 14.78, 14.16, 13.99, 10.65; mass spectrum (CI, isobutane, relative percent), m/e 325 (87 MH^+), 295 (38), 280 (17), 279 (12, M^+ – EtOH), 251 (26), 249 (21), 233 (10), 223 (13), 205 (25), 177 (21), 135 (11), 83 (52), 79 (12). Anal. Calcd for $C_{17}H_{24}O_6$: C, 62.93; H, 7.46. Found: C, 62.94; H, 7.57.

Cleavage of Bridgehead Enol Lactones with Potassium Carbonate in Ethanol. Preparation of Functionalized Ketones. The following is a typical procedure:

***trans*-3,4-Dicarboethoxy-3-[2-(ethoxycarbonyl)ethyl]bicyclo[4.4.0]decan-1-one (11).** In a 25-mL round-bottomed flask are placed enol lactone **10** (40 mg, 0.111 mmol), dry EtOH (10 mL), and anhydrous K_2CO_3 (1.00 g, 7.24 mmol). The reaction mixture was stirred at room temperature for 30 min. The EtOH was evaporated and the residue taken up in Et_2O (20 mL). The slurry was filtered through a Büchner funnel, and the collected K_2CO_3 was washed (Et_2O, 2 × 20 mL) until it remained white. The ether was evaporated and the yellow residue was chromatographed twice on SiO_2 with use of 1:1 hexane:ether as the eluent. The spot, R_f 0.21 (I_2 active), was collected to yield 30 mg (68%) of analytically pure decalone-ester **11** as a transparent oil. IR (CCl_4) 3000, 2925, 2838, 1735, 1455, 1390, 1310, 1180 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.15 (m, 6 H, 3 O$CH_2$$CH_3$), 3.10 (br d, 1 H, J = 4.46 Hz, C(*H*)CO_2Et), 2.86 (d, 1 H, J = 17.29 Hz, COC*H*), 2.72–2.51 (m, 2 H, contains COC*H*), 2.20 (distorted t, 2 H, CH_2CO), 2.13–1.95 (complex m, 2 H), 1.85–1.65 (M, 4 H), 1.60–1.45 (br M, 1 H), 1.35 (t, 3 H, J = 7.30 Hz, CH_3), 1.25–0.95 (m, contains 2 partially resolved triplets, 10 H, 2 CH_3 and aliphatic H); ^{13}C NMR ($CDCl_3$) δ 208.10, 173.34, 172.13, 171.87, 61.51, 60.51, 50.40, 51.39, 50.45, 48.13, 43.75, 41.59, 32.51, 31.19, 28.98, 25.76, 25.16, 25.02, 14.17, 14.01, 13.94; mass spectrum, m/e (CI, isobutane, relative percent) 397 (MH^+, 100), 351 (M^+ – EtOH, 29), 101 (19). Anal. Calcd for $C_{21}H_{32}O_7$: C, 63.62; H, 8.13. Found: C, 63.33; H, 7.97.

***cis*-3,4-Dicarboethoxy-3-[2-(ethoxycarbonyl)ethyl]bicyclo[4.4.0]decan-1-one (8)** was prepared from **7** by reaction and workup identical with that for enol lactone **10**. Purification of the residue by flash chromatographing twice on SiO_2 with 2:1 hexane:ether produces decalone ester **8** as a transparent oil (R_f 0.12) (75%): IR ($CHCl_3$) 2960, 2920, 2840, 1710, 1300, 1260, 1180, 1150, 1020 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.18 (m, 6 H, 2 O$CH_2$$CH_3$), 3.60–3.48 (m, 2 H), 3.40–3.25 (complex m, 2 H), 3.23–3.05 (m, 4 H), 1.93–1.60 (m, 6 H), 1.22 (m, 13 H, includes 3 O$CH_2$$CH_3$); ^{13}C NMR ($CDCl_3$) δ 206.08, 172.88, 172.32, 171.67, 61.46, 60.90, 60.61, 57.17, 52.81, 50.80, 46.46, 41.67, 32.52, 32.18, 29.54, 25.70, 25.49, 25.13, 14.23; mass spectrum, m/e (CI, isobutane, relative percent) 397 (MH^+, 100), 351 (M^+ – EtOH, 69), 89 (95); high-resolution mass spectrum calcd for $C_{21}H_{32}O_7$ 396.2148, found 396.2130.

