(100 mL), washed with water (10 mL) and brine (10 mL), dried, filtered, and concentrated. The crude product was purified by flash chromatography on silica gel to yield 26.8 mg (91%) of **63** as a colorless glass: IR (film, cm^{-1}) 1685; ^1H NMR (300 MHz, $CDCl_3$) δ 4.36 (t, J = 8.7 Hz, 1 H), 3.63 (dd, J = 11.1, 2.6 Hz, 1 H), 3.32 (d, J = 11.1 Hz, 1 H), 2.72 (d, J = 19.2 Hz, 1 H), 2.53 (dd, J = 19.2, 2.6 Hz, 1 H), 2.43-2.35 (m, 1 H), 2.32 (d, J = 1.6 Hz, 3 H), 2.18-2.12 (m, 2 H), 1.77-1.15 (series of m, 6 H), 1.55 (s, 2 H), 1.48 (s, 3 H), 1.38 (s, 3 H), 0.98 (s, 3 H), 0.95-0.85 (m, 2 H), 0.77 (d, J = 6.4 Hz, 3 H), 0.73-0.64 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 205.8, 153.6, 132.9, 99.4, 71.9, 68.5, 54.5, 48.7, 44.3, 39.9, 38.5, 36.5, 36.2, 35.9, 31.8, 31.0, 30.5, 29.8, 20.8, 20.7, 20.0, 19.2, 18.2; MS m/z (M^+) calcd 358.2508, obsd 358.2514. Anal. Calcd for $C_{23}H_{34}O_3 \cdot 0.5(C_2H_5)_2O$: C, 75.91; H, 9.94. Found: C, 75.95; H, 9.67.

(2a*R,3*S**,4a*S**,7*R**,7a*S**,10b*R**,10c*S**)-2a,3,4,4a,5,6,7,7a,8,9,-10b,10c-Dodecahydro-3-hydroxy-2a-(hydroxymethyl)-7,10,10c-trimethylnaphth[2,1,8-*cde*]azulen-1(2*H*)-one (64).** A mixture of **63** (36.5 mg, 0.1 mmol), pyridinium *p*-toluenesulfonate (15 mg, 0.06 mmol), and methanol (5 mL) was stirred at ambient temperature for 4 h, quenched with 10 drops of saturated $NaHCO_3$ solution, and concentrated. The residue was taken up in ether (25 mL), washed with brine (2 × 5 mL), dried, filtered, concentrated, and purified on a silica gel column to yield 32 mg (100%) of **64** as a colorless glass: IR ($CHCl_3$, cm^{-1}) 3610, 3470 (br), 1690; ^1H NMR (300 MHz, $CDCl_3$) δ 3.92 (d, J = 11.0 Hz, 1 H), 3.87 (dd, J = 13.4, 6.8 Hz, 1 H), 3.46 (br d, J = 11.0 Hz, 1 H), 3.29 (br s, 1 H), 2.96 (d, J = 1.6 Hz, 1 H), 2.87 (br s, 1 H), 2.56-2.46 (m, 2 H), 2.26-2.20 (m, 1 H), 2.17 (d, J = 2.1 Hz, 3 H), 1.85-1.23 (series of m, 10 H), 1.06 (s, 3 H), 0.98-0.87 (m, 1 H), 0.81 (d, J = 6.3 Hz, 3 H), 0.86-0.78 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 205.8, 152.5, 132.1, 73.3, 69.4, 52.2, 51.2, 47.9, 44.8, 40.2, 39.0, 38.5, 35.8, 35.3, 31.4, 29.4, 20.9, 20.8, 20.6, 15.9; MS m/z (M^+) calcd 318.2195, obsd 318.2172. Anal. Calcd for $C_{20}H_{30}O_3 \cdot 0.25H_2O$: C, 74.37; H, 9.52. Found: C, 74.22; H, 9.39.

(2a*R,3*S**,4a*S**,7*R**,7a*S**,10b*R**,10c*S**)-2a,3,4,4a,5,6,7,7a,8,9,-10b,10c-Dodecahydro-3-hydroxy-2a,7,10,10c-tetramethylnaphth[2,1,8-*cde*]azulen-1(2*H*)-one (10).** Diol **64** (20 mg, 0.06 mmol) and DBN (30 μL, 0.24 mmol) were dissolved in DMF (0.5 mL). Carbon disulfide (0.5 mL) was added, and the reaction mixture was stirred at ambient temperature under nitrogen for 1 h. After the introduction of methyl iodide (0.5 mL), stirring was continued for an additional hour prior to concentration in vacuo. The residue was partitioned between ethyl acetate (25 mL) and water (5 mL), and the organic phase was washed with brine (5 mL), dried, filtered, concentrated, and purified on a silica gel column to yield 18 mg (74%) of the xanthate as a light brown glass: ^1H NMR (300 MHz, $CDCl_3$) δ 4.86 (d, J = 11.1 Hz, 1 H), 4.44 (d, J = 11.1 Hz, 1 H), 3.90 (m, 1 H), 2.83 (br s, 1 H), 2.55 (s, 3 H), 2.50-2.30 (series of m, 3 H), 2.22 (d, J = 1.9 Hz, 3 H), 1.66-1.11 (series of m, 10 H), 1.07 (s, 3 H), 1.01-0.85 (series of m, 3 H), 0.80 (d, J = 6.4 Hz, 3 H).

To a solution of this xanthate (18 mg, 0.044 mmol) in 2 mL of toluene were added 21 μL (0.066 mmol) of tris(trimethylsilyl)silane and 2.5 mg (0.015 mmol) of AIBN. The mixture was stirred for 2 h at 110 °C under nitrogen, cooled, and evaporated in vacuo. The residue was purified on a silica gel column to yield 5 mg (38%) of **10** as a colorless syrup: IR ($CHCl_3$, cm^{-1}) 3475, 1690; ^1H NMR (300 MHz, $CDCl_3$) δ 4.05 (dd, J = 8.4, 7.9 Hz, 1 H), 2.59 (d, J = 18.3 Hz, 1 H), 2.44-2.36 (m, 1 H), 2.32 (s, 3 H), 2.20-2.17 (m, 1 H), 2.01 (d, J = 18.3 Hz, 1 H), 1.79-1.19 (series of m, 11 H), 1.15 (s, 3 H), 0.94-0.86 (m, 1 H), 0.90 (s, 3 H), 0.77 (d, J = 6.4 Hz, 3 H), 0.73-0.68 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 206.2, 153.2, 133.4, 72.0, 60.2, 49.1, 48.1, 41.7, 39.1, 36.6, 36.2, 36.0, 35.4, 31.7, 30.4, 30.3, 20.8, 20.8, 20.2, 17.6; MS m/z (M^+) calcd 302.2246, obsd 302.2241.

(2a*R,3*S**,4a*S**,7*R**,7a*S**,10a*S**,10b*R**,10c*S**)-Tetradecahydro-3-hydroxy-2a,7,10c-trimethyl-10-methylenenaphth[2,1,8-*cde*]azulen-1-(2*H*)-one (66).** A solution of **10** (5 mg, 0.017 mmol) in absolute ethanol (2 mL) was cooled to 0 °C, treated with benzeneselenol in ethanol (100 μL of 0.52 M, 0.052 mmol), and stirred at this temperature for 1 h. The reaction mixture was partitioned between ether (100 mL) and water (10 mL), and the ether layer was washed with brine (10 mL), dried, concentrated, and redissolved in THF (10 mL). This yellow solution was cooled to 0 °C, treated with 100 μL of 30% hydrogen peroxide, and allowed to warm to room temperature over 12 h. Dilution with ether (50 mL) was followed by washing with saturated $NaHCO_3$ solution (10 mL) and brine (10 mL), drying, and concentration. Chromatography of the residue on silica gel (elution with 25% ethyl acetate in petroleum ether) returned 1 mg of **10** along with 3 mg (60%) of **66** as a colorless syrup: IR ($CHCl_3$, cm^{-1}) 3500, 3320, 1730; ^1H NMR (300 MHz, $CDCl_3$) δ 5.60-5.45 (m, 2 H), 3.85 (s, 1 H), 3.58 (d, J = 10.5 Hz, 1 H), 2.29 (d, J = 14 Hz, 1 H), 2.12 (d, J = 14 Hz, 1 H), 1.75 (s, 1 H), 1.70-1.20 (series of m, 14 H), 1.23 (s, 3 H), 1.00 (s, 3 H), 0.01 (d, J = 6.3 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 217.3, 149.7, 117.1, 71.3, 61.7, 55.5, 53.1, 51.6, 40.8, 37.4, 36.2, 33.8, 33.1, 31.1, 29.4, 27.6, 25.1, 23.8, 20.6, 17.0.

Rhodium Trichloride-Catalyzed Isomerization of 66. A mixture of **66** (3 mg, 0.01 mmol) and rhodium trichloride heptahydrate (2 mg) in 1 mL of ethanol was heated to reflux for 3 h, cooled, diluted with ether (20 mL), and filtered through a small plug of silica gel to yield 1.25 mg of material identical to **10** by 300-MHz ^1H NMR.

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Supplementary Material Available: Crystallographic experimental procedure, solution and refinement of the structure, crystallographic details, tables of refined temperature factors, positional parameters, bond angles, and bond distances, and a diagram of the unit cell for **24** together with the final calculated (MM2) atomic coordinates for **10**, **11**, **66**, and **67** (21 pages). Ordering information is given on any current masthead page.

Stereocontrolled Access to the Most Highly Condensed Pentalenolactone Antibiotic. From Cycloheptatriene to Pentalenolactone P Methyl Ester

Leo A. Paquette,* Ho-Jung Kang, and Choon Sup Ra

Contribution from the Evans Chemical Laboratories, The Ohio State University, Columbus, Ohio 43210. *Received April 6, 1992*

Abstract: The first total synthesis of the title compound (**3b**) has been accomplished. Besides the immediate establishment of the trans cyclopropane–lactone relationship by an appropriate Diels–Alder reaction, other notable transformations include the regioselective chain-lengthening to generate **23**, oxadi-π-methane rearrangement, lactone ring construction by an intramolecular Michael reaction–oxidation sequence, and use of monomeric formaldehyde to introduce the final carbon atom. The chemistry outlined defines a strategy that is highly stereocontrolled and completely tolerant of a sterically congested cyclopropane ring that is carried through to the target from the very first step.

The assignment of structure and absolute configuration to pentalenolactone (**1**) was accomplished in 1969.[1] In the ensuing years, the broad spectrum of antibacterial,[2] antiviral,[3] and irreversible enzyme inactivator properties[4] of this sesquiterpene lactone

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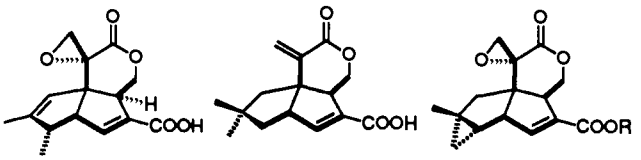
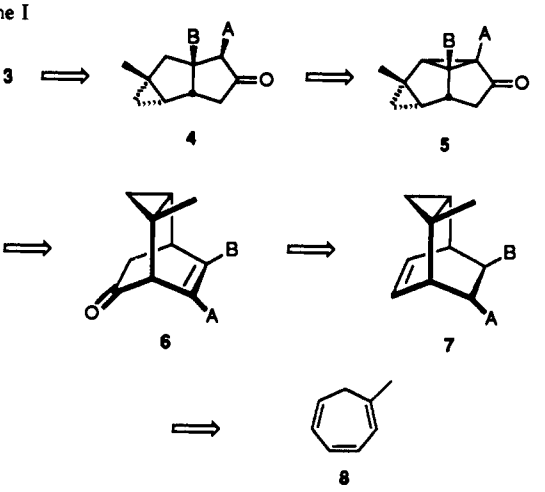
became recognized. These developments ushered in an era of notably innovative biosynthetic and preparative studies,[5,6] the underlying purposes of which have been to uncover the full potential of the *Streptomyces* species responsible for the production of various metabolites and to develop expedient laboratory routes to them.[7] The discovery of pentalenene, the parent hydrocarbon of the family,[8,9] and pentalenic acid, a less oxygenated precursor,[10,11] followed soon thereafter. More recently, the isolation and structure determination of pentalenolactones A,[12] B,[12] D,[12] E (**2**),[13,14] F,[12,15] G,[16] H,[10a] O,[17] and P[17] have been disclosed.

