(352 mg, 1.09 mmol) in dry EtOH (12 mL) were added triethyl orthoformate (1.7 mL, 10.3 mmol) and one drop of concentrated H_2SO_4, and the mixture was stirred at room temperature for 2 days. After addition of saturated $NaHCO_3$ (10 mL) to the reaction mixture, the solvent was concentrated in vacuo, and the residue was extracted with CH_2Cl_2. The extract was washed with water, dried over $MgSO_4$, and evaporated in vacuo to give a mixture of olefinic isomers **32** as a colorless oil (401 mg, 100%). According to method A, desulfurization of **32** (88 mg, 0.24 mmol) with aluminum amalgam (aluminum, 350 mg, 13.0 mmol) in 2% aqueous THF (20 mL) gave a 7:3 mixture (by ^1H NMR spectrum) of **33** and **34** as a colorless oil: 49 mg (90%); ^1H NMR ($CDCl_3$) δ 1.27 (t, 6, J = 7 Hz), 1.5–1.9 (m, 4), 1.83 (d, 0.9, J = 7 Hz), 2.2–2.4 (m, 2), 3.01 (m, 0.7), 4.16 (q, 2, J = 7 Hz), 4.18 (q, 2, J = 7 Hz), 5.1–6.0 (m, 2.1), 6.96 (q, 0.3, J = 7 Hz); IR (neat) 1730, 1635 cm^{-1}; mass spectrum, m/e 228 (M^+), 183, 81 (base peak).

Acknowledgment. This research was supported by Grants-in-Aid for Special Project Research "Nitrogen Organic Resources" and for Scientific Research-C (No. 557477) from the Ministry of Education, Science, and Culture, which are gratefully acknowledged. We thank Ms. A. Itoh for her technical cooperation.

Registry No. **1**, 32501-93-2; **7**, 133-13-1; **8**, 83219-76-5; **9**, 63383-27-7; **10**, 2049-80-1; (*E*)-**11**, 83219-90-3; (*Z*)-**11**, 83219-77-6; **12**, 83219-78-7; **13**, 609-14-3; **14**, 83219-79-8; **15** (isomer 1), 83219-80-1; **15** (isomer 2), 83219-95-8; **16**, 5837-78-5; **17**, 611-10-9; (*E*)-**18**, 83219-91-4; (*Z*)-**18**, 83219-81-2; **19**, 83219-82-3; **20**, 63383-28-8; **21**, 41302-34-5; (*E*)-**22**, 83219-92-5; (*Z*)-**22**, 83219-83-4; **23**, 83219-84-5; **24**, 83219-85-6; **25**, 765-69-5; **26**, 83219-86-7; **27** (isomer 1), 83289-18-3; **27** (isomer 2), 83289-19-4; **28**, 71545-36-3; **29**, 83219-87-8; (*E*)-**30**, 83219-88-9; (*Z*)-**30**, 83219-89-0; **31**, 83231-98-5; **33**, 83219-93-6; **34**, 83219-94-7; Me_3SiCN, 7677-24-9; ethyl 3-cyano-2-methyl-2-[(*Z*)-2-(phenylsulfonyl)vinyl]-3-(trimethylsiloxy)butanoate, 83219-96-9; ethyl 2-cyano-1-[(2-phenylsulfonyl)vinyl]-2-(trimethylsiloxy)cyclopentanecarboxylate, 83219-97-0; methyl 2-cyano-1-[2-phenylsulfonyl)vinyl]-2-(trimethylsiloxy)cyclohexanecarboxylate, 83219-98-1.