***trans*-3,4-Dicarboethoxy-3-[2-(ethoxycarbonyl)ethylbicyclo[4.3.0]nonan-1-one (23).** The reaction was conducted as above for 30 min at room temperature. Workup followed by flash column chromatography over SiO_2 with 2:1 hexanes:ether as the eluent produces the hydrindanone ester (R_f 0.09, I_2) as a colorless oil in 60% yield: IR ($CHCl_3$) 2980, 1725, 1450, 1380, 1230–1190 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.21 (q, 2 H, J = 7.10 Hz, O$CH_2$$CH_3$), 4.12 (2 overlapping quartets, J = 7.10 Hz, 4 H, O$CH_2$$CH_3$), 3.28 (d, 1 H, J = 5.68 Hz, C(*H*)CO_2Et), 3.03 (d, 1 H, J = 18.32 Hz, COC*H*), 2.63–2.40 (br m, 2 H, contains C(H)C_3), 2.35 (d, 1 H, J = 18.32 Hz, COC*H*), 2.23–2.05 (complex m, 3 H), 2.02–1.60 (m, 5 H), 1.25 (m, 1 H, contains 3 CH_2CH_3); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 174.90, 172.45, 172.04, 136.16, 134.01, 61.36, 60.42, 51.57, 41.60, 38.66, 33.42, 31.37, 30.09, 27.43, 26.07, 14.25, 14.05; low-resolution mass spectrum (CI, isobutane, relative percent), m/e 383 (MH^+, 35.30), 337 (100, M^+ – EtOH), 263 (28), 245 (12), 154 (11), 91 (11), 81 (13), 79 (13); high-resolution mass spectrum calcd for $C_{20}H_{30}O_7$ 382.1992, found 380.1990.

***cis*-3,4-Dicarboethoxy-3-[2-(ethoxycarbonyl)ethyl]bicyclo[4.4.0]decan-1-one (20)** prepared from **19** as previously described affords a crude yellow oil which was purified by flash chromatography over SiO_2 with 2:1 hexanes:ether as the eluent. Hydrindanone ester **20** (R_f 0.07, I_2) was subsequently recovered as a clear oil in 62% yield: IR (CCl_4) 2990, 1738, 1600, 1500, 1350, 1000 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.25 (m, 6 H, 3 OCH_2), 2.83–2.70 (br m, 2 H), 2.55 (d, 1 H, J = 16.05 Hz), 2.41 (d, 1 H, J = 11.37 Hz), 2.33–2.10 (m, 4 H), 2.03–1.58 (m, 6 H), 1.45–1.30 (m, 1 H), 1.23 (m, 9 H, 3 CH_3); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 209.76, 172.74, 172.54, 171.95, 61.62, 61.03, 60.68, 52.98, 51.45, 50.86, 44.15, 41.33, 31.93, 31.80, 29.45, 29.34, 23.85, 14.24, 13.95; mass spectrum (CI, isobutane, m/e, relative percent) 383 (MH^+, 4), 337 (M^+ – EtOH, 100), 308 (10), 263 (15); high-resolution mass spectrum calcd for $C_{20}H_{30}O_7$ 382.1992, found 382.1963.