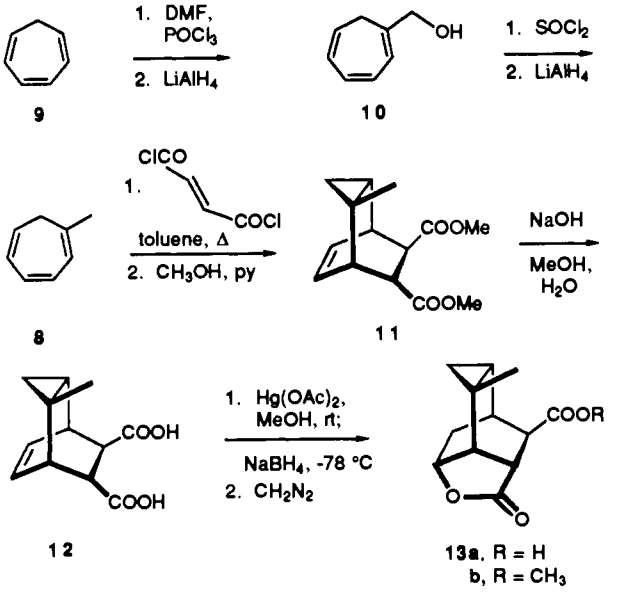


1 **2** **3a**, R = H; **b**, R = CH_3

Scheme I



Scheme II



Our interest in this class of compounds stems from their significant biological activity and their unusual structural features. In the latter context, pentalenolactone P (**3a**) has attracted particular attention since it represents the first of the pentalenolactones to contain a cyclopropane ring. Moreover, the enzymatic dehydrogenation responsible for elaboration of the three-membered ring[8f] has positioned it on the highly congested concave

(1) (a) Takeuchi, S.; Ogawa, Y.; Yonehara, H. *Tetrahedron Lett.* **1969**, 2737. (b) Martin, D. G.; Slomp, G.; Mizsak, S.; Duchamp, D. J.; Chidester, C. G. *Tetrahedron Lett.* **1970**, 4901. (c) Duchamp, D. J.; Chidester, C. G. *Acta Crystallogr. Sect. B* **1972**, *28*, 173.

(2) (a) Koe, B. K.; Sobin, B. A.; Celmer, W. D. *Antibiot. Annu.* **1957**, 672. (b) English, A. R.; McBride, T. J.; Lynch, J. E. *Antibiot. Annu.* **1957**, 682.

(3) Nakagawa, A.; Tomoda, H.; Hao, M. V.; Okano, K.; Iwai, Y.; Omura, S. *J. Antibiot.* **1985**, *38*, 1114.

(4) Cane, D. E.; Songh, J.-K. *Arch. Biochem. Biophys.* **1989**, *270*, 50 and relevant references cited therein.

(5) Biosynthesis: (a) Cane, D. E.; Rossi, T.; Pachlatko, J. P. *Tetrahedron Lett.* **1979**, 3639. (b) Cane, D. E.; Rossi, T.; Tillman, A. M.; Pachlatko, J. P. *J. Am. Chem. Soc.* **1981**, *103*, 1838. (c) Takahashi, S.; Takeuchi, M.; Arai, M.; Seto, H.; Otake, N. *J. Antibiot.* **1983**, *36*, 226. (d) Maurer, K. H.; Mecke, D. *J. Antibiot.* **1986**, *39*, 266.

(6) Synthesis: (a) Danishefsky, S.; Hirama, M.; Gombatz, K.; Harayama, T.; Berman, E.; Schuda, P. F. *J. Am. Chem. Soc.* **1978**, *100*, 6536; **1979**, *101*, 7020. (b) Parsons, W. H.; Schlessinger, R. H.; Quesada, M. L. *J. Am. Chem. Soc.* **1980**, *102*, 889. (c) Parsons, W. H.; Schlesinger, R. H. *Bull. Soc. Chim. Fr.* **1980**, 327. (d) Ohtsuka, T.; Shirahama, H.; Matsumoto, T. *Chem. Lett.* **1984**, 1923.

(7) Reviews: (a) Paquette, L. A. *Top. Curr. Chem.* **1984**, *119*, 1. (b) Paquette, L. A.; Doherty, A. M. *Polyquinane Chemistry*; Springer-Verlag: Heidelberg, 1987; Chapters 8 and 9.

(8) Isolation and biosynthesis: (a) Seto, H.; Yonehara, H. *J. Antibiot.* **1980**, *33*, 92. (b) Cane, D. E.; Tillman, A. M. *J. Am. Chem. Soc.* **1983**, *105*, 122. (c) Cane, D. E.; Abell, C.; Tillman, A. M. *Bioorg. Chem.* **1984**, *12*, 312. (d) Cane, D. E.; Abell, C.; Lattman, R.; Kane, C. T.; Hubbard, B. R.; Harrison, P. H. M. *J. Am. Chem. Soc.* **1988**, *110*, 4081. (e) Harrison, P. H. M.; Oliver, J. S.; Cane, D. E. *J. Am. Chem. Soc.* **1988**, *110*, 5922. (f) Cane, D. E.; Oliver, J. S.; Harrison, P. H. M.; Abell, C.; Hubbard, B. R.; Kane, C. T.; Lattman, R. *J. Am. Chem. Soc.* **1990**, *112*, 4513.

(9) Synthesis: (a) Annis, G. D.; Paquette, L. A. *J. Am. Chem. Soc.* **1982**, *104*, 4504. (b) Paquette, L. A.; Annis, G. D. *J. Am. Chem. Soc.* **1983**, *105*, 7358. (c) Pattenden, G.; Teague, S. J. *Tetrahedron Lett.* **1984**, *25*, 3021. (d) Piers, E.; Karunaratne, V. *J. Chem. Soc., Chem. Commun.* **1984**, 959. (e) Crimmins, M. T.; DeLoach, J. A. *J. Am. Chem. Soc.* **1986**, *108*, 800. (f) Mehta, G.; Rao, K. S. *J. Chem. Soc., Chem. Commun.* **1985**, 1464. (g) Hua, D. H. *J. Am. Chem. Soc.* **1986**, *108*, 3835. (h) Mehta, G.; Rao, K. S. *J. Am. Chem. Soc.* **1986**, *108*, 8015. (i) Imanishi, T.; Ninbari, F.; Yamashita, M.; Iwata, C. *Chem. Pharm. Bull.* **1986**, *34*, 2268. (j) Hudlicky, T.; Natchus, M. G.; SInai-Zingde, G. *J. Org. Chem.* **1987**, *52*, 4641. (k) Imanishi, T.; Munetaka, M.; Ninbari, F.; Yamashita, M.; Iwata, C. *Chem. Pharm. Bull.* **1988**, *36*, 1371. (l) Schore, N. E.; Rowley, E. G. *J. Am. Chem. Soc.* **1988**, *110*, 5224. (m) Pattenden, G.; Teague, S. J. *Tetrahedron* **1987**, *43*, 5637. (n) Hudlicky, T.; Sinai-Zingde, G.; Natchus, M. G.; Ranu, B. C.; Papadopoluos, P. *Tetrahedron* **1987**, *43*, 5685. (o) Ihara, M.; Katogi, M.; Fukumoto, K.; Kametani, T. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2963. (p) Piers, E.; Karunaratne, V. *Can. J. Chem.* **1989**, *67*, 160. (q) Imanishi, T.; Yameshita, M.; Hirokawa, Y.; Tanaka, T.; Iwata, C. *Chem. Pharm. Bull.* **1990**, *38*, 1124. (r) Shizuri, Y.; Maki, S.; Ohkubo, M.; Yamamura, S. *Tetrahedron Lett.* **1990**, *21*, 7167. (s) Wu, Y. J.; Burnell, D. J. *J. Chem. Soc., Chem. Commun.* **1991**, 764.

(10) Isolation and biosynthesis: (a) Seto, H.; Sasaki, T.; Uzawa, J.; Takeuchi, S.; Yonehara, H. *Tetrahedron Lett.* **1978**, 4411. (b) Sakai, K.; Ohtsuka, T.; Misumi, S.; Shirahama, H.; Matsumoto, T. *Chem. Lett.* **1981**, 355.

(11) Synthesis: (a) Consult ref 9n,o. (b) Crimmins, M. T.; DeLoach, J. A. *J. Org. Chem.* **1984**, *49*, 2076. (c) Ihara, M.; Katogi, M.; Fukumoto, K.; Kametani, T. *J. Chem. Soc., Chem. Commun.* **1987**, 721. (d) Agnel, G.; Negishi, E. *J. Am. Chem. Soc.* **1991**, *113*, 7424.

(12) Cane, D. E.; Sohng, J.-K.; Williard, P. G. *J. Org. Chem.* **1992**, *57*, 845.

(13) Isolation and biosynthesis: (a) Cane, D. E.; Rossi, T. *Tetrahedron Lett.* **1979**, 2973. (b) Murata, Y.; Ohtsuka, T.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1981**, 4313.

(14) Synthesis: (a) Paquette, L. A.; Schostarez, H.; Annis, G. D. *J. Am. Chem. Soc.* **1981**, *103*, 6526. (b) Paquette, L. A.; Annis, G. D.; Schostarez, H. *J. Am. Chem. Soc.* **1982**, *104*, 6646. (c) Ohtsuka, T.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1983**, *24*, 3851. (d) Cane, D. E.; Thomas, P. J. *J. Am. Chem. Soc.* **1984**, *106*, 5295. (e) Taber, D. F.; Schuchardt, J. L. *J. Am. Chem. Soc.* **1985**, *107*, 5289. (f) Marino, J. P.; Silveira, C.; Comasseto, J.; Petragnani, N. *J. Org. Chem.* **1987**, *52*, 4139. (g) Taber, D. F.; Schuchardt, J. L. *Tetrahedron* **1987**, *43*, 5677. (h) Hua, D. H.; Coulter, M. J.; Badejo, I. *Tetrahedron Lett.* **1987**, *28*, 5465. (i) Mori, K.; Tsuji, M. *Tetrahedron* **1988**, *44*, 2835.

(15) (a) Reference 14d. (b) Tillman, A. M.; Cane, D. E. *J. Antibiot.* **1983**, *36*, 170. (c) Seto, H.; Noguchi, H.; Sankawa, U.; Iitaka, Y. *J. Antibiot.* **1984**, *37*, 816. (d) Williard, P. G.; Sohng, J. K.; Cane, D. R. *J. Antibiot.* **1988**, *41*, 130.

(16) (a) Reference 15c. (b) Seto, H.; Sasaki, T.; Yonehara, H.; Uzawa, J. *Tetrahedron Lett.* **1978**, 923. (c) Ohtsuka, T.; SHirahama, H.; Matsumoto, T. *Chem. Lett.* **1984**, 1923. (d) Pirrung, M. C.; Thomson, S. A. *J. Org. Chem.* **1988**, *37*, 227.

(17) Seto, H.; Sasaki, T.; Yonehara, H.; Takahashi, S.; Takeuchi, M.; Kuwano, H.; Arai, M. *J. Antibiot.* **1984**, *37*, 1076.

surface of the core diquinane framework. The challenge offered by this unusual structural feature and the possible role of **3a** as precursor to a tertiary carbocation centrally important to production of other pentalenolactones[8d] prompted us to undertake the first synthesis of this highly functionalized pentacyclic lactone as its stable methyl ester **3b**. An effective strategy for the fully stereocontrolled elaboration of this distinctive natural product is detailed herein.[18]

Results and Discussion

Any synthesis of **3** must deal with the key stereochemical issue of setting the requisite trans relationship of the cyclopropane and lactone rings. Elements of stereoelectronic control were considered in the retrosynthetic analysis, such that the regioselectivity observed during the reductive cleavage of ketones related to **5**[19] could be utilized to an advantage (Scheme I). Since the oxadi-π-methane rearrangement provides convenient access to tricyclooctanones of this general type,[20] application of this photoisomerization would require the availability of **6** as the β,γ-unsaturated ketone precursor. In analogy with less highly substituted examples, the expectation was that the conversion of **6** to **5** would proceed with full retention of stereochemistry.

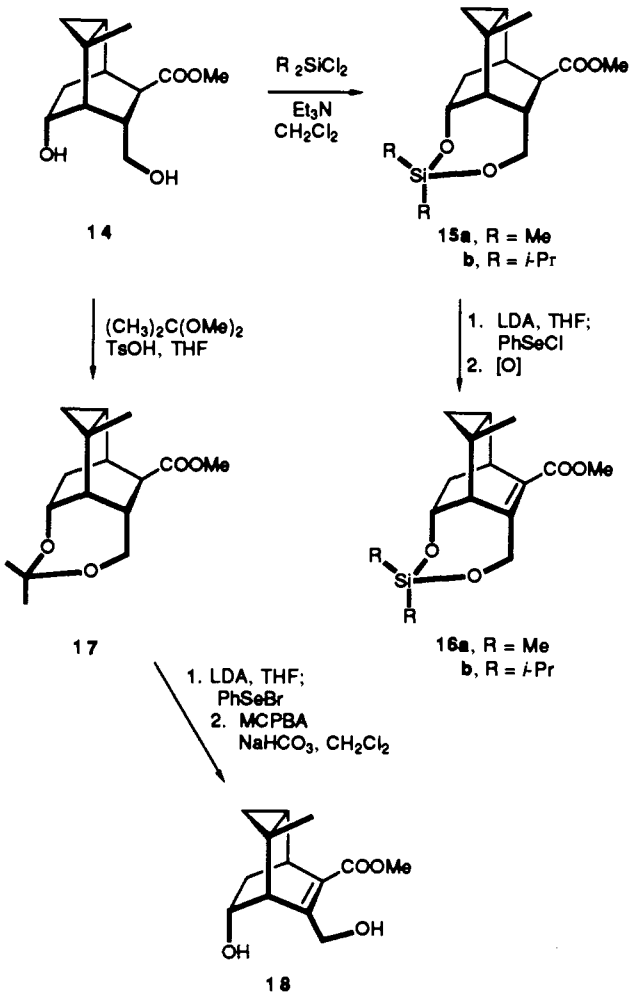
This being the case, a practical method of elaborating **6** from 1-methylcycloheptatriene (**8**) was visualized. As a class, cycloheptatrienes participate in Diels–Alder reactions by prior electrocyclization to their norcaradiene valence tautomers.[21] The use of a sufficiently reactive 2π reagent was, of course, mandated. Beyond that, the substituents present on the dienophile were required to be chemically distinguishable at a suitably advanced stage of molecular construction. This limitation proved to be nontrivial. In preliminary experiments, **8** was found to be quite inert as a Diels–Alder diene. Consequently, only highly reactive dienophiles were serviceable.