Sequential (π-Allyl)palladium Alkylations

Richard S. Valpey, David J. Miller, James M. Estes, and Stephen A. Godleski*

Department of Chemistry, University of Rochester, Rochester, New York 14627

Received March 4, 1982

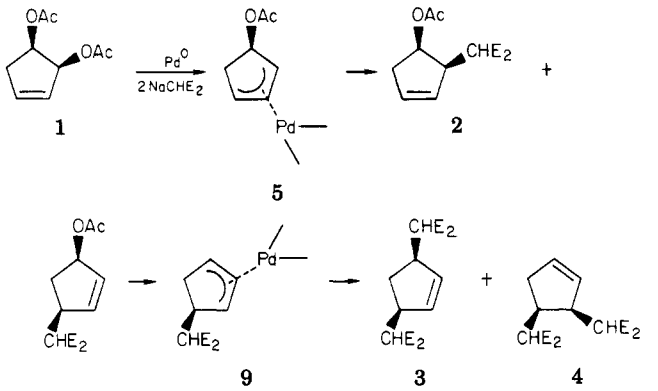
Sequential π-allyl alkylation reactions have been studied by using diallylic and allylic–homoallylic cyclopentenyl diesters as substrates. The regio- and stereochemistry of these reactions have been determined. The use of an acetate–pivalate diester allowed discrete addition of two different nucleophiles in this reaction.

We envisioned sequential π-allyl alkylation reactions as having the potential for considerable synthetic utility. To date, only a single example of such a process has been investigated, and it involved a discrete, two-step procedure for the construction of cyclopropanes.[1] Specifically, we sought the development and application of this methodology for the preparation of the five-membered ring containing antileukemic alkaloid cephalotaxine[2] as well as prostaglandin analogues.

The tandem π-allyl intermediates in this double alkylation process allow the two new bonds to be made with complete stereospecificity, their stereochemistry being dictated by the relative stereochemistry of the initial diallylic or allylic–homoallylic π-allyl precursor.[3] In addition, π-allyl alkylations are known[4] to tolerate a number of active electrophiles (e.g., carbonyl groups) in the key bond-forming steps, further widening the applicability of this process.

The use of a cyclopentene precursor to test the feasibility of this reaction, in addition to the indicated synthetic relevance, provides a particularly stringent challenge. This is based on our a priori analysis that the major competing reaction would be a base-induced elimination of HOR to give a diene, a process to which a cyclopentene substrate should be particularly susceptible.

Scheme I[a]



[a] E = $CO_2C_2H_5$.

Results and Discussion

Our investigation of sequential π-allyl alkylation reactions was initiated by using simple cyclopentene substrates in order to determine the viability of this process as well as to gain information regarding its regio- and stereochemistry.

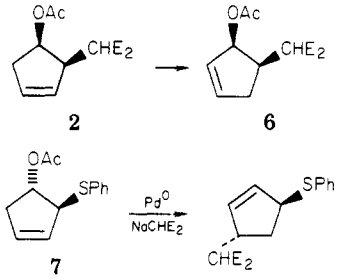
The bis(π-allyl) substrate *cis*-3,4-diacetoxycyclopent-1-ene (**1**)[5] was prepared by acetylation of the corresponding diol.[6] In principle, three products (**2**–**4**, Scheme I) could

(1) Genet, J. P.; Pian, F.; Ficini, J. *Tetrahedron Lett.* **1980**, *21*, 3183.
(2) Paudler, W. W.; Kerley, G. I.; McKay, J. *J. Org. Chem.* **1963**, *28*, 2194. Paudler, W. W.; McKay, J. *Ibid.* **1973**, *38*, 2110.
(3) Stereospecificity in π-allyl alkylation, i.e., complete retention of configuration with respect to the allylic C–X bond in nucleophilic addition: Trost, B. M.; Weber, L. *J. Am. Chem. Soc.* **1975**, *97*, 1611.
(4) Trost, B. M.; Dietsche, T. J.; Fullerton, T. J. *J. Org. Chem.* **1974**, *39*, 737.
(5) For the preparation of *cis*-3,4-diacetoxycyclopent-1-ene (1) see: Owen, L. N.; Smith, P. N. *J. Chem. Soc.* **1952**, 4035.

0022-3263/82/1947-4717$01.25/0

be obtained by reaction of 1 with a palladium(0) catalyst and 2 equiv of diethyl sodiomalonate.

In the event, however, treatment of 1 with a catalytic amount of $Pd(PPh_3)_4$ and 2 equiv of diethyl sodiomalonate in THF at 65 °C gave only the dimalonated material 3 (>90% yield). That no monoalkylated material (2) was formed can be attributed either to the remaining acetoxy in intermediate 5 sterically prohibiting attack at the proximal allyl terminus or to the ability of palladium to catalyze olefin isomerization in 2 to give 6 which can be reacted further. We have observed such isomerization in the precursor 7 which provided only 8 under comparable reaction conditions.



