and 1,3-cyclooctadiene with disiamylborane. GC pure (100%) compounds were obtained by preparative GC using a 6 ft × 0.5 in. column packed with 20% SP-2100 on Chromosorb W (60–80 mesh).

1-(2-Cyclohexenyl)-1-ethanol: IR (neat) ν_{max} 3359, 1642 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.5–6.0 (m, 2 H), 3.6–3.9 (m, 1 H), 1.4–2.3 (m, 8 H), 1.2 (d, J = 4 Hz, 3 H); ^{13}C NMR ($CDCl_3$) ppm 129.87, 128.34, 70.61, 42.90, 25.32, 23.73, 21.36, 19.95.

1-(2-Cycloheptenyl)-1-ethanol: IR (neat) ν_{max} 3355, 1644 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.6–6.1 (m, 2 H), 3.8 (m, 1 H), 1.3–2.5 (m, 10 H), 1.1 (d, J = 4 Hz, 3H); ^{13}C NMR ($CDCl_3$) ppm 133.41, 132.37, 70.88, 46.97, 30.32, 28.93, 28.67, 26.89, 19.58.

1-(2-Cyclooctenyl)-1-ethanol: IR (neat) ν_{max} 3358, 1644 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.3–5.9 (m, 2 H), 3.65 (m, 1 H), 1.3–2.6 (m, 12 H), 1.1 (d, J = 4 Hz, 3 H); ^{13}C NMR ($CDCl_3$) ppm 130.60, 130.50, 71.53, 43.94, 31.80, 29.42, 26.91, 26.73, 25.61, 21.30.

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Intramolecular Anionic Cyclization Route to Capped [3]Peristylanes

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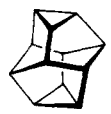
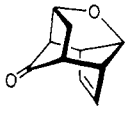
A short route to capped [3]peristylanes, in particular the polycyclic ether **9**, is described. The synthesis begins with the known unsaturated ketone **3** and proceeds by way of a two-carbon chain extension, chemospecific reduction, epoxidation, and anionic cyclization to form the first additional framework C–C bond. Following tosylation, the cyclopropane ring is elaborated under anionic conditions. The regioselectivity of ring closure is discussed in the context of MM2 calculations. Although nitrile **8** could be transformed by conventional methods to the carboxylic acid, subsequent Hunsdiecker degradation of this intermediate proved unworkable. On the other hand, **8** proved subject to decyanation when heated with potassium hydride in tetrahydrofuran. The response of **8** and **9** to the action of trimethylsilyl iodide was briefly examined. In both examples, the cyclopropane ring was cleaved while the ether linkage was unaffected.

The molecular array *p*-[$3^2.5^6$]octahedrane (**1**)[1] is the smallest member of a family of polycyclic saturated $(CH_2)_n$ systems having a central *n*-membered ring (for **1**, n = 6) connected by alternate carbon atoms to two $(n/2)$-membered rings.[2] Dramatic alterations in structural topology are expected to accompany changes in n. To this time, the pentagonal dodecahedrane and select derivatives (n = 5) have been the only representatives studied.[3] We are interested in defining the precise nature of these geometric perturbations and in correlating the various structural features with chemical reactivity.[4] For this reason, **1** has been chosen as a synthetic target of interest, although a less symmetric dimethyl analogue has been recently prepared.[5]



1

2



3

Examination of the carbocyclic framework of **1** in a retrosynthetic sense has led us to consider the readily available diketone **2**[6] as a potentially suitable starting material. Two symmetrically disposed carbon atoms are seen to be lacking and these must ultimately serve as the linchpins for construction of the two cyclopropane rings. In the present paper, methods are described that resulted in the desired chemical construction on one surface of **2** *under mild conditions* (thus avoiding framework rearrangement[7,8]).

Ganter and co-workers have convincingly demonstrated that the carbonyl groups in **2** are sterically compressed.[9] This situation, which markedly lowers the reactivity of these centers (particularly following nucleophilic attack at one of them), can be ameliorated by bridging across half of the molecule as in **3**. This substance is prepared from **2** by reduction with lithium tri-*tert*-butoxyaluminum hydride and cyclization with 2 N sodium hydroxide in methanol.[8,9] Accordingly, we have utilized **3** in this initial study. Our investigation has culminated in an eight-step synthesis of **9** via a route potentially applicable to the elaboration of **1**.