Synthetic Studies Preparatory to Photorearrangement. 1-Methylcyclopheptatriene (**8**) was prepared by an adaptation of Kato's method,[22] which proceeds via Vilsmeier formylation of cycloheptatriene (**9**) and stepwise reduction of the resultant 1-carboxaldehyde (Scheme II). Condensation of **8** with fumaryl chloride was initially accomplished in CH_2Cl_2 solution under high-pressure conditions (150 000 psi). Direct treatment of the product with methanol containing pyridine eventuated in the efficient isolation (80%) of pure diester **11**.[23] This Diels–Alder reaction could be accomplished somewhat less efficiently (50%) in refluxing toluene. Since the latter conditions proved more amenable to scale-up, large amounts of **11** were prepared in this way.

With **11** in hand, its ester groups were distinguished by saponification to **12** and oxymercuration. In this way, the steric role of the methyl substituent on the stereochemical course of the [4 + 2] cycloaddition was parlayed to considerable advantage. Thus, the proximal endo carbonyl was thereby transformed uniquely into a lactone subunit. Furthermore, a single carbon atom of the etheno bridge was now suitably oxygenated.

Lactone **13b** is a rather strained molecule. As a consequence, smooth conversion to diol **14** could be achieved with sodium borohydride. Protection of the hydroxyl groups in **14** could be effected in 80% and 56% yields, respectively, by condensation with dimethyl- and diisopropyldichlorosilanes in the presence of triethylamine (Scheme III).[24] Although **15a** and **15b** were both

Scheme III



destroyed when heated with benzeneselenenic anhydride in chlorobenzene,[25] the targeted α,β-unsaturated esters **16a** and **16b** could be produced by oxidative elimination of the corresponding α-phenylseleno intermediate. However, neither **16a** nor **16b** could be obtained in excess of 30% because of excessive decomposition.[24] The need of a more robust protecting group prompted consideration of acetonide **17**. In this instance, oxidation of the α-selenenylated intermediate with MCPBA was observed to proceed cleanly with concomitant acetal cleavage to afford **18** in 72% overall yield. Evidently, the substantial strain introduced upon installation of the conjugated double bond accelerates hydrolysis to regenerate the diol.

A number of pilot experiments[24] suggested that our long-term goals would be best served if regioselective chain extension were implemented in advance of the photoisomerization step. Accordingly, **18** was exhaustively silylated, and the ester functionality was reduced with Dibal-H (Scheme IV). The subsequent conversion of **19** to **21a** was most satisfactorily achieved by perruthenate oxidation[26] to deliver the aldehyde, Wittig olefination to generate conjugated diene **20**, and regioselective hydroboration of this highly functionalized intermediate with 9-BBN.[27] The overall yield of this three-step sequence was 84%.

As expected, dihydroxy pivalate **22a** was formed cleanly on exposure of **21b** to 48% HF in acetonitrile.[28] Regioselective

(18) Preliminary communication: Kang, H.-J.; Ra, C. S.; Paquette, L. A. *J. Am. Chem. Soc.* **1991**, *113*, 9384.
(19) Demuth, M. In *Comprehensive Organic Synthesis, Volume 5*; Pergamon Press, in press.
(20) Demuth, M.; Schaffner, K. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 820.
(21) (a) Hoffmann, R. *Tetrahedron Lett.* **1970**, 2907. (b) Ciganek, E. *J. Am. Chem. Soc.* **1965**, *87*, 1149. (c) Maier, G. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 402.
(22) Asao, T.; Kuroda, S.; Kato, K. *Chem. Lett.* **1978**, 41.
(23) The less reactive dimethyl fumarate gave no evidence of entering into cycloaddition with **8** under these conditions of extreme pressure.
(24) Kang, H.-J. Ph.D. Thesis, The Ohio State University, Columbus, OH, 1991.
(25) (a) Barton, D. H. R.; Lester, D. J.; Ley, S. V. *J. Chem. Soc., Chem. Commun.* **1978**, 130. (b) Barton, D. H. R.; Morzycki, J. W.; Motherwell, W. B.; Ley, S. V. *J. Chem. Soc., Chem. Commun.* **1981**, 1044.
(26) (a) Griffith, W. P.; Ley, S. V.; Whitcombe, G. P.; White, A. D. *J. Chem. Soc., Chem. Commun.* **1987**, 1625. (b) Griffith, W. P.; Ley, S. V. *Aldrichimica Acta* **1990**, *23*, 13.
(27) Kabalka, G. W.; Shoup, T. M.; Goudgaon, N. M. *Tetrahedron Lett.* **1989**, *30*, 1483.

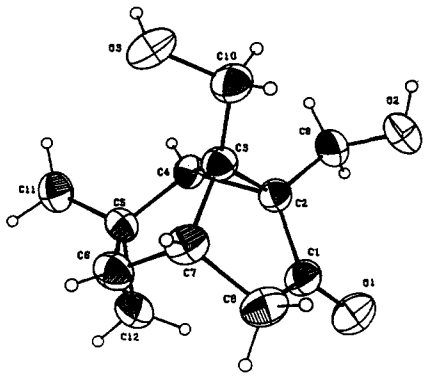
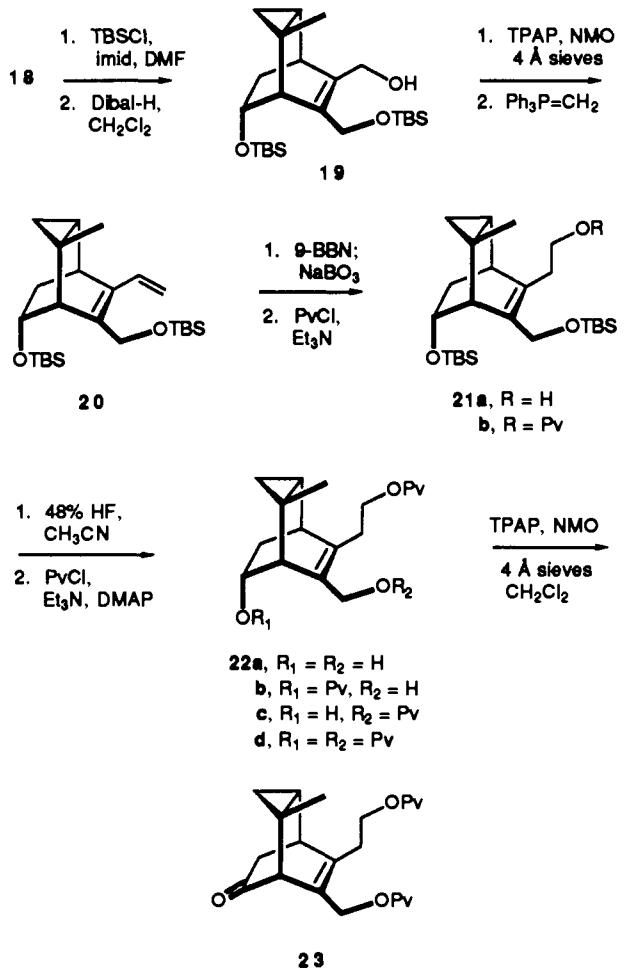


Figure 1. Computer-generated drawing of i (see ref 29) derived from the X-ray coordinates.

Scheme IV

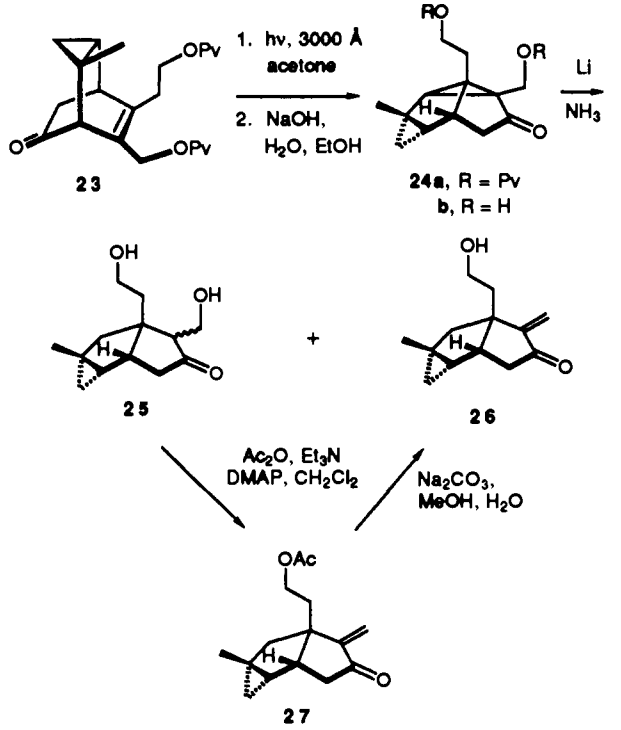


conversion of **22a** to **22c** (74%) was achieved by overnight reaction with a slight excess of pivaloyl chloride in CH_2Cl_2 containing triethylamine and DMAP. An appreciation of the degree of steric control governing this acylation can be gained by the limited extent to which **22b** (11%) and **22d** (6%) are formed competitively. At this point, perruthenate oxidation of **22c** made available the pivotal tricyclic β,γ-unsaturated ketone **23** (97%).

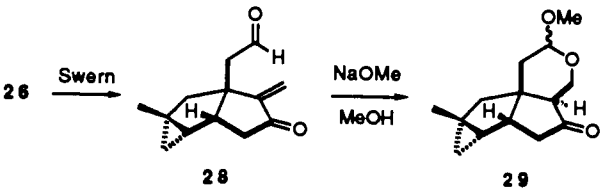
Photorearrangement and Lactone Annulation. Following the development of a concise route to **23**, a large segment of the structural network of pentalenolactone P was quickly elaborated by light-induced photoisomerization. The most efficacious means uncovered for achieving high-yield conversion to **24a** involved merely irradiating acetone solutions of the ketone with a bank

(28) Newton, R. F.; Reynolds, D. R.; Finch, M. A. W.; Kelly, D. R.; Roberts, S. M. *Tetrahedron Lett.* **1979**, *20*, 3981.

Scheme V



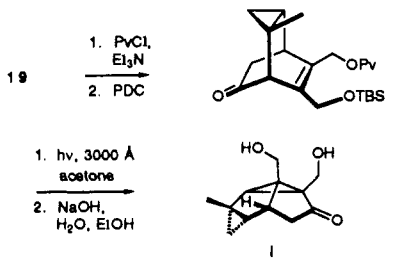
Scheme VI



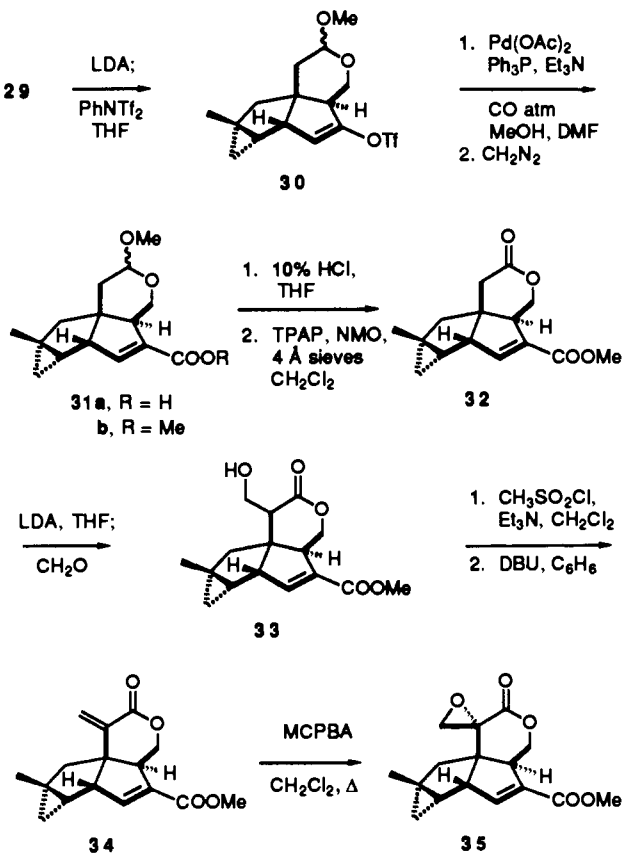
of 3000-Å lamps in a Rayonet reactor (Scheme V). Subsequent saponification of the dicyclopropyl ketone afforded the very polar, crystalline diol **24b**. The multifaceted structural features of this intermediate compare closely to those of a lower homologue prepared by analogous means,[24,29] for which X-ray crystallographic confirmation is available (Figure 1). As a consequence, the stage was set for examination of the reductive cleavage step.