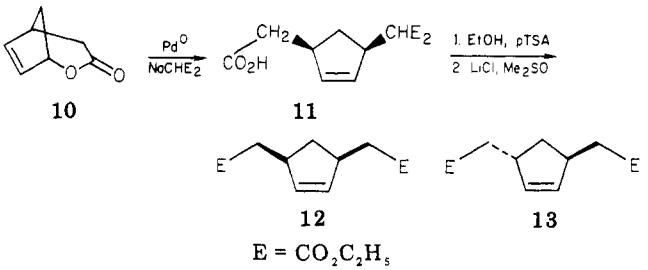
2 6 7 8

E = $CO_2C_2H_5$

The exclusive obtention of the dimalonated isomer 3 over 4 can be attributed to steric inhibition of attack on the allyl terminus proximal to the diethyl malonate in the second π-allyl intermediate, 9.

Performance of the necessary control reactions with identical reaction conditions except that no catalyst was added resulted in isolation of only unchanged starting material.

The regiochemistry of the dialkylation product 3 was obvious from the symmetry displayed in the ^1H and ^{13}C NMR. The stereochemistry of 3 was proven by independent chemical syntheses as follows. Treatment of the lactone, 4-oxabicyclo[3.2.1]oct-6-en-3-one (10),[7] with diethyl sodiomalonate and $Pd(PPh_3)_4$ in THF at 65 °C for 2 h provided the cis ester acid 11 as required by the overall



10 11 12 13

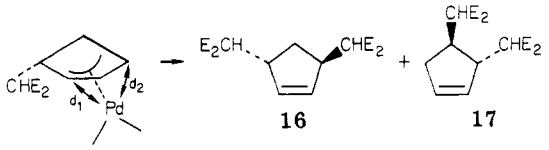
E = $CO_2C_2H_5$

retention of configuration known to be followed[3] in mono-π-allyl alkylations. Esterification (EtOH, pTSA) and decarboxylation (LiCl, Me_2SO) gave the cis diester 12. Preparation of the trans diester 13 was accomplished by reaction of 10 with diethyl sodiomalonate in THF (65 °C, 36 h) in the absence of Pd° catalyst, followed by esterification and decarboxylation.

The conversion of 3 to 12 was completed by decarboxylation (LiCl, Me_2SO). Conversion of 3 to 12 established 3 as the cis isomer, indicating the anticipated retention of configuration in the sequential π-allyl alkylation.

The *trans*-3,4- and *trans*-3,5-diacetoxycyclopent-1-enes (14 and 15)[8] were prepared from the corresponding diols. Reaction of either 14 or 15 with a catalytic amount of $Pd(PPh_3)_4$ and 2 equiv of diethylsodiomalonate in THF (65 °C) gave predominantly the *trans*-dimalonated product 16 (83%) along with a small amount of "1,2" material 17 (8%). The trans stereochemistry of 16 was confirmed by its decarboxylation (LiCl, Me_2SO) which was found to produce 13. The stereochemistry of 17 was not established but is assumed to be trans.

The predominance of the "1,3" dialkylation product 16 can be rationalized on the basis of an asymmetric ($d_2 > d_1$) π-allyl complex which is preferentially attacked on the terminus less closely associated with the Pd. Also, π-allyl alkylations are known to proceed predominantly[9,10] on the termini remote from an electronegative substituent.

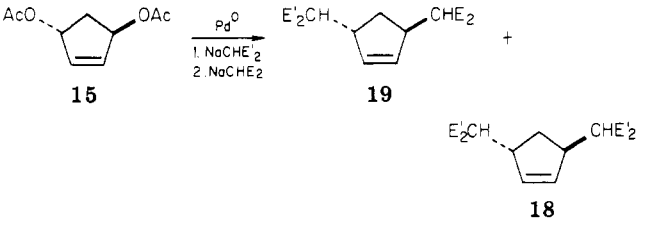


16 17

E = $CO_2C_2H_5$

Although only minor amounts of the more desirable (prostaglandin-like) trans-3,4 isomer 17 were obtained, the ability to sequentially add *two different* nucleophiles was still of interest as a means of extending the general synthetic utility of the methodology.