Condensation of **3** with the anion of diethyl (cyanomethyl)phosphonate proceeded with customary good efficiency (81%) to give **4** as an inseparable 4:1 mixture of isomers. Reduction of the admixed α,β-unsaturated nitriles with magnesium in methanol[10] occurred with complete

(1) For an explanation of this nomenclature, see footnote 4 in Paquette, L. A.; Browne, A. R.; Doecke, C. W.; Williams, R. V. *J. Am. Chem.* **1983**, *105*, 4113.

(2) Garratt, P. J.; White, J. F. *J. Org. Chem.* **1977**, *42*, 1733.

(3) (a) Paquette, L. A.; Balogh, D. W.; Usha, R.; Kountz, D.; Christoph, G. G. *Science (Washington, D.C.)* **1981**, *211*, 575. (b) Paquette, L. A.; Balogh, D. W. *J. Am. Chem. Soc.* **1982**, *104*, 774. (c) Christoph, G. G.; Engel, P.; Usha, R.; Balogh, D. W.; Paquette, L. A. *Ibid.* **1982**, *104*, 784. (d) Paquette, L. A.; Ternansky, R. J.; Balogh, D. W. *Ibid.* **1982**, *104*, 4502. (e) Ternansky, R. J.; Balogh, D. W.; Paquette, L. A. *Ibid.* **1982**, *104*, 4503. (f) Paquette, L. A.; Ternansky, R. J.; Balogh, D. W.; Taylor, W. J. *Ibid.* **1983**, *105*, 5441. (g) Paquette, L. A.; Ternansky, R. J.; Balogh, D. W.; Kentgen, G. *Ibid.* **1983**, *105*, 5446.

(4) For preliminary studies aimed at the member of this series where n = 4, consult Paquette, L. A.; Fischer, J. W.; Browne, A. R.; Doecke, C. W. *J. Am. Chem. Soc.* **1985**, *107*, 686.

(5) A dimethyl derivative of **1** is known: Hirao, K.; Ohuchi, Y.; Yonemitsu, O. *J. Chem. Soc., Chem. Commun.* **1982**, 99.

(6) (a) Baggiolini, E.; Herzog, E. G.; Iwasaki, S.; Sehorta, R.; Schaffner, K. *Helv. Chim. Acta* **1967**, *50*, 297. (b) Klinsman, U.; Gauthier, J.; Schaffner, K.; Pasternak, M.; Fuchs, B. *Ibid.* **1972**, *55*, 2643.

(7) Doecke, C. W.; Garratt, P. J. *Tetrahedron Lett.* **1981**, *22*, 1051.

(8) (a) Ammann, W.; Jäggi, F. J.; Ganter, C. *Helv. Chim. Acta* **1980**, *63*, 2019. (b) Ramos Tombo, G. M.; Chakrabarti, S.; Ganter, C. *Ibid.* **1983**, *66*, 914.

(9) (a) Pfund, R. A.; Ganter, C. *Helv. Chim. Acta* **1979**, *62*, 228. (b) Ammann, W.; Ganter, C. *Ibid.* **1977**, *60*, 1924.

(10) Profitt, J. A.; Watt, D. S.; Corey, E. J. *J. Org. Chem.* **1975**, *40*, 127.

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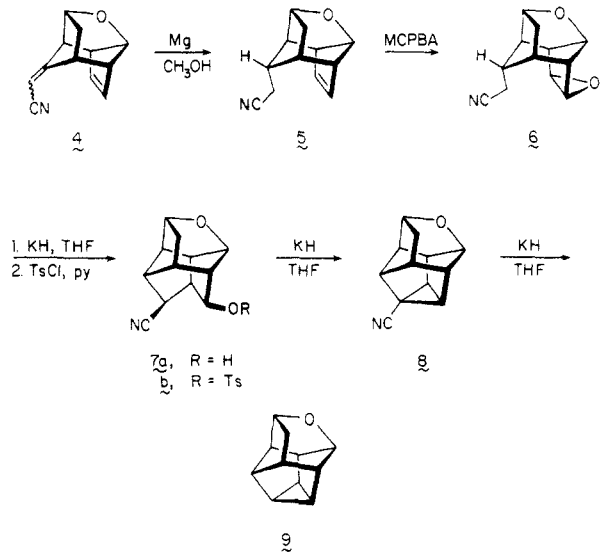
regiocontrol and with delivery of hydrogen to the β carbon from its convex face to provide **5** (94%). Consideration of the geometry of **5** predicts that epoxidation of its double bond should occur uniquely from that direction syn to the oxa bridge. Indeed, **6** was formed in essentially quantitative yield.