While precedent suggested that dissolving metal reduction of **24b** would result in regioselective rupture of the central cyclopropane bond, no guidance was available to guarantee that the second cyclopropane ring would be insulated from related electron-transfer chemistry. Furthermore, the integrity of the hydroxymethyl group could not be assured. In the event, the stereoelectronic factors present in **24b** proved adequate to limit reduction to the dihydro level. Two products were formed, both arising from regiocontrolled rupture of the "conjugated" three-membered ring. Of these, **25** usually dominated over its dehydrated counterpart **26** by a factor that varied from 2:1 to 1:1, depending on the run. Satisfyingly, the acetylation of this mixture led uniquely to **27**, as β-elimination within esterified **25** occurs

(29) The sequence utilized to produce i was as follows:



Scheme VII



readily under these conditions. When this treatment was followed by careful saponification, keto alcohol **26** was easily acquired in a high state of purity. More prolonged exposure of **26** to the alkaline conditions on recourse to a stronger base such as K_2CO_3 was found to promote premature intramolecular Michael addition to the exomethylene ketone.

Although the oxidation of **26** to keto aldehyde **28** could be accomplished with TPAP[26] in 70% yield, the Swern reagent gave still better results (Scheme VI). Spot-to-spot conversion was welcomed in this instance because of the considerable sensitivity of this intermediate. In practice, **28** was exposed to sodium methoxide in methanol as soon as possible. These efforts were rewarded by rapid formation of the hemiacetal anion and slower conjugate addition of the nucleophilic functional group to the enone with formation of a cyclic acetal.[14a,b] The overall yield of **29** was 62%. The anomeric ratio was 4.8:1 (^{1}H NMR analysis).

Chemical Modification of the Framework. Once acetal **29** became available, two possible strategies were considered for achieving the total synthesis of **3b**. The first involves immediate transformation of the acetal moiety into an epoxy lactone subunit with subsequent conversion of the ketone carbonyl into the α,β-unsaturated ester component. This plan has several possible advantages, including the following: (1) utilization of harsh conditions for enolization α to the lactone as necessary; (b) double-bond isomerization would be avoided during acetal hydrolysis;[14b] and (c) no need would exist for controlled oxidation of the methylene lactone in the presence of the unsaturated ester. Nonetheless, the scenario in the second route, which deals with the increase in structural complexity in the reverse order, was considered more workable.

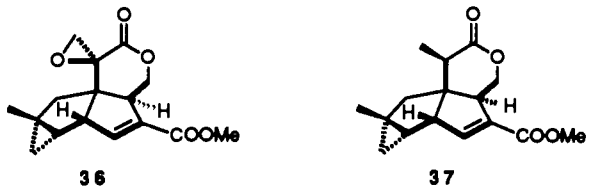
Consequently, the carbomethoxy group was installed first in a totally regioselective fashion by transformation of **29** to enol triflate **30**,[30] followed by $Pd(OAc)_2$-catalyzed methoxycarbonylation[31] and treatment with diazomethane (Scheme VII).

Next, the lactone ring was unmasked by acidic hydrolysis to the lactol and oxidation with TPAP.[26] Methylenation α to the lactone carbonyl now had to be implemented. Three different tactics had earlier been deployed for this purpose. In their synthesis of pentalenolactone,[6a] Danishefsky et al. utilized Bredereck's reagent.[32] Paquette and co-workers made use of Stiles' reagent[33] in their successful preparation of pentalenolactone E methyl ester.[14a,b] Recently, Eschenmoser's salt[34] was employed by Pirrung et al. to arrive at pentalenolactone G.[16d] The difficulties associated with such methylenations are perhaps best reflected in Magnus' thwarted synthesis of pentalenolactone H.[35]

The steric congestion about this reaction center, a neopentyl carbon, contributes substantially to its sluggish reactivity. In the present instance, the β-methyl group on the cyclopropane ring in **32** further exacerbates approach to the β-face. In preliminary experiments, the reagents discussed above did not show promise when admixed on a small scale with the lactone enolate. Gras' procedure[36] led only to slow decomposition. Phenylselenenylation[37] and methylation could be accomplished, but all second functionalization maneuvers at the α-carbon failed to set the stage for methylenation.

Recourse to solutions of monomeric formaldehyde in tetrahydrofuran[38] resulted in efficient conversion (86%) to **33**. Examination of the high-field ^{1}H NMR spectrum of this product showed the $\alpha:\beta$ isomer ratio to be 10:1. This epimeric mixture was not separated, but was directly mesylated and subjected to elimination with DBU in benzene at room temperature.

We were then able to take advantage of two schemes for epoxidizing this penultimate intermediate regioselectively. The first entailed direct epoxidation with MCPBA[39] and gave **35** along with small amounts of β-oxirane **36** in 18% combined yield. The precise stereoisomeric ratio was not determined. A modest improvement in the yield was seen when the three-step sequence[6a] involving Dibal-H/*t*-BuOOH, $VO(acac)_2$/TPAP, and NMO was utilized instead. It is worth noting that this approach to **35** gave predominantly **37**, the product of 1,4-reduction. In this instance, the **35**:**36** ratio was 2.7:1. That pentalenolactone P methyl ester had indeed been produced via both routes was confirmed by careful comparison of the IR, ^{1}H NMR, and ^{13}C NMR spectra with those of authentic **35** kindly provided by Professor David Cane.[40]



Summary. The total synthesis of *dl*-pentalenolactone P methyl ester has been accomplished for the first time from readily available **8** in 32 synthetic operations and an overall yield of 0.3%. The requisite trans relationship of the cyclopropane and lactone rings was immediately secured by Diels–Alder cycloaddition and

(30) McMurry, J. E.; Scott, W. J. *Tetrahedron Lett.* **1983**, *24*, 979.
(31) Cacchi, S.; Morera, E.; Ortar, G. *Tetrahedron Lett.* **1985**, *26*, 1109.
(32) (a) Bredereck, H.; Simchen, G.; Rebsdta, S.; Kantlehner, W.; Horn, P.; Wahl, R.; Hoffmann, H.; Grieshaber, P. *Chem. Ber.* **1968**, *101*, 41. (b) Gutzwiller, Y.; Pizzolato, G.; Uskokovic, M. *J. Am. Chem. Soc.* **1971**, *93*, 5907. (c) Ban, Y.; Taga, N.; Oishi, T. *Tetrahedron Lett.* **1974**, 187.
(33) (a) Finkbeiner, H. L.; Stiles, M. *J. Am. Chem. Soc.* **1963**, *85*, 616. (b) Parker, W. L.; Johnson, F. *J. Org. Chem.* **1973**, *38*, 2489.
(34) (a) Schreiber, J.; Maag, H.; Hashimoto, N.; Eschenmoser, A. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 330. (b) Danishefsky, S.; Kitahara, T.; Mckee, R.; Schuda, P. F. *J. Am. Chem. Soc.* **1976**, *98*, 6715. (c) Roberts, J. L.; Borromeo, P. S.; Poulter, C. D. *Tetrahedron Lett.* **1977**, 1621.
(35) Magnus, P.; Slater, M. J.; Principe, L. M. *J. Org. Chem.* **1989**, *54*, 5148.
(36) (a) Gras, J. L. *Tetrahedron Lett.* **1978**, 2111. (b) Disanayaka, B. W.; Weedon, A. C. *Synthesis* **1983**, 952.
(37) Grieco, P. A.; Miyashita, M. *J. Org. Chem.* **1974**, *39*, 120.
(38) Schlosser, M.; Jenny, T.; Guggisberg, Y. *Synlett* **1990**, 704.
(39) Valente, V. R.; Wolfhagen, J. L. *J. Org. Chem.* **1966**, *31*, 2509.
(40) We thank Prof. David Cane (Brown University) for providing us with an authentic sample of **3b** and relevant spectra and Dr. Shuji Takahashi (Sankyo Co., Ltd.) for making available copies of the high-field ^{1}H NMR spectrum of **3a**.

preserved during the ensuing photoisomerization and reductive cleavage steps. Although the present exercise was not enantioselective, a number of intermediates would appear well suited to chemical resolution or enzymatic discrimination, thus enabling in principle comparable access to the dextro- or levorotatory antipode as desired.

Experimental Section

Melting points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 1320 spectrometer. ^{1}H NMR spectra were recorded at 300 MHz and ^{13}C NMR spectra at 75 or 62 MHz as indicated. Mass spectra were recorded on a Kratos MS-30 instrument at The Ohio State University Chemical Instrument Center. Elemental analyses were performed at the Scandinavian Microanalytical Laboratory, Herlev, Denmark. All MPLC separations were conducted on Merck Lobar columns (Lichroprep Si-60) with the help of a Fluid Metering INC pump and a Waters Associates Model R403 differential refractometer detector. The organic extracts were dried over anhydrous magnesium sulfate. Solvents were reagent grade and in all cases dried prior to use.

1-Formylcycloheptatriene.[22] To freshly distilled cycloheptatriene (276 g, 3.00 mol) to dry *N,N*-dimethylformamide (550 g, 7.50 mol) cooled to 0 °C was slowly added phosphorus oxychloride (690 g, 4.50 mol) over 45 min. After additional stirring for 20 min with slow warming to room temperature, the mixture was heated at 60–65 °C in an oil bath for 15 h. An additional quantity of Vilsmeier reagent (from DMF (330 g, 4.50 mol) and phosphorus oxychloride (5.60 g, 3.0 mmol)) was introduced over 20 min to the cold reaction mixture, and heating was resumed for an additional 15 h. The cooled mixture was poured onto ice (2 L) over 30 min and extracted with ether (3 × 1000 mL). Following the usual workup, the concentrated dark oil was purified by distillation in vacuo (57 °C/1 Torr) to furnish the aldehyde as a pale green oil (91.5 g, 25%). Yields ranged from 25 to 40%.

1-Methylcycloheptatriene (8).[22] To a solution of the above aldehyde (58.5 g, 487 mmol) in dry ether (500 mL) cooled to 0 °C was slowly added lithium aluminum hydride (10.0 g, 260 mmol). The reaction mixture was stirred for 1 h before being quenched by careful addition of 2 N NaOH solution (150 mL). The crude product was extracted into ether (3 × 400 mL) and concentrated to give **10**. The alcohol was dissolved in cold (0 °C) benzene (200 mL) and treated with thionyl chloride (75.2 g, 633 mmol). After 30 min at this temperature, the cold purple solution was carefully quenched with saturated $NaHCO_3$ solution (200 mL). Following the usual workup, the dried organic layers were concentrated to provide the chloromethyl derivative (62 g, 91%), which was immediately subjected to the following reduction.

A cooled (0 °C) solution of the chloride in ether (500 mL) was treated portionwise with lithium aluminum hydride (13.3 g, 350 mmol) over 1.5 h. The reaction mixture was stirred for an additional 1.5 h with slow warming to room temperature before it was heated to reflux for 1 h, carefully quenched by portionwise addition of 2 N NaOH solution (200 mL), and extracted with ether (5 × 200 mL). After the removal of a majority of the solvent by distillation from the dried organic phases, the product was purified by vacuum distillation (58–60 °C, 26 Torr) to furnish **8** as a colorless oil (35.3 g, 68% overall): IR (neat, cm^{-1}) 3068, 3010, 2960, 1622, 1538, 1440, 1353; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.45 (m, 2 H), 6.11 (m, 1 H), 5.97 (m, 1 H), 5.35 (m, 1 H), 2.32 (d, J = 7.0 Hz, 2 H), 2.00 (d, J = 0.3 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 132.9, 130.7, 128.6, 126.5, 121.8, 120.5, 34.0, 24.3.

4-*exo*-Methyl-8-*exo*,9-*endo*-bis(methoxycarbonyl)-*endo*-tricyclo[3.2.2.0^{2,4}]non-6-ene (11). A solution of **8** (818 mg, 7.70 mmol) and fumaroyl chloride (1.07 g, 7.00 mmol) in CH_2Cl_2 (4.5 mL) was placed under 150 000 psi for 4 days. The resulting pale brown solution was diluted with dry CH_2Cl_2 (5 mL), cooled to 0 °C, and treated with anhydrous methanol (2 mL) containing pyridine (1 mL). The reaction mixture was stirred overnight with slow warming to room temperature. Following the usual workup, purification of the residue by MPLC on silica gel (elution with 8% ethyl acetate in petroleum ether) gave **11** as a viscous oil (1.40 g, 80%), which spontaneously solidified at room temperature: mp 70–72 °C; IR (neat, cm^{-1}) 1720; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.82 (m, 2 H), 3.72 (s, 3 H), 3.63 (s, 3 H), 3.51 (m, 1 H), 3.20 (m, 1 H), 2.95 (m, 2 H), 2.00 (s, 3 H), 0.61 (m, 1 H), 0.31 (m, 1 H), −0.05 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 174.8, 173.9, 129.8, 128.8, 51.9, 51.8, 46.6, 42.6, 39.5, 34.7, 19.4, 14.6, 13.6, 10.9; HRMS m/z (M$^+$) calcd 219.1021, obsd 219.1055. Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 66.83; H, 7.23.