Reaction of the bis(π-allyl) precursor 15 with a catalytic amount of $Pd(PPh_3)_4$ and 1 equiv of dimethyl malonate followed when the first alkylation was complete by 1 equiv of diethyl malonate resulted in a 2:1 ratio of bis(dimethyl malonate) alkylated 18 to diethyl dimethyl dimalonated



15 19 18

E = CO_2CH_3, E = $CO_2C_2H_5$

material 19. Transesterification was ruled out by spectral analysis (^1H NMR and mass spectra) which revealed that no trimethyl or triethyl species were present. Attempts to achieve a higher percentage of 19 by variation of reaction conditions (time, temperature, catalyst, solvent) were uniformally unsuccessful.

In an effort to allow discrete alkylation of two different nucleophiles to proceed, we next pursued the use of two leaving groups differing in reactivity toward nucleophilic displacement by palladium. Previous results in our laboratory[11] indicated that an allylic pivalate was slower to alkylate than an allylic acetate and suggested that an allylic acetate–pivalate substrate might be successful in this regard.

(6) For the preparation of the *cis*-diol see: Korach, M.; Nielsen, D. R.; Rideout, W. H. *J. Am. Chem. Soc.* **1960**, *82*, 4328. DePuy, C. H.; Zaweski, E. F. *Ibid.* **1959**, *81*, 4920. Sable, H. Z.; Anderson, T.; Tolbert, B.; Posternak, T. *Helv. Chim. Acta* **1963**, *46*, 1157.

(7) Kende, A. S.; Chu, J. *J. Org. Chem.* **1973**, *38*, 2252.

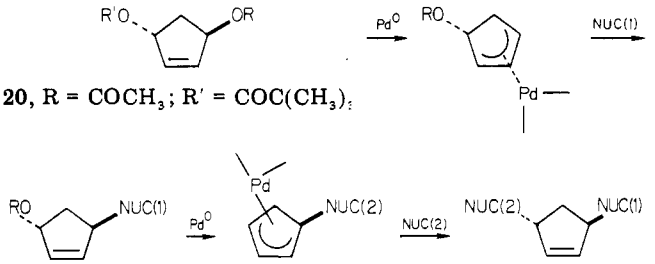
(8) For the preparation of the *trans*-diol see ref 6 and: Blumquist, A. T.; Mayes, W. G. *J. Org. Chem.* **1945**, *10*, 134. Tanaka, T.; Kurozumi, S.; Turu, T.; Milra, S.; Kobayashi, M.; Ishimoto, S. *Tetrahedron* **1976**, *32*, 1713. Korach, M.; Nielsen, D. R.; Rideout, W. H. *Org. Synth.* **1962**, *42*, 50.

(9) Tsuji, J.; Sakai, K.; Nagashima, H.; Shimizu, I. *Tetrahedron Lett.* **1981**, *22*, 131.

(10) Trost, B. M.; Molander, G. A. *J. Am. Chem. Soc.* **1981**, *103*, 5969.

(11) Comparison of reaction times and severity of reaction conditions in our spirocycle work indicated that allyl pivalates were less reactive than allylic acetates. See: Godleski, S. A.; Valpey, R. S. *J. Org. Chem.* **1982**, *47*, 381.

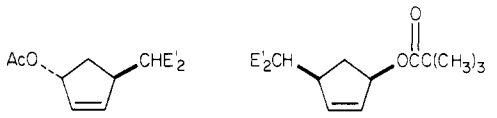
The allylic acetate–pivalate **20** was prepared from the corresponding diol. Reaction of **20** with 1 equiv of di-



20, R = $COCH_3$; R' = $COC(CH_3)_3$

methyl malonate, followed by 1 equiv of diethyl malonate under the usual Pd-catalyzed reaction conditions, gave the diethyl dimethyl dimalonated **19** and bis(dimethyl dimalonated) **18** in a 5:1 **19**/**18** ratio, largely realizing our goal. Small amounts (<5%) of 3,4-dialkylation products were observed spectroscopically but not isolated.