The stereochemical questions relevant to the conversion of **4** to **6** could not be unequivocally ascertained by detailed ^{1}H NMR analysis. However, the correctness of the assumptions was established in ring closure of **6** leading to alcohol **7a** (78%) upon exposure to potassium hydride in

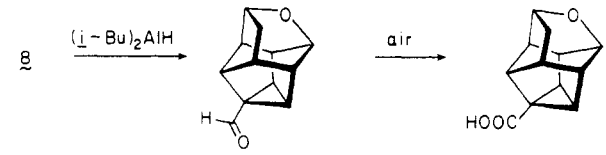


refluxing tetrahydrofuran for 30 min. Although two possible cyclization pathways are open to **6**, only one is followed within the limits of spectroscopic detection. Although our penultimate goal of arriving at **8** can be served by either isomer, it is of some interest to ponder the underlying reason for this selectivity. The pair of options can be reduced to construction of the carbocyclic ring systems A and B, where the hydroxy and cyano groups

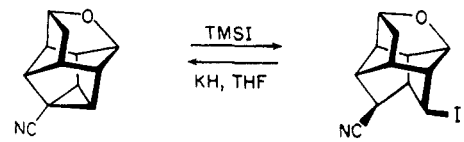
have been excised to simplify matters. To the extent that the differing levels of ring strain present in these two structures are experienced by the anion of **6** while advancing toward the two relevant transition states, B should be favored. Thus, MM2 optimizations targeted at A and B show A to be 7.7 kcal/mol less stable than B.[11] Apparently, the added antagonist twist that the molecule must accommodate during C–C bond formation as in A is adequate to deter the operation of this reaction channel. In contrast, the carbon atoms in the framework of B are conjoined without undue additional strain.

In accord with our original expectations, tosylate **7b** underwent ready cyclization when heated with potassium hydride in tetrahydrofuran solvent for 30 min. Careful analysis of reaction mixtures heated for twice this length of time revealed that **9** was now co-formed with **8**. This interesting decyanation could be effected independently on pure **8**, although the yield of isolated **9** proved always to be in the 8–9% range. This inefficiency could be traced in part to the high volatility of **9**, but other ill-defined degradation side reactions certainly operate competitively. The more notable features of the 300-MHz ^{1}H NMR spectrum of **9** include three distinctively different cyclopropyl signals at δ 2.09–1.72 and a pair of unit area >CHO absorptions at δ 4.46 (t, J = 5.3 Hz) and 4.34–4.31 (m).

The success of the **8** → **9** conversion was especially welcomed when it was discovered subsequently that carboxylic acid **11**, prepared conventionally from **8**, failed to undergo controlled Hunsdiecker degradation when subjected to several modifications of this reaction. The materials isolated appeared to be products of more extensive chemical change.



Were the ether linkages in **8** and **9** to prove more receptive to electrophile-induced cleavage than the constituent cyclopropane rings, the possibility existed for repetition of the protocol just completed to achieve arrival at **1**. Trimethylsilyl iodide was the reagent most extensively examined. As concerns **8**, smooth conversion to **12** was observed. The endo orientation of its cyano group



is assumed on the basis of kinetically controlled protonation during the workup procedure. Treatment of **12** with potassium hydride returned **8**. Analogous handling of **9** afforded two isomeric products resulting from cleavage of its cyclopropane ring (^{1}H NMR analysis). No search was made to optimize these conditions since it was abundantly clear that the necessary chemoselectivity was not being realized.

Nevertheless, capped [3]peristylanes are now known to be accessible under anionic conditions. One of our current goals involves the exploration of possibilities for preparing the parent octahedrane **1** via comparable routes beginning with diketone **2**.