***trans*-2,3-Dimethyl-*cis*-4,5-dicarboethoxy-5-[2-(ethoxycarbonyl)-ethyl]cyclohexanone (17). Reaction of 16.** Purification by flash chromatography (1:1 hexanes:ether) affords the pure cyclohexanone ester **17** (R_f 0.3, I_2 active) as a colorless transparent oil in 67% yield: ^1H NMR (500 MHz, $CDCl_3$) δ 4.15 (m, 6 H, 3 OCH_2), 3.14 (collapsed AB quartet, 1 H, J = 4.5, 1.4 Hz, C(H)CO_2Et), 2.78 (d, 1 H, J = 14.4 Hz, COC*H*), 2.67 (collapsed AB quartet, 1 H, J = 14.5, 1.5 Hz, COC*H*), 2.61 (sextet, 1 H, J = 6.65 Hz, CO(CH_3)*H*), 2.17 (t, 2 H, J = 8.03 Hz, $-CH_2C-$), 2.00 (m, 1 H $CHCH_2C$), 1.76 (m, 1 H, $CHCH_2$), 1.67 (m, 1 H, C(CH_3)*H*), 1.28 (t, 3 H, J = 7.13 Hz, CH_2CH_3), 1.24 (t, 6 H, J = 8.0 Hz, 2 CH_2CH_3), 1.01 (d, 3 H, J = 6.75 Hz, C(CH_3)*H*), 0.98 (d, 3 H, J = 6.0 Hz, CO(CH_3)*H*); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 209.04, 173.54, 172.42, 172.04, 61.77, 60.80, 51.89, 50.98, 45.63, 43.51, 37.74, 32.74, 30.95, 29.22, 17.96, 14.37, 14.18, 11.69; mass spectrum (CI, isobutane, relative percent), m/e 371 (MH^+, 57), 326 (18), 325 (100, M^+ – EtOH), 296 (18), 251 (31), 195 (16), 177 (21), 135 (11); high-resolution mass spectrum calcd for $C_{19}H_{30}O_7$ 370.1922, found 370.2000.

***cis*-2,3-Dimethyl-4,5-dicarboethoxy-5-[2-(ethoxycarbonyl)ethyl]cyclohexanone (14).** The reaction of **14** was conducted as above. Flash column chromatography (1:1 hexanes:ether) produces a single component, R_f 0.33 (I_2). Cyclohexanone ester **14** was subsequently obtained in 48% yield as a clear, colorless oil: IR ($CHCl_3$) 2990, 2250, 1750–1710, 1480–1440, 1380, 1300 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.25 (m, 6 H, $-OCH_2-$), 2.51 (d, 1 H, J = 9.60 Hz, COC*H*), 2.49 (d, 1 H, J = 6.50 Hz, C(H)CO_2Et), 2.29 (m, 2), 2.20–2.08 (m, 2 H, contains COC*H* and $COCCH_3(H)$), 1.88–1.72 (m, 2 H), 1.22 (m, 9 H, CH_3), 1.14 (d, 3 H, J = 6.50 Hz, $CH_3C(H)$), 0.99 (d, 3 H, J = 6.35 Hz, CH_3CHCO); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 206.95, 172.93, 173.50, 172.22, 61.53, 61.00, 60.56, 58.18, 50.04, 49.19, 46.24, 38.10, 32.02, 29.40, 19.11, 14.19,

13.93, 11.90; mass spectrum (CI, isobutane, relative percent), *m/e* 371 (MH^+, 26), 325 (100, M^+ – EtOH), 251 (26), 195 (8), 177 (12); high-resolution mass spectrum calcd for $C_{19}H_{31}O_7$ 370.1992, found 371.2071 (MH^+).

Preparation of the Bridgehead Epoxides. The procedure outlined below is illustrative of the general method:

1,13-Epoxy-*trans*-6,7-dicarboethoxytricyclo[7.4^{8,13}.1.0]tetradeca-2-oxa-3-one (27). To a 50-mL round-bottomed flask is added enol lactone **10** (340 mg, 0.970 mmol) and CH_2Cl_2 (25 mL). MCPBA (80–85%, 265 mg, 1.54 mmol) is introduced into the flask and the reaction mixture stirred at room temperature for 1 h at which time TLC (1:1 hexanes:ether) shows complete disappearance of the starting lactone (R_f 0.49) and the appearance of the epoxide as a strongly I_2-active spot (R_f 0.44). The reaction mixture was poured into an aqueous solution (25 mL) of $NaHCO_3$ (1.0 g) and sodium thiosulfate (1.0 g) and then stirred at room temperature for 30 min. The layers were then separated, and the aqueous layer was extracted with CH_2Cl_2 (1 × 25 mL). The combined CH_2Cl_2 layers were dried ($MgSO_4$), filtered, and evaporated, producing 310 mg of a transparent oil. This oil was purified by flash column chromatography on SiO_2 with use of 2:1 hexane:ether as the eluent. The fractions having R_f 0.19 were collected and evaporated, yielding 255 mg (72%) of crystalline epoxide **32** (mp 82–84 °C): IR ($CHCl_3$) 2940, 2860, 1730, 1300–1100, 1030 cm^{-1}; ^1H NMR (500 mHz, $CDCl_3$) δ 4.15 (m, 4 H, OCH_2CH_3), 3.48 (d, 1 H, J = 9.25 Hz, C(*H*)CO_2Et), 2.68 (dddd, 1 H, J = 9.30, 4.70, 2.65 Hz, COC*H*), 2.48 (d, 1 H, J = 14.85 Hz, C-$(O)_2CH$), 2.26–2.08 (m, 3 H, contains $C(O)_2CH$), 2.05 (complex m, 1 H, COC*H*), 1.89–1.60 (m, 6 H), 1.51–1.40 (m, 1 H), 1.26 (m, 6 H, 2 OCH_2CH_3); ^{13}C NMR ($CDCl_3$) δ 174.48, 172.05, 170.66, 86.33, 66.09, 61.92, 60.96, 50.65, 46.72, 38.96, 38.51, 32.77, 30.57, 23.34, 23.17, 20.40, 19.05, 14.37, 14.16; mass spectrum (CI, isobutane, relative percent) 367 (MH^+, 85), 352 (11), 349 (47), 321 ($M^+ - CH_3CH_2OH$, 100), 303 (13), 275 (19), 247 (19), 227 (11); high-resolution mass spectrum calcd for $C_{19}H_{26}O_7$ 366.1678, found 366.1691.

1,13-Epoxy-*cis*-6,7-dicarboethoxytricyclo[7.4^{8,13}.1.0]tetradeca-2-oxa-3-one (31). Into a clean, dry, 25-mL, round-bottomed flask, equipped with a stir bar, are placed recrystallized enol lactone **7** (89 mg, 0.250 mmol) and dry CH_2Cl_2 (5 mL). MCPBA (74 mg, 0.428 mmol) is added at once and the solution stirred for 50 min. The solution was poured into H_2O (5 mL) containing $NaHCO_3$ (100 mg) and $Na_2S_2O_3$ (100 mg) and stirred for 0.5 h. The aqueous layer was separated and extracted with CH_2Cl_2 (2 × 20 mL). The CH_2Cl_2 extracts were combined, dried ($MgSO_4$), filtered, and evaporated, affording 84 mg of white powder. This powder was recrystallized from 3:1 hexanes:ethyl acetate, producing 66 mg (72%) of colorless needles, mp 121–123 °C: ^1H NMR (250 MHz, $CDCl_3$) δ 4.10 (m, 4 H, 2 OCH_2), 2.76 (m, 2 H), 2.55 (m, 2 H), 2.43 (d, 1 H, J = 15.3 Hz), 2.08 (m, 2 H), 1.92–1.54 (br m, 8 H), 1.46–1.30 (br m, 1 H), 1.22 (t, 3 H, J = 6.95 Hz, 2 CH_3); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 173.48, 173.07, 169.06, 85.95, 64.26, 61.63, 61.07, 52.77, 47.55, 40.97, 35.88, 34.80, 31.99, 25.83, 23.16, 19.60, 18.87; IR ($CHCl_3$) 2990, 2940, 1750 (br vs), 1510, 1370, 1250 (br vs), 1150 (br vs), 1010 cm^{-1}; low-resolution mass spectrum (CI, isobutane, relative percent) 368 (17), 367 (87, MH^+), 322 (18), 321 (100, $M^+ - C_2H_5OH$), 303 (12), 275 (15); high-resolution mass spectrum calcd for $C_{19}H_{26}O_7$ 366.1679, found 366.1631.