Quenching the reaction after monoalkylation revealed, however, that the predominant product present was the *allylic acetate* **21**![12] A possible partial rationale that we



21 **24**

E' = CO_2CH_3

can apply to this result is that the pivalate effectively screens the palladium from approach on the face opposite the acetate, prohibiting oxidative addition, but the suggested enhanced rate of pivalate displacement in **20** over acetate displacement in **15** remains puzzling.

Use of the *cis*-3-acetoxy-5-pivaloxy compound **22** resulted in increased selectivity for the methyl–ethyl dialkylation product **23** than that observed from the diacetate **1** (ratio increased from 1:1.4 to 3.8:1 in favor of **23**) but a much poorer overall yield (~40%). Attempted isolation of the monoalkylated intermediate **24** proved unexpectedly difficult, but ^1H NMR clearly indicated the *presence of pivalate and complete absence of acetate*, suggesting that the anticipated selectivity was now being realized. We expect the latter selectivity to be the usual case, and we are investigating this phenomenon in additional substrates.

Conclusions

Diallylic and allylic–homoallylic diesters have been found to be effective precursors for sequential π-allyl alkylations. The regio- and stereochemistry of this new palladium reaction have been determined. The use of acetate–pivalate allylic esters has allowed selective incorporation of two different nucleophiles in this reaction.

Experimental Section

General Methods. Infrared spectra were determined on a Perkin-Elmer PE 467 and are reported in reciprocal centimeters. ^1H NMR were recorded on a JEOLCO H-100 (100 MHz) or a Bruker WH-400 (400 MHz). Chemical shifts are reported in δ units and coupling constants in hertz, and splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; b, broad. ^{13}C NMR were recorded on a PFT-100 (25.2 MHz) with chemical shifts reported downfield from Me_4Si in parts per million. Mass spectra were recorded on a Du Pont 21-490B at an ionizing voltage of 20 eV. Melting points were determined on a Mel-Temp apparatus and are uncorrected. Microanalyses were performed by Galbraith Laboratories, Knoxville, TN. Medium-pressure liquid chromatography (MPLC) was done with Woelm silica gel (32–63 μm) in the indicated solvent. Et_2O, DME, and THF were distilled immediately before use from benzophenone ketyl. Pyridine, hexane, CH_2Cl_2, and NEt_3 were distilled from CaH_2.

Preparation of *cis*-3,5-Bis[bis(ethoxycarbonyl)methyl]-cyclopentene (3). *cis*-3,4-Diacetoxycyclopentene (0.36 g, 1.9 mmol) was dissolved in 2 mL of THF. To this were added tetrakis(triphenylphosphine)palladium(0) (0.9 g, 0.08 mmol) and 2 mL of a 2 M solution of diethyl sodiomalonate in THF. The reaction mixture was heated for 3 h at 65 °C. The mixture was cooled and filtered through Celite, and the solvent was removed under reduced pressure. The resulting oil was taken up in ethyl acetate, washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The mixture was purified by medium-pressure liquid chromatography on silica gel with ether/hexane (1:1) as the eluting solvent. The product was isolated in 90% yield (0.66 g): ^1H NMR (100 MHz, $CDCl_3$) 5.70 (s, 2 H), 4.10 (q, 8 H), 3.40 (m, 2 H), 3.30 (m, 2 H), 2.30 (m, 2 H), 1.25 (t, 12 H); ^{13}C NMR (25.15 MHz) ($CDCl_3$, Me_4Si) 14.1 (q), 32.9 (t), 44.9 (d), 57.2 (d), 61.3 (t), 133.3 (d), 168.3 (s); mass spectrum, *m/e* 396. Anal. Calcd for $C_{19}H_{28}O_8$: C, 59.37; H, 7.29. Found: C, 59.44; H, 7.32.

Preparation of *cis*-3,5-Bis[(ethoxycarbonyl)methyl]-cyclopentene (12). Preparation A. Compound **3** (0.37 g, 0.93 mmol) was dissolved in 5.6 mL of Me_2SO and 0.02 mL of water to which was added lithium chloride (0.16 g, 3.7 mmol). This mixture was heated at reflux for 8 h. The solution was cooled to room temperature, partitioned between ethyl acetate and water, washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The product was purified by medium-pressure liquid chromatography with ether/hexane (1:1) as the eluting solvent to give 0.18 g (80%) of a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) 5.69 (s, 2 H), 4.14 (q, 4 H), 3.09 (m, 2 H), 2.43 (m, 3 H), 2.21 (m, 2 H), 1.26 (t, 6 H), 1.08 (m, 1 H); literature values are in ref 13.