Hydrolysis and Lactonization of 11. Diester **11** (110 mg, 0.440 mmol) was hydrolyzed with NaOH (88 mg, 2.20 mmol) in refluxing 40% aqueous CH_3OH solution (2 mL) over 5 h. The cooled mixture was acidified to pH 1 by addition of 1 N HCl, extracted with CH_2Cl_2 (3 × 10 mL), dried, and concentrated to give diacid **12** (91.5 mg, 94%), which was sufficiently pure (^{1}H NMR) to be reacted directly: ^{1}H NMR (80 MHz, $CDCl_3$) δ 5.98–5.78 (m, 2 H), 3.65–3.49 (m, 1 H), 3.41–3.18 (m, 1 H), 3.15–2.80 (m, 2 H), 1.28 (s, 3 H), 1.08–0.69 (m, 1 H), 0.49–0.38 (m, 1 H), 0.18 to −0.07 (m, 1 H).

To a solution of **12** (50.0 mg, 0.225 mmol) in anhydrous methanol (1 mL) was added mercuric acetate (72 mg, 0.225 mmol). The reaction mixture was stirred for 15 h at 30 °C, cooled to −78 °C, treated with sodium borohydride (5 mg), and stirred for 1 h with slow warming to room temperature. Following acidification to pH 1 with 1 N HCl, the product was extracted into CH_2Cl_2 (3 × 10 mL). ^{1}H NMR analysis at this stage usually showed ca. 80% conversion. Complete conversion was achieved by a second cycle of the above mixture with 0.3 equiv of mercuric salt (21 mg). Lactonic acid **13a** was converted into ester **13b** by treatment with diazomethane in ether. MPLC purification (silica gel, elution with 25% ethyl acetate in petroleum ether) following the usual workup gave **13b** as a colorless oil, which solidified at room temperature (39.8 mg, 75%): mp 77–78 °C; IR (neat, cm^{-1}) 1780, 1735; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.39 (t, J = 6.1 Hz, 1 H), 3.75 (s, 3 H), 3.29 (d, J = 4.7 Hz, 1 H), 2.75 (m, 3 H), 1.80 (m, 1 H), 1.55 (m, 1 H), 1.15 (s, 3 H), 0.70 (m, 1 H), 0.35 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 179.1, 172.3, 76.8, 52.2, 43.4, 41.7, 37.4, 30.6, 28.6, 22.4, 16.5, 11.5, 10.6; HRMS m/z (M$^+$) calcd 236.1048, obsd 236.1068. Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: C, 65.78; H, 6.89.

Methyl (1*S,2*R**,4*R**,6*R**,7*R**,8*R**)-8-Hydroxy-7-(hydroxymethyl)-2-methyltricyclo[3.2.2.0^{2,4}]nonane-6-carboxylate (14).** To a solution of **13b** (2.06 g, 87.3 mmol) in methanol (25 mL) was added sodium borohydride (800 mg, excess) at room temperature, and the resulting solution was stirred overnight, quenched with 5% HCl, and freed of methanol. The residue was extracted with ether (3 × 30 mL), and the combined organic layers were dried and evaporated to give a crude product, which was purified on silica gel (elution with EtOAc) to afford **14** (1.82 g, 87%) as a white solid: mp 87.0–87.5 °C; IR (KBr, cm^{-1}) 3220, 1725; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.06 (br s, 2 H), 3.84–3.64 (m, 3 H), 3.71 (s, 3 H), 2.81 (dd, J = 2.0, 7.3 Hz, 1 H), 2.61 (m, 1 H), 2.48 (m, 1 H), 1.86 (ddd, J = 4.0, 10.2, 14.3 Hz, 1 H), 1.75 (t, J = 2.4 Hz, 1 H), 1.15–1.04 (m, 1 H), 1.12 (s, 3 H), 0.64 (quint, J = 3.73 Hz, 1 H), 1.06 (dd, J = 3.3, 6.2 Hz, 1 H), 0.14 (dd, J = 6.3, 7.8 Hz, 1 H); ^{13}C NMR (62 MHz, $CDCl_3$, ppm) 175.8, 66.5, 64.0, 51.7, 44.3, 42.6, 37.2, 35.6, 30.2, 22.1, 18.0, 17.5, 11.9; HRMS m/z (M$^+$ − H_2O) calcd 222.1256, obsd 222.1269.

Methyl (1*R,5a*R**,6*R**,7*S**,7a*R**,8a*R**,8b*S**)-Octahydro-3,3,8a-trimethyl-1,7-methano-1*H*-cyclopropa[*g*]-2,4-benzodioxepin-6-carboxylate (17).** To a THF solution (70 mL) of **14** (1.82 g, 7.58 mmol) was added 2,2-dimethoxypropane (5.50 g, 53 mmol) and TsOH (70 mg, 0.41 mmol). The resulting solution was stirred for 2 h before saturated $NaHCO_3$ solution (30 mL) was added to it. The organic solvents were evaporated, and the residue was extracted into CH_2Cl_2 (3 × 30 mL). The usual workup and purification on silica gel (elution with 8% EtOAc in petroleum ether) furnished **17** (1.29 g, 61%) along with recovered starting material (367 mg, 20%): IR (neat, cm^{-1}) 1735; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.00 (dd, J = 9.5, 12.1 Hz, 1 H), 3.81–3.75 (m, 1 H), 3.69 (s, 3 H), 3.47 (dd, J = 6.5, 12.1 Hz, 1 H), 2.78–2.69 (m, 1 H), 2.50 (t, J = 3.5 Hz, 1 H), 2.37 (d, J = 4.9 Hz, 2 H), 1.77 (ddd, J = 2.8, 8.7, 14.5 Hz, 1 H), 1.41 (s, 3 H), 1.26 (dm, J = 14.5 Hz, 1 H), 1.21 (s, 3 H), 1.08 (s, 3 H), 0.65 (quint, J = 3.6 Hz, 1 H), 0.42 (dd, J = 3.3, 5.9 Hz, 1 H), 0.068 (dd, J = 6.0, 7.5 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 175.9, 101.1, 69.7, 66.9, 51.8, 51.2, 35.8, 34.7, 33.9, 28.0, 27.3, 23.7, 22.5, 17.4, 14.3, 11.1; HRMS m/z (M$^+$ − CH_3) calcd 265,1440, obsd 265.1472. Anal. Calcd for $C_{16}H_{24}O_4$: C, 68.54; H, 8.63. Found: C, 68.63; H, 8.55.

Methyl (1*R,2*R**,4*R**,5*S**,8*R**)-8-Hydroxy-7-(hydroxymethyl)-2-methyltricyclo[3.2.2.0^{2,4}]non-6-ene-6-carboxylate (18).** To a THF solution (2.5 mL) of diisopropylamine (0.85 mL) at −20 °C was added *n*-butyllithium (2.43 mL, 3.65 mmol, 1.5 M in hexane), and this solution was stirred for 20 min, cooled to −78 °C, and treated dropwise with **17** (330 mg, 1.18 mmol). The reaction mixture was warmed to −30 °C over 1 h and cooled to −78 °C before PhSeBr (prepared in situ from PhSeSePh (800 mg) and Br_2 (0.19 mL) in 3 mL of THF) was introduced, and the mixture was stirred at −78 °C for 30 min and warmed to room temperature over 1 h. Quenching with saturated NH_4Cl solution, followed by the usual workup and purification by MPLC (elution with 8% EtOAc in petroleum ether) gave the desired β-selenide (410 mg, 79%), the α-selenide (35 mg, 7%), and unreacted starting material (28 mg).

To a CH_2Cl_2 solution (10 mL) of the above β-selenide (410 mg, 1.06 mmol) containing $NaHCO_3$ (178 mg, 2.12 mmol) was added MCPBA (366 mg, 2.12 mmol) portionwise at room temperature. The resulting mixture was stirred for 1 h and quenched with saturated $NaHCO_3$ solution. The aqueous phase was extracted with ether (3 × 30 mL), and the combined organic layers were washed with saturated $NaHCO_3$ and dried. Concentration followed by purification on silica gel (elution with 75% EtOAc in petroleum ether) afforded **18** (205 mg, 92%) as a colorless

oil: IR (neat, cm^{-1}) 1705, 1620; ^1H NMR (300 MHz, $CDCl_3$) δ 4.90 (d, J = 13.4 Hz, 1 H), 4.24 (d, J = 13.4 Hz, 1 H), 3.94 (m, 1 H), 3.79 (s, 3 H), 3.40 (m, 1 H), 3.05 (d, J = 3.2 Hz, 1 H), 2.82 (br s, 1 H), 1.91 (ddd, J = 2.6, 7.9, 13.9 Hz, 1 H), 1.02 (s, 3 H), 0.90 (dm, J = 11.3 Hz, 1 H), 0.88–0.74 (m, 2 H), 0.43 (dd, J = 6.3, 7.2 Hz, 1 H) (one OH proton not observed); ^{13}C NMR (75 MHz, $CDCl_3$) 166.6, 159.1, 135.2, 94.1, 67.7, 62.1, 51.6, 48.6, 34.8, 32.9, 25.3, 23.7, 23.3, 19.3; HRMS m/z (M^+) calcd 238.1205, obsd 238.1263.

(1*R,2*R**,4*R**,5*S**,8*R**)-8-(*tert*-Butyldimethylsiloxy)-7-[(*tert*-butyldimethylsiloxy)methyl]-2-methyltricyclo[3.2.2.0^{2,4}]non-6-ene-6-methanol (19).** To a stirred solution of **18** (2.00 g, 8.40 mmol) in 20 mL of DMF was added TBSCl (3.80 g, 25.2 mmol) and imidazole (5.72 g, 84.0 mmol), and the resulting mixture was stirred at room temperature overnight before being poured into H_2O (200 mL) and extracted with ether (3 × 200 mL). Normal workup and solvent evaporation was followed by purification of the crude product on silica gel.

The bis-silylated ester was dissolved in 30 mL of CH_2Cl_2 and cooled to −78 °C. Dibal-H (25 mL, 1.0 M in hexane) was introduced in a slow, dropwise fashion, and the resulting mixture was stirred at that temperature for 1 h before being quenched with methanol at −78 °C. The reaction mixture was warmed to room temperature, and a 5% solution of sodium potassium tartrate (100 mL) was added. Stirring was continued until clear phase separation was obtained. Extraction of the aqueous phase with ether (3 × 50 mL) followed by drying and evaporation of the combined organic layers produced crude material that was purified on silica gel (elution with 12% EtOAc in petroleum ether) to give **19** (2.95 g, 80% overall) as a white solid: mp 73.5–74.0 °C; IR (KBr, cm^{-1}) 3380; ^1H NMR (300 MHz, $CDCl_3$) δ 4.55 (d, J = 12.4 Hz, 1 H), 4.38 (dd, J = 5.4, 12.3 Hz, 1 H), 4.23 (dd, J = 6.4, 12.2 Hz, 1 H), 4.06 (d, J = 12.4 Hz, 1 H), 3.84 (dt, J = 7.7, 2.9 Hz, 1 H), 2.79 (m, 1 H), 2.57 (d, J = 3.2 Hz, 1 H), 1.80–1.72 (m, 2 H), 1.02 (s, 3 H), 0.93 (s, 9 H), 0.86–0.82 (m, 1 H), 0.81 (s, 9 H), 0.67 (m, 2 H), 0.31 (m, 1 H), 0.10 (s, 6 H), 0.002 (s, 3 H), −0.02 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 141.0, 140.6, 69.7, 63.0, 60.6, 46.3, 35.9, 34.9, 26.0, 25.8, 25.7, 23.5, 23.3, 18.4, 17.9, 17.8, −4.7, −5.4; HRMS m/z (M^+) calcd 438.2985, obsd 438.2957. Anal. Calcd for $C_{24}H_{46}O_3Si_2$: C, 65.69; H, 10.57. Found: C, 65.48; H, 10.59.

***tert*-Butyl[[(1*S**,2*R**,4*R**,5*R**,6*R**)-9-[(*tert*-butyldimethylsiloxy)methyl]-4-methyl-8-vinyltricyclo[3.2.2.0^{2,4}]non-8-en-6-yl]oxy]dimethylsilane (20).** To a CH_2Cl_2 solution (15 mL) of **19** (3.00 g, 6.84 mmol) was added NMO (1.60 g, 13.7 mmol), 4-Å molecular sieves (3.42 g, 500 mg/mmol), and TPAP (120 mg, 0.342 mmol). The reaction mixture was stirred for 1 h at room temperature, diluted with 10% ethyl acetate in petroleum ether (30 mL), and filtered through a silica gel pad (elution with 10% EtOAc in petroleum ether). Solvent evaporation gave the aldehyde, which was used directly in the next step.