Preparation of the Decalone Lactones. The procedure below illustrates the general method.

***cis*-4-(2-Carboethoxyethyl)-5-carboethoxytricyclo[6.4^{6,1}.2.1]dodec-11-oxa-2,12-dione (29).** In a 25-mL round-bottomed flask are placed crystalline epoxide **27** (1.80 mg, 0.490 mmol), dry EtOH (5 mL), and anhydrous K_2CO_3 (1.00 g, 7.24 mmol). The slurry was stirred at room temperature for 15 min when TLC showed disappearance of the epoxide (R_f 0.44, 1:1 hexane:ether, strongly I_2 active) and the appearance of two other spots (R_f 0.51 and 0.46, both strongly I_2 active). Most of the ethanol was removed at reduced pressure, and the residue was taken up in CH_2Cl_2 (25 mL). The CH_2Cl_2 layer was washed with H_2O (2 × 10 mL), dried ($MgSO_4$), filtered, and evaporated. Recrystallization from hexanes:ethyl acetate (3:1) returns the pure decalone lactone **29** as thin needles (mp 118 °C) in 56% yield: ^1H NMR (250 MHz, $CDCl_3$) δ 4.18 (m, 4 H, $-OCH_2-$), 3.53 (d, 1 H, J = 19.28 Hz, COC*H*), 3.18 (dd, 1 H, J = 11.65, 1.75 Hz, C(*H*)CO_2Et), 2.53 (distorted t, 2 H, $COCH_2$), 2.50–2.28 (m, 2 H, contains C(O)C*H* and axial bridgehead H), 2.02 (distorted t, 2 H, $COCH_2CH_2$), 1.85–1.42 (6 H, ring $-CH_2-$), 1.27 (q, 6 H, J = 6.82 Hz, 2 CH_2CH_3); ^{13}C NMR ($CDCl_3$) δ 203.63, 173.07, 169.66, 86.06, 61.42, 60.77, 45.48, 44.54, 42.18, 39.06, 28.85, 29.85, 29.34, 27.49, 26.73, 25.36, 22.58, 14.37; mass spectrum, *m/e* (CI, isobutane, relative percent) 367 (MH^+, 100), 321 (M^+ – EtOH, 25), 227 (10), 125 (11), 71 (30); high-resolution mass spectrum calcd for $C_{19}H_{26}O_7$ 366.1679, found 366.1667.

1-Ethyl-6-(1-(1-cyclohexenyl)ethenyl)hex-2-endioate (24). To HgO (344 mg, 1.52 mmol) in a 25-mL flask was added MeOH (116 μL, 2.86 mmol) and $BF_3{\cdot}OEt_2$ (116 μL, 0.82 mmol). The mixture was heated to 50 °C for 5 min and then 1-ethyl hex-2-enoate in Et_2O (4 mL) was added. The suspension was cooled to −23 °C and 1-ethynyl-1-cyclohexene (7.6 mL, 7.65 mmol) was added dropwise. The cooling bath was removed, and the mixture was stirred for 6 h. Et_2O and H_2O were added, and the organic phase was separated, washed with saturated $NaHCO_3$ solution, and then dried ($MgSO_4$). After concentration, the residue was chromatographed on 100 g of SiO_2 (1:1 Skelly F/Et_2O) and then rechromatographed on 50 g of SiO_2 (4:1 Skelly F/Et_2O) to obtain 1.453 g of **24** (45%).