Preparation B. 4-Oxabicyclo[3.2.1]oct-6-en-3-one (0.15 g, 1.2 mmol) was reacted with diethyl sodiomalonate (0.6 mL of a 2 M solution) in THF in the presence of tetrakis(triphenylphosphine)palladium(0) (0.07 g, 0.06 mmol) catalyst. The reaction was complete in 2 h at 65 °C. The mixture was then partitioned between ethyl acetate and 10% H_2SO_4, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The product was immediately used in the next reaction. The diester acid (0.27 g, 0.98 mmol) was dissolved in benzene (5 mL) and ethanol (2 mL). A catalytic amount of *p*-toluenesulfonic acid was added, and the mixture was stirred at room temperature overnight. The solvent was removed at atmospheric pressure, and the residue was taken up in ethyl acetate, washed with H_2O, dried, and concentrated at reduced pressure. MPLC (hexane/ether, 1:1) yielded 0.25 g of the triester which was immediately used in the decarboxylation reaction. The triester (0.25 g, 0.8 mmol) was dissolved in 5 mL of Me_2SO and 0.5 mL H_2O, to which was added lithium chloride (0.10 g, 2.5 mmol). This mixture was heated at reflux for 6 h followed by partitioning between ethyl acetate and water. The organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The product was purified by medium-pressure liquid chromatography on silica gel with ether/hexane (1:1) to give 0.15 g (80%) of a colorless oil. The product exhibited spectral characteristics identical with those of the product from preparation A.

Preparation of *trans*-3,5-Bis[(ethoxycarbonyl)methyl]-cyclopentane (13). 4-Oxabicyclo[3.2.1]oct-6-en-3-one (0.42 g, 3.5 mmol) was reacted with diethyl sodiomalonate (4 mL, 1 M in THF) in 5 mL of refluxing THF for 36 h. The mixture was partitioned between ethyl acetate and 10% H_2SO_4, dried over

(12) Approximately 75% of the reaction mixture was the monoalkylated allylic acetate **21**, ~10% was the bis dimethylmalonated product, and a small amount (~10%) was the monoalkylated allylic pivalate.

(13) Trost, B. M.; Verhoeven, T. *J. Am. Chem. Soc.* **1980**, *102*, 4730.

(14) **Note Added in Proof**: After the submission of our manuscript a paper appeared by Backvall describing his efforts on diallylic systems other than cyclopentene: Backvall, J. E.; Nordberg, R. E.; Nystrom, J. E. *Tetrahedron Lett.* **1982**, *23*, 1617.

anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting crude diester acid (0.9 g, 3.2 mmol) was dissolved in benzene (10 mL) and ethanol (3 mL). A catalytic amount of *p*-toluenesulfonic acid was added, and the mixture was stirred at room temperature overnight. The mixture was taken up in ethyl acetate, washed with water, dried, and concentrated. The crude triester (0.9 g, 2.8 mmol) was dissolved in Me_3SO (10 mL) and H_2O (1 mL), to which was added lithium chloride (0.5 g, 1.2 mmol). The mixture was heated at reflux for 6 h. The resulting mixture was partitioned between ethyl acetate and water. The organic phase was dried over Na_2SO_4 and concentrated. The product was purified by MPLC with ether/hexane (1:1) as the eluting solvent to yield 0.35 g (43%) of **13** as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) 5.72 (s, 2 H), 4.13 (q, 4 H), 3.25 (m, 2 H), 2.32 (m, 4 H), 1.79 (t, 2 H), 1.26 (t, 6 H).