To a stirred THF solution (20 mL) of methyltriphenylphosphonium iodide (4.70 g, 11.6 mmol) was added *n*-butyllithium (6.8 mL, 10.2 mmol) at −20 °C, and the resulting mixture was warmed to 0 °C. The above aldehyde dissolved in 10 mL of THF was added to the Wittig reagent, and the resulting mixture was stirred for 1 h at 0 °C. After the reaction mixture was warmed to room temperature, saturated NH_4Cl solution was introduced. Ether extraction (3 × 100 mL) followed by normal workup and purification on silica gel (elution with 4% EtOAc in petroleum ether) gave **20** (2.78 g, 93% overall) as a colorless oil: IR (neat, cm^{-1}) 1635; ^1H NMR (300 MHz, $CDCl_3$) δ 6.81 (dd, J = 10.9, 17.3 Hz, 1 H), 5.24 (d, J = 17.2 Hz, 1 H), 4.98 (d, J = 10.9 Hz, 1 H), 4.71 (d, J = 12.2 Hz, 1 H), 4.04 (d, J = 12.2 Hz, 1 H), 3.89 (dt, J = 7.7, 2.9 Hz, 1 H), 3.13 (m, 1 H), 2.74 (d, J = 3.1 Hz, 1 H), 1.76 (ddd, J = 2.6, 7.7, 13.2 Hz, 1 H), 1.03 (s, 3 H), 0.93 (s, 9 H), 0.83–0.72 (m, 1 H), 0.81 (s, 9 H), 0.69–0.61 (m, 2 H), 0.29 (m, 1 H), 0.099 (s, 3 H), 0.096 (s, 3 H), 0.00 (s, 3 H), −0.03 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 143.4, 139.0, 130.8, 110.2, 70.5, 62.1, 45.9, 35.5, 30.7, 26.1, 25.9, 25.0, 23.6, 23.2, 18.5, 18.0, 17.2, −4.6, −5.3; HRMS m/z (M^+) calcd 434.3036, obsd 434.3040. Anal. Calcd for $C_{25}H_{46}O_2Si_2$: C, 69.06; H, 10.66. Found: C, 69.17; H, 10.63.

(1*R,2*R**,4*R**,5*S**,8*R**)-8-[(*tert*-Butyldimethylsiloxy)methyl]-7-[(*tert*-butyldimethylsiloxy)methyl]-2-methyltricyclo[3.2.2.0^{2,4}]non-6-ene-6-ethanol (21a).** To a stirred THF solution (20 mL) of **20** (8.80 g, 20.2 mmol) was added 9-BBN (80 mL, 40 mmol, 0.5 M in THF), and the resulting solution was stirred for 4 h at room temperature, cooled to 0 °C, and quenched by slow addition of H_2O (100 mL). Sodium perborate (19 g) was introduced, and the resulting solution was stirred overnight. After extraction with ether (3 × 300 mL), the usual workup and MPLC purification (elution with 8% EtOAc in petroleum ether) afforded **21a** (8.30 g, 90%) as a colorless oil: IR (neat, cm^{-1}) 3490; ^1H NMR (300 MHz, $CDCl_3$) δ 4.56 (d, J = 11.6 Hz, 1 H), 3.93 (d, J = 11.6 Hz, 1 H), 3.85 (m, 1 H), 3.72–3.52 (m, 2 H), 2.72–2.65 (m, 1 H), 2.70 (d, J = 3.2 Hz, 1 H), 2.60 (m, 1 H), 2.37 (dt, J = 13.3, 4.0 Hz, 1 H), 2.04 (dd, J = 4.0, 9.2 Hz, 1 H), 1.82 (ddd, J = 2.2, 7.5, 13.6 Hz, 1 H), 1.06 (s, 3 H), 0.93 (s, 9 H), 0.83 (s, 9 H), 0.74 (dm, J = 14.2 Hz, 1 H), 0.69–0.62 (m, 2 H), 0.31 (m, 1 H), 0.09 (s, 6 H), 0.03 (s, 3 H), 0.00 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 142.5, 136.8, 69.9, 62.2, 59.7, 46.1, 36.2 (2 C), 34.2, 25.9, 25.6, 25.2, 23.4, 22.8, 18.2, 17.7, 17.3, −4.9, −5.0, −5.5; HRMS m/z (M^+) calcd 452.3142, obsd 452.3142.

(1*R,2*R**,4*R**,5*S**,8*R**)-8-(*tert*-Butyldimethylsiloxy)-7-[(*tert*-butyldimethylsiloxy)methyl]-2-methyltricyclo[3.2.2.0^{2,4}]non-6-ene-6-ethanol Pivalate (21b).** To a stirred solution of **21a** (321 mg, 0.709 mmol) in 10 mL of CH_2Cl_2 was added Et_3N (0.49 mL, 3.54 mmol), DMAP (8.6 mg, 10 mol %), and pivaloyl chloride (0.13 mL, 1.06 mmol). The mixture was stirred overnight at room temperature and diluted with an additional 50 mL of CH_2Cl_2. Customary workup and concentration gave the crude product, which was purified on silica gel (elution with 8% EtOAc in petroleum ether) to give pure **21b** (370 mg, 97%) as a colorless oil: IR (neat, cm^{-1}) 1720; ^1H NMR (300 MHz, $CDCl_3$) δ 4.50 (d, J = 11.7 Hz, 1 H), 4.09 (m, 2 H), 3.99 (d, J = 11.7 Hz, 1 H), 3.82 (m, 1 H), 2.66–2.49 (series of m, 4 H), 1.72 (ddd, J = 2.5, 7.6, 13.2 Hz, 1 H), 1.19 (s, 9 H), 1.01 (s, 3 H), 0.92 (s, 9 H), 0.81 (s, 9 H), 0.81–0.77 (m, 1 H), 0.62 (m, 2 H), 0.28 (m, 1 H), 0.084 (s, 3 H), 0.081 (s, 3 H), −0.01 (s, 3 H), −0.03 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 178.6, 140.3, 137.0, 69.7, 63.5, 62.4, 45.5, 38.7, 36.5, 35.8, 30.2, 27.3, 26.0, 25.8, 25.6, 23.5, 18.4, 17.9, 17.7, −4.65, −4.68, −5.3 (one C not observed); HRMS m/z (M^+) calcd 536.3717, obsd 536.3720. Anal. Calcd for $C_{30}H_{56}O_4Si_2$: C, 67.11; H, 10.51. Found: C, 67.18; H, 10.54.

(1*R,2*R**,4*R**,5*S**,8*R**)-8-Hydroxy-7-(hydroxymethyl)-2-methyltricyclo[3.2.2.0^{2,4}]non-6-ene-6-ethanol 6-Pivalate (22a).** To a solution of **21b** (1.82 g, 3.39 mmol) in 10 mL of CH_3CN was added HF (15 mL, 5% v/v of 48% HF–CH_3CN) at 0 °C. The reaction mixture was stirred for 2 h before being diluted with ether (100 mL) and washed with H_2O and saturated $NaHCO_3$ solution. Concentration of the organic phase and purification of the residue on silica gel (elution with 75% EtOAc in petroleum ether containing 2% EtOH) gave **22a** (990 mg, 95%) as a colorless oil: IR (neat, cm^{-1}) 3350, 1730; ^1H NMR (300 MHz, $CDCl_3$) δ 4.47 (d, J = 10.9 Hz, 1 H), 4.16 (m, 2 H), 3.92 (d, J = 10.9 Hz, 1 H), 3.86 (m, 1 H), 2.76–2.37 (series of m, 6 H), 1.87 (ddd, J = 2.6, 7.8, 13.7 Hz, 1 H), 1.18 (s, 9 H), 0.99 (s, 3 H), 0.85 (dm, J = 15.2 Hz, 1 H), 0.76 (dd, J = 3.4, 6.2 Hz, 1 H), 0.65 (m, 1 H), 0.37 (dd, J = 6.3, 7.3 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 178.6, 142.6, 138.3, 67.6, 63.0, 59.7, 47.7, 38.6, 36.2, 35.4, 29.9, 27.1, 24.9, 24.2, 23.4, 18.7; HRMS m/z (M^+) calcd 308.1987, obsd 308.1965.

(1*R,2*R**,4*R**,5*S**,8*R**)-8-Hydroxy-7-(hydroxymethyl)-2-methyltricyclo[3.2.2.0^{2,4}]non-6-ene-6-ethanol 6,7-Dipivalate (22c).** To a CH_2Cl_2 solution (77 mL) of **22a** (1.19 g, 3.86 mmol) was added Et_3N (2.69 mL, 19.3 mmol), DMAP (47.2 mg, 0.386 mmol), and pivaloyl chloride (0.52 mL, 4.25 mmol). The resulting mixture was stirred overnight at room temperature before saturated $NaHCO_3$ solution was added. The aqueous layer was extracted with ether (3 × 100 mL), and the combined organic phases were dried and evaporated. The residue was purified by MPLC (elution with 18% EtOAc in petroleum ether) to give **22c** (1.13 g, 74%) along with regioisomer **22b** (11%) and tripivalate **22d** (6%).

For **22c**: IR (neat, cm^{-1}) 3500, 1725; ^1H NMR (300 MHz, $CDCl_3$) δ 4.67 (dd, J = 12.2, 21.4 Hz, 2 H), 4.13 (m, 2 H), 3.78 (m, 1 H), 2.72–2.48 (series of m, 4 H), 1.86 (ddd, J = 2.6, 8.0, 13.8 Hz, 1 H), 1.63 (br s, 1 H), 1.17 (s, 9 H), 1.14 (s, 9 H), 0.98 (s, 3 H), 0.79 (dm, J = 16.4 Hz, 1 H), 0.75 (m, 1 H), 0.61 (m, 1 H), 0.34 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 178.5, 178.2, 144.9, 134.6, 68.2, 63.6, 62.6, 47.1, 38.6, 38.4, 36.3, 35.0, 30.1, 27.1, 27.0, 25.0, 24.3, 23.3, 18.6; HRMS m/z (M^+) calcd 392.2563, obsd 392.2565. Products **22b** and **22d** were not characterized.

(1*S,2*R**,4*R**,5*R**)-8-(2-Hydroxyethyl)-9-(hydroxymethyl)-4-methyltricyclo[3.2.2.0^{2,4}]non-8-en-6-one Dipivalate (23).** To a stirred solution of **22c** (1.13 g, 2.88 mmol) in 10 mL of CH_2Cl_2 were added NMO (675 mg, 5.77 mmol), 4-Å molecular sieves (1.4 g, 0.5 g/mmol), and TPAP (51 mg, 0.144 mmol). The resulting mixture was stirred at room temperature for 40 min, diluted with 10% ethyl acetate in petroleum ether (25 mL), filtered through a silica gel column (elution with 18% EtOAc in petroleum ether), and evaporated to give **23** (1.09 g, 97%) as a colorless oil: IR (neat, cm^{-1}) 1725; ^1H NMR (300 MHz, $CDCl_3$) δ 4.74 (d, J = 12.6 Hz, 1 H), 4.61 (d, J = 12.6 Hz, 1 H), 4.19 (t, J = 6.4 Hz, 2 H), 3.17 (s, 1 H), 3.05 (m, 1 H), 2.67 (m, 2 H), 1.89 (dd, J = 2.5, 18.2 Hz, 1 H), 1.73 (dd, J = 3.0, 18.2 Hz, 1 H), 1.20 (s, 9 H), 1.16 (s, 9 H), 1.13 (s, 3 H), 1.10–0.94 (m, 1 H), 0.90 (dd, J = 3.7, 7.1 Hz, 1 H), 0.65 (t, J = 7.3 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 209.1, 178.24, 178.16, 147.1, 133.1, 61.9, 61.6, 58.3, 38.8, 38.5, 37.1, 35.7, 30.3, 27.10, 27.05, 26.1, 24.8, 22.1, 18.4; HRMS m/z (M^+) calcd 390.2406, obsd 390.2405. Anal. Calcd for $C_{23}H_{34}O_5$: C, 70.74; H, 8.78. Found: C, 70.34; H, 8.81.

(2a*S,2b*S**,2c*S**,3a*S**,3b*R**,3c*S**)-Octahydro-2a,3c-bis(hydroxymethyl)-2c-methyl-2*H*-dicyclopropa[*a*,*cd*]pentalen-2-one Dipivalate (24a).** A solution of **23** (1.14 g, 2.92 mmol) in acetone (570 mL) was

deoxygenated by bubbling nitrogen through for 30 min in a quartz tube. This solution was irradiated with a bank of 12 3000-Å lamps in a Rayonet reactor. After 12 h, the reaction mixture was concentrated and subjected to MPLC purification (elution with 14% EtOAc in petroleum ether) to give **24a** (1.04 g, 91%) as a colorless oil: IR (neat, cm^{-1}) 1725; ^1H NMR (300 MHz, $CDCl_3$) δ 4.67 (d, J = 12.2 Hz, 1 H), 4.27 (t, J = 6.7 Hz, 2 H), 3.57 (d, J = 12.2 Hz, 1 H), 2.94 (d, J = 7.3 Hz, 1 H), 2.37–2.21 (m, 2 H), 2.14–1.90 (m, 2 H), 1.80 (s, 1 H), 1.65 (dt, J = 3.8, 8.5, 1 H), 1.32 (s, 3 H), 1.22 (s, 9 H), 1.13 (s, 9 H), 0.93 (dd, J = 3.8, 6.8 Hz, 1 H), 0.50 (dd, J = 6.8, 8.7 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 212.4, 178.4, 177.9, 66.3, 63.5, 62.5, 50.6, 50.3, 48.0, 41.3, 38.7, 37.5 (2 C), 31.7, 28.8, 27.2, 27.0, 23.1, 22.1; HRMS m/z (M^+) calcd 390.2406, obsd 390.2402. Anal. Calcd for $C_{23}H_{34}O_5$: C, 70.74; H, 8.78. Found: C, 70.53; H, 8.82.