Compound 24: IR (film) 2982, 2880, 1760, 1726, 1374, 1210; ^1H NMR (250 MHz, $CDCl_3$) δ 6.94 (m, 1 H, C*H*=$CHCO_2Et$), 5.85 (M, 2 H, =*CH*CO_2Et and diene =C*H*), 4.92 (d, 1 H, J = 1.7 Hz, C=CH_2), 4.65 (d, 1 H, J = 1.7 Hz, C=CH_2), 4.17 (q, 2 H, J = 6.8 Hz, CH_2CH_3), 2.62 (m, 4 H, CH_2CH_2CH=CH–), 2.15 (m, 4 H, ring allylic), 1.65 (m, 4 H, ring alkyl), 1.28 (t, 3 H, J = 6.8 Hz, CH_2CH_3); ^{13}C NMR (62.9 MHz, $CDCl_3$) 170.76, 166.4, 153.9, 146.3, 130.5, 126.1, 122.8, 100.1, 60.5, 32.6, 27.4, 25.5, 24.9, 22.4, 22.0, 14.5; high-resolution mass spectrum, calcd for $C_{16}H_{22}O_4$ 278.1518, found 278.1534.

8-Carboethoxy-13-oxatricyclo[7.4.1.0.2.7]tetradec-1(2)-en-12-one (25). The cycloaddition was run by heating in a Carius tube compound **24** (100 mg, 0.359 mmol) and xylene (15 mL) to 190 °C for 16 h. After concentration the oil was purified by column chromatography (10 g, SiO_2, 1.25:1 Skelly F/Et_2O) to yield 73 mg (73%) of cycloadduct.

Compound 25: IR 2962, 2926, 2870, 1758, 1733, 1380, 1118; ^1H NMR (250 MHz, $CDCl_3$) δ 4.18 (dq, 2 H, J = 1.1, 7.5 Hz, CH_2CH_3), 2.34–2.60 (m, 6 H), 1.32–2.15 (m, 11 H), 1.28 (t, 3 H, J = 7.5 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$) 175.6, 173.7, 143.6, 126.8, 60.8, 51.7, 39.0, 38.5, 34.1, 31.6, 25.6, 20.8, 20.5, 20.2, 14.5; high-resolution mass spectrum, calcd for $C_{16}H_{22}O_4$ 278.1518, found 278.1509.

4-(2-Carboethoxyethyl)-5-carboethoxybicyclo[4.4.0]decan-2-one (26). A mixture of compound **25** (53 mg, 0.191 mmol), Na_2CO_3 (5 g), and EtOH (50 mL) in a 100-mL flask was stirred for 24 h at 25 °C. Saturated NH_4Cl solution, Et_2O, and H_2O were added and then the organic phase was washed with H_2O and dried ($MgSO_4$). After concentration the oil was chromatographed on 2 g of SiO_2 (1:1 Skelly F/Et_2O) to yield 43 mg (69%) of decalone **26**.

Compound 26: IR 2976, 1750, 1720, 1360, 1190; ^1H NMR (250 MHz, $CDCl_3$) δ 4.21 (q, J = 8.2 Hz, 2 H, CH_2CH_3), 4.11 (q, 2 H, J = 7.3 Hz, CH_2CH_3), 2.49 (d, 1 H, J = 9.3 Hz), 1.92–2.45 (m, 9 H), 1.47–1.86 (m, 8 H), 1.30 (t, 3 H, J = 7.3 Hz, CH_3), 1.24 (t, 3 H, J = 8.2 Hz, CH_3); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 209.6, 174.1, 173.0, 60.8, 60.6, 55.6, 52.9, 45.2, 32.0, 31.0, 29.6, 25.5, 25.2, 25.1, 14.4, 14.3; high-resolution mass spectrum, calcd for $C_{18}H_{28}O_5$ 324.1937, found 324.1928.

Acknowledgment. We are grateful to the National Institutes of Health for Financial support of this work. We are also grateful to William England for assistance with the X-ray crystallography.

Supplementary Material Available: Tables of positional parameters, anisotropic temperature factors, bond angles, and interatomic distances for bridgehead enol lactone **7** and lactone **29** (5 pages). Ordering information is given on any current masthead page.