***trans*-3,5-Bis[bis(ethoxycarbonyl)methyl]cyclopent-1-ene (16).** *trans*-3,5-Diacetoxycyclopentene (**15**; 0.325 g, 1.77 mmol) and $Pd(PPh_3)_4$ (0.196 g, 0.17 mmol) were dissolved in 1 mL of distilled THF. To this solution was added diethyl sodiomalonate (3.5 mL, 1.0 M in THF). The mixture was heated at reflux under an N_2 atmosphere for 4 h and cooled to room temperature, and the THF was removed at reduced pressure. The residue was dissolved in ether, washed with brine, dried over anhydrous $MgSO_4$, and concentrated at reduced pressure. The product was purified by MPLC with ether/hexane (1:6) as the eluting solvent, affording 0.581 g (83%) of **16** as colorless oil: NMR ($CDCl_3$) 5.7 (s, 2 H), 4.1 (q, 8 H, J = 7.4 Hz), 3.3 (m, 2 H), 1.9 (t, 2 H), 1.2 (t, 12 H, J = 7.4 Hz); ^{13}C NMR ($CDCl_3$) 168, 133, 61, 56.5, 56.0, 44, 14; IR (CCl_4) 29.0, 1735; mass spectrum, m/e 184. Anal. Calcd for $C_{19}H_{28}O_8$: C, 59.37; H, 7.29. Found: C, 59.36; H, 7.42.

***trans*-3-Acetoxy-5-pivaloxycyclopent-1-ene (20).** *trans*-3,5-Dihydroxycyclopent-1-ene (0.389 g, 3.89 mmol) was dissolved in 5 mL of CH_2Cl_2 containing 0.7 mL (3.89 mmol) of triethylamine. Freshly distilled trimethyl acetic anhydride (0.72 mL, 3.57 mmol) was then added, followed by *N*-(dimethylamino)pyridine (0.43 g, 3.57 mmol). The mixture was stirred at room temperature for 4 h, and then the solvent was removed under reduced pressure. The residue was dissolved in ethyl acetate (20 mL), extracted with brine, dried over anhydrous Na_2SO_4, and concentrated. The crude product was subjected to MPLC (ether/hexane, 1:5), yielding 0.386 (2.1 mmol) of *trans*-3-hydroxy-5-pivaloxycyclopent-1-ene (42%). This compound was immediately subjected to acetylation under the following conditions. The alcohol ester (0.054 g, 0.29 mmol) was dissolved in 1 mL of CH_2Cl_2. Triethylamine (42 μL, 0.30 mmol), acetic anhydride (28 μL, 0.30 mmol), and *N*-(dimethylamino)pyridine (0.004 g, 0.03 mmol) were then added, and the mixture was stirred at room temperature for 3 h. The solvent was removed by evaporation at reduced pressure. The residue was taken up in 10 mL of ethyl acetate, washed with H_2O (5 mL), dried over anhydrous $MgSO_4$, and concentrated, yielding a colorless oil: 0.06 g (99%); ^1H NMR ($CDCl_3$) 6.2 (s, 2 H), 5.8 (t, 2 H, J = 4 Hz), 2.2 (t, 2 H, J = 4 Hz), 2.0 (s, 3 H), 1.1 (s, 9 H); IR (CCl_4) 2860, 1735; mass spectrum, m/e 167.

***cis*-3-Acetoxy-5-pivaloxycyclopent-1-ene (22).** The cis diester **22** was prepared in a fashion identical with that for **20** by starting with the corresponding diol.[6] *cis*-3,5-Dihydroxycyclopentene (2.76 mmol) gave 0.25 g (40%) of **22**: ^1H NMR ($CDCl_3$) 6.0 (s, 2 H), 5.5 (br s, 2 H), 2.8 (dt, 1 H), J = 15, 7.5 Hz), 2.0 (s, 3 H), 1.6 (dt, J = 15, 4 Hz), 1.1 (s, 9 H); IR (CCl_4) 2860, 1735; mass spectrum, m/e 167.