(2a*S,2b*S**,2c*S**,3a*S**,3b*R**,3c*R**)-Octahydro-3c-(2-hydroxyethyl)-2a-(hydroxymethyl)-2c-methyl-2*H*-dicyclopropa[*a*,*cd*]pentalen-2-one (24b).** To a stirred solution of **24a** (1.81 g, 4.64 mmol) in H_2O (10 mL) and ethanol (20 mL) at room temperature was added sodium hydroxide (557 mg, 14 mmol). The reaction mixture was stirred for 2 days and quenched with saturated NH_4Cl solution (20 mL). Ethanol was removed under reduced pressure, and the residual solution was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were washed with H_2O, dried, and concentrated. The residue was purified on silica gel (elution with EtOAc containing with 2% EtOH) to afford **24b** (825 mg, 80%) as a white solid: IR ($CHCl_3$, cm^{-1}) 3380, 1715; ^1H NMR (300 MHz, $CDCl_3$) δ 4.23 (d, J = 12.4 Hz, 1 H), 3.92–3.76 (m, 2 H), 3.19 (br s, 1 H), 3.04 (d, J = 12.4 Hz, 1 H), 2.92 (m, 1 H), 2.49–2.35 (m, 2 H), 2.20 (dd, J = 1.6, 16.4 Hz, 1 H), 1.76 (m, 1 H), 1.67–1.60 (m, 1 H), 1.61 (s, 1 H), 1.31 (s, 3 H), 0.86 (dd, J = 3.8, 6.6 Hz, 1 H), 0.48 (dd, J = 6.6, 8.7 Hz, 1 H) (one OH proton not observed); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 215.8, 66.0, 60.6, 60.0, 53.8, 49.2, 48.6, 39.7, 37.2, 31.8, 31.2, 23.0, 22.1; HRMS m/z (M^+) calcd 222.1256, obsd 222.1273.

(1a*S,1b*R**,4a*R**,5a*R**)-Octahydro-4a-(2-hydroxyethyl)-5a-methyl-4-methylene-3*H*-cyclopropa[*a*]pentalen-3-one (26).** Small pieces of lithium wire (1.2 g), which had been washed with anhydrous pentane, were rapidly added to cold (−78 °C), vigorously stirred ammonia (700 mL) that had been distilled over sodium. Stirring was continued for 30 min before **24b** (825 mg, 3.72 mmol) in 20 mL of THF and 80 mL of ether was introduced. The reaction mixture was stirred for 2 h at −78 °C before being quenched with NH_4Cl (25 g). The dry ice bath was removed, and NH_3 was allowed to evaporate overnight. The residue was dissolved in H_2O (300 mL) and extracted with CH_2Cl_2 (3 × 200 mL). The combined organic layers were washed with H_2O (200 mL), dried, and concentrated. The concentrate was purified by MPLC (elution with 50% EtOAc in petroleum ether) to give **26** (288 mg, 38%). Dihydroxy ketone **25** was collected by back-flushing the column with ethyl acetate containing 2% ethanol.

To a solution of **25**, DMAP (24 mg), and Et_3N (1.4 mL, 10 mmol) in 6 mL of CH_2Cl_2 was added acetic anhydride (0.28 mL, 3 mmol) at −20 °C. The reaction mixture was stirred for 3 h and warmed to 0 °C before being quenched with saturated $NaHCO_3$ solution (10 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL), and the combined organic layers were washed with H_2O, dried, and concentrated. The residue was purified by MPLC (elution with 18% EtOAc in petroleum ether) to afford **27** (225 mg), which was directly subjected to hydrolysis.

To a solution of **27** (225 mg, 0.907 mmol) in 12 mL of methanol and 5 mL of H_2O was added Na_2CO_3 (96 mg, 0.907 mmol) in 1 mL of H_2O at room temperature. The resulting mixture was stirred for 40 min and quenched with saturated NH_4Cl solution (3 mL). Methanol was removed under reduced pressure, and the residue was extracted with ether (3 × 50 mL). Normal workup and MPLC purification (elution with 50% EtOAc in petroleum ether) gave additional **26** (183 mg, 62% combined yield) as a colorless oil: IR (neat, cm^{-1}) 3430, 1720, 1620; ^1H NMR (300 MHz, $CDCl_3$) δ 6.01 (s, 1 H), 5.29 (s, 1 H), 3.59 (m, 2 H), 2.78 (m, 1 H), 2.50 (dd, J = 8.1, 19.4 Hz, 1 H), 2.39 (dd, J = 1.8, 19.4 Hz, 1 H), 2.19 (d, J = 13.1 Hz, 1 H), 2.04 (dd, J = 1.5, 13.1 Hz, 1 H), 1.78 (m, 2 H), 1.28 (br s, 1 H), 1.24–1.18 (m, 1 H), 1.17 (s, 3 H), 0.24 (m, 1 H), 0.12 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 209.4, 153.1, 117.3, 59.0, 53.0, 48.8, 45.0, 44.9, 41.1, 31.1, 25.4, 21.6, 13.6; HRMS m/z (M^+) calcd 206.1306, obsd 206.1303.

(4a*S,6a*R**,6b*S**,7a*R**,8a*R**)-Decahydro-2-methoxy-7a-methyl-5*H*-cyclopropa[4,5]pentaleno[1,6a-*c*]pyran-5-one (29).** To a stirred CH_2Cl_2 solution (2.5 mL) of oxalyl chloride (25 μL, 0.291 mmol) was added DMSO (0.1 mL, excess) at −78 °C, and the resulting mixture was stirred for 20 min before **26** (30 mg, 0.145 mmol) was introduced. The reaction mixture was stirred for 20 min at that temperature, and Et_3N (0.3 mL) was then added dropwise. The solution was stirred for 10 min, warmed to room temperature, and extracted with ether (3 × 10 mL). The combined organic layers were washed with saturated $NaHCO_3$ solution (10 mL), dried, and concentrated to give aldehyde **28**, which was quickly passed through a silica gel pad (elution with 25% EtOAc in petroleum ether) and used in the next step.

The above material was dissolved in anhydrous methanol (4 mL), and NaOMe (35 μL, 1.0 M in MeOH) was introduced. The resulting mixture was stirred overnight at room temperature before being quenched with saturated NH_4Cl solution (5 mL). Methanol was removed under reduced pressure, and the residual solution was diluted with ether (20 mL). The usual workup followed by purification on silica gel (elution with 18% EtOAc in petroleum ether) gave **29** (25 mg, 62% overall): IR (neat, cm^{-1}) 1735; ^1H NMR (300 MHz, $CDCl_3$, major epimer) δ 4.39 (dd, J = 3.2, 8.0 Hz, 1 H), 4.00 (dd, J = 4.8, 11.9 Hz, 1 H), 3.63 (dd, J = 6.1, 11.9 Hz, 1 H), 3.33 (s, 3 H), 2.68 (m, 1 H), 2.48 (dd, J = 9.1, 19.4 Hz, 1 H), 2.31 (dm, J = 19.4 Hz, 1 H), 2.17 (d, J = 13.4 Hz, 1 H), 2.04 (t, J = 5.3 Hz, 1 H), 1.82 (d, J = 13.6 Hz, 2 H), 1.53 (dd, J = 8.1, 13.8 Hz, 1 H), 1.33–1.25 (m, 1 H), 1.22 (s, 3 H), 0.35 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$, major epimer, ppm) 218.5, 99.1, 58.9, 55.3, 55.0, 48.4, 47.6 (2 C), 41.8, 41.1, 31.6, 27.4, 22.6, 15.9; HRMS m/z (M^+) calcd 236.1412, obsd 236.1398.

Methyl (4a*R,6a*R**,6b*S**,7a*R**,8a*R**)-1,2,4a,6a,6b,7,7a,8-Octahydro-2-methoxy-7a-methyl-4*H*-cyclopropa[4,5]pentaleno[1,6a-*c*]pyran-5-carboxylate (31b).** To a stirred solution (4 mL) of diisopropylamine (0.12 mL, 0.826 mmol) was added *n*-butyllithium (0.51 mL, 0.764 mmol, 1.5 M in hexane) at −20 °C, and the solution was stirred for 20 min before being cooled to −78 °C. Acetal **29** (150 mg, 0.636 mmol) in 3 mL of THF was added to the LDA solution, and the resulting mixture was stirred for 1 h before *N*-phenyltriflimide (273 mg, 0.764 mmol) in 2 mL of THF was introduced. The reaction mixture was warmed to 0 °C, stirred overnight, diluted with petroleum ether (10 mL), filtered through a TLC-grade silica gel pad (elution with 18% EtOAc in petroleum ether), and evaporated to give **30**, which was used in the next step without further purification.

To a stirred solution of **30** in 2 mL of DMF was added Ph_3P (80 mg, 0.305 mmol), $Pd(OAc)_2$ (23 mg, 0.103 mmol), Et_3N (0.3 mL), and methanol (0.5 mL). The resulting mixture was purged with CO for 10 min, stirred at room temperature for 3 h under atmospheric CO, and poured into ether (30 mL) and H_2O (20 mL). The usual workup gave a mixture of **31a** and **31b**, which was dissolved in ether and treated with excess diazomethane in ether. Solvent evaporation followed by MPLC purification (elution with 14% EtOAc in petroleum ether) afforded **31b** (117 mg, 66% overall) as a colorless oil (4.8:1 mixture of anomers).

Major anomer: IR (neat, cm^{-1}) 1715, 1625; ^1H NMR (300 MHz, $CDCl_3$) δ 6.74 (m, 1 H), 4.64 (dd, J = 5.8, 8.1 Hz, 1 H), 4.04 (dd, J = 7.8, 11.8 Hz, 1 H), 3.70 (s, 3 H), 3.40 (t, J = 11.2 Hz, 1 H), 3.34 (s, 3 H), 3.09 (m, 1 H), 2.84 (m, 1 H), 2.09 (d, J = 13.4 Hz, 1 H), 1.79–1.64 (m, 3 H), 1.18 (s, 3 H), 1.16–1.10 (m, 1 H), 0.31 (m, 1 H), 0.22 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 165.4, 146.7, 133.9, 98.0, 61.2, 60.0, 54.8, 52.2, 51.9, 51.4, 47.9, 39.4, 28.5 (2 C), 22.7, 15.7; HRMS m/z (M^+ − OMe) calcd 247.1334, obsd 247.1332.

Minor anomer: IR (neat, cm^{-1}) 1715, 1625; ^1H NMR (300 MHz, $CDCl_3$) δ 6.65 (m, 1 H), 4.61 (dd, J = 5.0, 8.0 Hz, 1 H), 3.90 (dd, J = 4.0, 12.0 Hz, 1 H), 3.74 (dd, J = 2.0, 15.6 Hz, 1 H), 3.72 (s, 3 H), 3.36 (s, 3 H), 3.34–3.29 (m, 1 H), 2.56 (dd, J = 1.8, 3.8 Hz, 1 H), 2.06 (dd, J = 5.0, 14.3 Hz, 1 H), 1.83–1.65 (m, 3 H), 1.27–1.21 (m, 1 H), 1.19 (s, 3 H), 0.43 (dd, J = 5.0, 8.1 Hz, 1 H), 0.28 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 165.2, 146.6, 134.8, 98.5, 59.6, 58.1, 55.0, 54.7, 51.6, 51.3, 51.0, 38.7, 28.8, 26.5, 22.9, 19.5; HRMS m/z (M^+ − OMe) calcd 247.1334, obsd 247.1311.

Methyl (4a*R,6a*R**,6b*S**,7a*R**,8a*R**)-1,2,4a,6a,6b,7,7a,8-Octahydro-7a-methyl-2-oxo-4*H*-cyclopropa[4,5]pentaleno[1,6a-*c*]pyran-5-carboxylate (32).** A stirred THF solution (2 mL) of **31b** (35 mg, 0.126 mmol) was treated with 10% HCl (1 mL), and the resulting solution was stirred at room temperature for 4.5 h before being neutralized with saturated $NaHCO_3$ solution and extracted with ether (3 × 10 mL). Normal workup and concentration gave the hemiacetal, which was oxidized directly.