***trans*-3-[Bis(ethoxycarbonyl)methyl]-5-[bis(methoxycarbonyl)methyl]cyclopent-1-ene (19).** *trans*-3-Acetoxy-5-pivaloxycyclopent-1-ene (**20**; 0.042 g, 0.18 mmol) and $Pd(PPh_3)_4$ (0.01 g, 0.009 mmol) were dissolved in 1 mL of THF. To this mixture was added a DME solution of dimethyl sodiomalonate (0.38 mL, 0.49 M solution). The solution was then heated at 60 °C for 3 h under a N_2 atmosphere. The reaction mixture was cooled to room temperature, diethyl sodiomalonate (0.5 mL, 2.1 M in THF) was added, and the solution was heated at reflux for 4 h. The mixture was cooled, concentrated at reduced pressure, and dissolved in ether (20 mL). The ether was washed with H_2O (10 mL), dried over anhydrous $MgSO_4$, and concentrated. The resulting product mixture was subjected to MPLC (ether/hexane, 1:3). The isolated yields were as follows: *trans*-3,5-bis[bis(ethoxycarbonyl)methyl]cyclopent-1-ene (**16**), 5 mg (0.018 mmol, 10%); *trans*-3,5-bis[bis(methoxycarbonyl)methyl]cyclopent-1-ene (**18**), 4 mg (0.017 mmol, 9%); *trans*-5-[bis(methoxycarbonyl)-methyl]cyclopent-1-ene (**19**), 35 mg (0.098 mmol, 54%).

The spectral data for **19** were as follows: ^1H NMR ($CDCl_3$) 5.7 (s, 2 H), 4.1 (q, 4 H, J = 7 Hz), 3.7 (s, 6 H), 3.3 (m, 4 H), 1.9 (m, 2 H), 1.2 (t, 6 H, J = 7 Hz); IR (CCl_4) 2890, 1735; mass spectrum, m/e 356. Anal. Calcd for $C_{17}H_{24}O_8$: C, 57.30; H, 6.74. Found: C, 57.38; H, 6.91.

***cis*-3-[Bis(ethoxycarbonyl)methyl]-5-[bis(methoxycarbonyl)methyl]cyclopent-1-ene (23)** was prepared in a manner exactly analogous to **19**. The isolated yields of the product mixture starting with 74 mg of *cis*-3-acetoxy-5-pivaloylcyclopentene were as follows: **3**, 7 mg (0.018 mmol, 5.5%); *cis*-3,5-bis[bis(methoxycarbonyl)methyl]cyclopentene, 6 mg (0.026 mmol, 7.9%); **23**, 36 mg (0.101 mmol, 30%).

The spectral data were for **23** as follows: ^1H NMR ($CDCl_3$) 5.7 (s, 2 H), 4.1 (q, 4 H, J = 7 Hz), 3.7 (s, 6 H), 3.3 (m, 4 H), 2.3 (m, 1 H), 1.2 (t, m, 7 H, J = 7 Hz); IR (CCl_4) 2196, 1735; mass spectrum, m/e 356. Anal. Calcd for $C_{17}H_{24}O_8$: C, 57.30; H, 6.74. Found: C, 57.50; H, 6.81.

Acknowledgment. We gratefully acknowledge the agencies that supported this research [NIH (Grant No. GM 27328), the Merck Foundation, CIBA-GEIGY Corp.] and a Weizmann Postdoctoral Fellowship to D.J.M.

Registry No. **1**, 78796-68-6; **3**, 83219-62-9; **10**, 5650-65-7; **11**, 83219-63-0; **12**, 83219-64-1; **13**, 83219-65-2; **15**, 59415-74-6; **16**, 83219-66-3; **17**, 83219-67-4; **18**, 83219-68-5; **19**, 83219-69-6; **20**, 83219-70-9; **22**, 83219-71-0; **23**, 83219-72-1; $Pd(PPh_3)_4$, 14221-01-3; $NaCH(CO_2C_2H_5)_2$, 996-82-7; $NaCH(CO_2CH_3)_2$, 18424-76-5; *cis*-3-[bis(ethoxycarbonyl)methyl]-5-[(ethoxycarbonyl)methyl]cyclopentene, 83219-73-2; *trans*-3,5-dihydroxycyclopent-1-ene, 694-47-3; *trans*-3-hydroxy-5-pivaloxycyclopent-1-ene, 83219-74-3; *cis*-3,5-dihydroxycyclopentene, 29783-26-4; *cis*-3,5-bis[bis(methoxycarbonyl)-methyl]cyclopentene, 83219-75-4.