To a stirred solution of the above hemiacetal in 3 mL of CH_2Cl_2 was added NMO (29.5 mg, 0.252 mmol), 4-Å molecular sieves (63 mg), and TPAP (2.2 mg, catalytic amount). The reaction mixture was stirred at room temperature for 40 min before being diluted with 30% ethyl acetate in petroleum ether (5 mL) and filtered through a silica gel pad. Concentration and MPLC purification (elution with 33% EtOAc in petroleum ether) gave **32** (29 mg, 88% overall) as a colorless oil: IR (neat, cm^{-1}) 1750, 1710, 1625; ^1H NMR (300 MHz, $CDCl_3$) δ 6.75 (t, J = 2.1 Hz, 1 H), 4.45 (dd, J = 4.4, 11.8 Hz, 1 H), 4.36 (dd, J = 4.1, 11.8 Hz, 1 H), 3.74 (s, 3 H), 3.29 (m, 1 H), 2.93 (m, 1 H), 2.52 (s, 2 H), 2.12 (d, J = 13.7 Hz, 1 H), 1.83 (dd, J = 1.3, 13.7 Hz, 1 H), 1.27 (m, 1 H), 1.20 (s, 3 H), 0.39 (m, 1 H), 0.13 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 172.0, 164.5, 147.5, 131.9, 67.2, 60.1, 53.8, 52.3, 51.5, 49.6, 42.3, 29.0, 27.4, 22.2, 16.2; HRMS m/z (M^+) calcd 262.1205, obsd 262.1224.

Methyl (4a*R,6a*R**,6b*S**,7a*R**,8a*R**)-1,2,4a,6a,6b,7,7a,8-Octahydro-1-(hydroxymethyl)-7a-methyl-2-oxo-4*H*-cyclopropa[4,5]pentaleno[1,6a-*c*]pyran-5-carboxylate (33).** To a THF solution (2 mL) of diisopropylamine (83 μL, 0.60 mmol) was added *n*-butyllithium (0.28 mL, 0.45 mmol, 1.6 M in hexane) at −20 °C, and the mixture was stirred for 20 min. The resulting solution was cooled to −78 °C, and **32** (78 mg, 0.298 mmol) dissolved in THF (2 mL) was added dropwise. The enolate solution was warmed to −50 °C over 1 h before 2 mL of monomeric formaldehyde in THF (prepared by the Schlosser procedure[38]) was added. The reaction mixture was stirred for 30 min at −50 °C, warmed slowly to room temperature, quenched with saturated NH_4Cl solution (3 mL), and extracted with ether (3 × 30 mL). Normal workup followed by chromatography on silica gel (elution with 66% EtOAc in petroleum ether) gave **33** (65 mg, 86%, α:β = 10:1) as a colorless oil. The yield is based on 13% recovery of starting lactone **32**: IR ($CHCl_3$, cm^{-1}) 3570, 1725, 1630; ^1H NMR (300 MHz, $CDCl_3$, major isomer) δ 6.76 (t, *J* = 2.1 Hz, 1 H), 4.82 (dd, *J* = 7.2, 11.7 Hz, 1 H), 4.27 (m, 1 H), 3.82 (t, *J* = 11.6 Hz, 1 H), 3.80 (m, 1 H), 3.75 (s, 3 H), 3.61 (m, 1 H), 3.06 (m, 1 H), 2.66 (dd, *J* = 3.2, 8.3 Hz, 1 H), 2.55 (dd, *J* = 4.0, 9.5 Hz, 1 H), 1.99 (dd, *J* = 1.1, 14.3 Hz, 1 H), 1.63 (d, *J* = 14.3 Hz, 1 H), 1.28 (m, 1 H), 1.16 (s, 3 H), 0.44 (m, 1 H), 0.14 (t, *J* = 4.5 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 174.5, 164.3, 146.9, 131.8, 68.6, 58.9, 58.4, 54.6, 54.0, 51.6, 48.5, 45.3, 28.5, 27.6, 21.6, 17.3; HRMS *m/z* (M^+) calcd 292.1311, obsd 292.1294.

Methyl (4a*R,6a*R**,6b*S**,7a*R**,8a*R**)-1,2,4a,6a,6b,7,7a,8-Octahydro-7a-methyl-1-methylene-2-oxo-4*H*-cyclopropa[4,5]pentaleno[1,6a-*c*]pyran-5-carboxylate (34).** To a stirred solution of **33** (65 mg, 0.223 mmol) and Et_3N (0.2 mL, excess) in 3 mL of CH_2Cl_2 was added methanesulfonyl chloride (52 μL, 0.67 mmol) at 0 °C. The reaction mixture was warmed to room temperature, and stirring was maintained for 1.5 h prior to quenching with saturated $NaHCO_3$ solution (3 mL). The aqueous phase was extracted with ether (3 × 10 mL), and the combined organic layers were washed with H_2O, dried, and concentrated in vacuo to give crude mesylate, which was dissolved in benzene (3 mL). To this solution was added DBU (0.13 mL, 0.89 mmol) at room temperature over a period of 5 min. After the mixture was stirred for 30 min, saturated NH_4Cl solution (5 mL) was introduced and the resulting solution was extracted with ether (3 × 10 mL). The combined organic layers were dried, and the volatiles were removed in vacuo. The residual oil was chromatographed on silica gel (elution with 25% EtOAc in petroleum ether) to afford **34** (57 mg, 93% overall) as a colorless oil: IR ($CHCl_3$, cm^{-1}) 1720, 1630; ^1H NMR (300 MHz, $CDCl_3$) δ 6.74 (m, 1 H), 6.09 (s, 1 H), 5.74 (s, 1 H), 4.29 (dd, *J* = 4.1, 11.4 Hz, 1 H), 4.21 (dd, *J* = 6.0, 11.4 Hz, 1 H), 3.75 (s, 3 H), 3.52 (m, 1 H), 2.98 (m, 1 H), 2.26 (dd, *J* = 1.2, 14.0 Hz, 1 H), 1.93 (d, *J* = 14.0 Hz, 1 H), 1.38 (m, 1 H), 1.25 (s, 3 H), 0.50 (m, 1 H), 0.33 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 168.7, 164.3, 147.4, 144.2, 131.6, 122.2, 66.9, 61.0, 60.9, 52.3, 51.5, 48.4, 29.3, 27.6, 22.3, 18.2; HRMS *m/z* (M^+) calcd 274.1205, obsd 274.1206.

Methyl (1*R,4a*R**,6a*R**,6b*S**,7a*R**,8a*R**)-4a,6a,6b,7,7a,8-Hexahydro-7a-methyl-2-oxospiro[4*H*-cyclopropa[4,5]pentaleno[1,6a-*c*]pyran-1(2*H*),2′-oxirane]-5-carboxylate. Pentalenolactone P Methyl Ester (35). Procedure A.** To a stirred solution of **34** (6 mg, 0.0219 mmol) in 3 mL of CH_2Cl_2 was added MCPBA (7.6 mg, 0.044 mmol) at room temperature. After the mixture had been refluxed for 1 day, 5% Na_2SO_3 solution (3 mL) was added to destroy excess peroxy acid, and the resulting solution was extracted with ether (3 × 10 mL). The combined organic layers were washed with saturated $NaHCO_3$ solution, dried, and concentrated. The residue was chromatographed on silica gel (elution with 18% EtOAc in petroleum ether) to give pentalenolactone P methyl ester (**35**) and small amount of β-epoxide isomer **36** (0.7 mg, combined 18%, based on the 37% (2.2 mg) recovery of starting **34**). The ratio of **35** to **36** was not determined.

Procedure B. To a stirred solution of **34** (10 mg, 0.0365 mmol) in DME (0.6 mL) and toluene (1.1 mL) was added dropwise Dibal-H (37 mL, 0.037 mmol, 1.0 M in hexane). The mixture was stirred for 30 min, and saturated $NaHCO_3$ solution (2 mL) was added. The resulting solution was stirred at −78 °C for 10 min, allowed to warm to room temperature, and extracted with ether (3 × 10 mL). The combined organic extracts were dried and concentrated to afford the crude lactol, which was dissolved in benzene (2 mL). To this solution was added $VO(acac)_2$ (1.0 mg, catalytic amount) and ^{t}BuOOH (18 μL, 0.055 mmol, 3.0 M in 2,2,4-trimethylpentane). After the reaction mixture had stirred at room temperature for 30 min, H_2O (5 mL) and saturated Na_2SO_3 solution (0.5 mL) were added, and the resulting solution was extracted with ether (3 × 10 mL). The combined organic extracts were washed with H_2O, dried, and evaporated to give crude epoxy lactol, which was taken up in 2 mL of CH_2Cl_2.

To this stirred solution was added NMO (8.5 mg, 0.073 mmol), 4-Å molecular sieves, and TPAP (0.6 mg, catalytic amount). The reaction mixture was stirred for 20 min at room temperature, diluted with 30% ethyl acetate in petroleum ether, and filtered through a silica gel column. Solvent evaporation and purification on a silica gel TLC plate (elution with 18% EtOAc in petroleum ether) gave pentalenolactone **35** (1.7 mg, 19%), β-epoxide isomer **36** (0.6 mg, 7%), and β-methyl lactone **37** (4.0 mg, 45%) based upon 17% (1.7 mg) recovery of starting **34**. Synthetic pentalenolactone P methyl ester was further purified on a Perkin-Elmer series-2 LC system equipped with an LC-75 UV detector using a 4.6 mm i.d. × 25 cm Zorbox-Sil column, eluting with 50:1 CH_2Cl_2–EtOAc at a solvent flow rate of 2.5 mL/min.

For **35**: FT-IR ($CHCl_3$, cm^{-1}) 1765, 1713, 1632; ^1H NMR (300 MHz, $CDCl_3$) δ 6.77 (m, 1 H), 4.79 (dd, *J* = 6.0, 11.8 Hz, 1 H), 4.13 (dd, *J* = 8.4, 11.8 Hz, 1 H), 3.76 (s, 3 H), 3.26–3.19 (m, 2 H), 3.09 (d, *J* = 4.7 Hz, 1 H), 2.88 (d, *J* = 4.7 Hz, 1 H), 2.06 (dd, *J* = 1.5, 13.8 Hz, 1 H), 1.95 (d, *J* = 13.8 Hz, 1 H), 1.29–1.23 (m, 1 H), 1.19 (s, 3 H), 0.42 (m, 1 H), 0.18 (dd, *J* = 3.8, 5.4 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 169.9, 164.3, 146.9, 132.7, 68.0, 58.1, 56.3, 53.7, 53.3, 51.8, 49.3, 43.9, 28.9, 28.1, 22.0, 16.3; HRMS *m/z* (M^+ − OMe) calcd 259.0970, obsd 259.0977.

For **36**: FT-IR ($CHCl_3$, cm^{-1}) 1763, 1711, 1634; ^1H NMR (300 MHz, $CDCl_3$) δ 6.78 (t, *J* = 2.2 Hz, 1 H), 4.63 (dd, *J* = 3.9, 11.5 Hz, 1 H), 4.38 (dd, *J* = 3.1, 11.5 Hz, 1 H), 3.77 (s, 3 H), 3.63 (m, 1 H), 3.11 (m, 1 H), 3.05 (d, *J* = 5.0 Hz, 1 H), 3.01 (d, *J* = 5.0 Hz, 1 H), 1.78 (d, *J* = 13.3 Hz, 1 H), 1.70 (dd, *J* = 1.3, 13.3 Hz, 1 H), 1.26 (m, 1 H), 1.19 (s, 3 H), 0.41 (m, 1 H), 0.15 (dd, *J* = 3.8, 5.4 Hz, 1 H); HRMS *m/z* (M^+ − OMe) calcd 259.0970, obsd 259.0958.

For **37**: IR ($CHCl_3$, cm^{-1}) 1740, 1710, 1630; ^1H NMR (300 MHz, $CDCl_3$) δ 6.66 (t, *J* = 2.2 Hz, 1 H), 4.67 (dd, *J* = 1.3, 11.9 Hz, 1 H), 4.24 (dd, *J* = 3.2, 11.9 Hz, 1 H), 3.74 (s, 3 H), 3.39 (m, 1 H), 2.95 (m, 1 H), 2.63 (q, *J* = 6.6 Hz, 1 H), 2.09 (dd, *J* = 1.4, 14.0 Hz, 1 H), 1.97 (d, *J* = 14.0 Hz, 1 H), 1.31 (d, *J* = 6.6 Hz, 3 H), 1.26 (m, 1 H), 1.21 (s, 3 H), 0.42 (m, 1 H), 0.12 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 174.7, 164.5, 147.6, 131.7, 65.4, 59.3, 54.2, 54.0, 51.5, 49.6, 41.4, 29.6, 26.7, 21.8, 17.4, 10.2; HRMS *m/z* (M^+) calcd 276.1361, obsd 276.1368.

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Supplementary Material Available: Summary of data collection and data refinement, crystallographic experimental details, and tables of bond distances, bond angles, least-squares planes, final fractional coordinates, and thermal parameters for **i** (7 pages); table of observed and calculated structure factors for **i** (3 pages). Ordering information is given on any current masthead page.