Experimental Section

(2,3,4,4a,7,7a-Hexahydro-4,2,7-ethanylylidenecyclopenta[*b*]pyran-8-ylidene)acetonitrile (4). A nitrogen-blanketed solution of diethyl cyanomethylphosphonate (5.95 g, 33.6 mmol) in anhydrous tetrahydrofuran (10 mL) was vigorously stirred at 0 °C while *n*-butyllithium in hexane (20.9 mL of 1.55 M, 33.5 mmol) was introduced slowly via syringe. The resulting sludge was stirred at room temperature for 1 h, at which points a solution of **3** (1.36 g, 8.4 mmol) in dry tetrahydrofuran was added dropwise. The reaction mixture was heated at reflux for 84 h, cooled, and treated with water (30 mL). The solution was saturated with sodium chloride and extracted with ether (3 × 25 mL). The combined organic layers were washed with 6 M hydrochloric acid (25 mL) and saturated sodium bicarbonate solution (25 mL) prior to drying. Solvent evaporation gave an orange oil, which was taken up in ether and passed through a short Florisil column. The oil so obtained slowly crystallized and was triturated with hexanes to give **4** (1.25 g, 80.6%) as a powdery white solid, mp 109–110 °C after sublimation. The substance was approximately a 4:1 mixture of isomers. The following are the spectral properties of the major constituent: IR ($CHCl_3$) cm^{-1} 2980, 2150, 1350, 1080, 1070, 940; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.89 (t, J = 1.7 Hz, 2 H), 4.96 (s, 1 H), 4.88 (m, 1 H), 4.43 (t, J = 4.1 Hz, 1 H), 3.38 (m,

(11) Houk, K. N.; Brown, F., private communication.

1 H), 2.99 (m, 1 H), 2.66 (br s, 1 H), 2.56 (m, 1 H), 1.94 (d, J = 12.2 Hz, 1 H), 1.62 (dt, J = 12.1, 4.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$) ppm 174.54, 134.04, 128.59, 116.55, 89.96, 87.90, 81.20, 53.86, 48.29, 46.86, 45.63, 33.32; MS, m/z calcd (M^+) 185.0840, obsd 185.0743.

Anal. Calcd for $C_{12}H_{11}NO$: C, 77.81, H, 5.99. Found: C, 77.80; H, 6.17.

2,3,4,4a,7,7a-Hexahydro-4,2,7-ethanylylidenecyclopenta-[*b*]pyran-8-acetonitrile (5). Magnesium turnings (6.9 g, 0.283 mol) were added to a stirred solution of **4** (1.3 g, 7.0 mmol) in dry methanol (138 mL). After the vigorous reaction had subsided, the mixture was stirred at room temperature for 24 h. The magnesium salts were dissolved by addition of 6 M hydrochloric acid (130 mL). When the solution had cooled, the product was extracted into ether (4 × 50 mL) and dichloromethane (1 × 50 mL, 3 × 25 mL). The combined organic layers were washed with brine (2 × 100 mL), dried, and evaporated to leave a brown oil. This material was purified by passage through a Florisil column (ether elution) and obtained as a colorless semisolid (1.25 g, 95%), mp 60–69 °C, which was utilized directly in the next step: IR ($CHCl_3$) cm^{-1} 2750, 2150, 1355, 1070, 990, 940, 880; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.01–5.94 (m, 2 H), 4.89–4.86 (m, 1 H), 4.34–4.32 (m, 1 H), 2.99–2.82 (m, 2 H), 2.69–2.60 (m, 2 H), 2.41–2.23 (m, 2 H), 2.03–2.00 (m, 1 H), 1.77 (d, J = 11.8 Hz, 1 H), 1.60 (dt, J = 11.8, 4.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$) ppm 134.24, 132.30, 119.58, 91.53, 82.99, 48.56, 45.34, 43.73, 43.01, 39.14, 38.39, 18.90; MS, m/z calcd (M^+) 187.0997, obsd 187.0987.

Octahydro-6,2,4-ethanylylideneoxireno[3,4]cyclopenta-[1,2-*b*]pyran-7-acetonitrile (6). A cold (0 °C), magnetically stirred solution of **5** (1.25 g, 6.68 mmol) in dichloromethane (12 mL) was treated in one portion with *m*-chloroperbenzoic acid (1.40 g, 7.0 mmol), and the oxidation was allowed to proceed for 1 h at 0 °C and for 6 h at room temperature. Water (50 mL) and dichloromethane (50 mL) were added and the layers were separated. The aqueous phase was extracted with dichloromethane (50 mL), and the combined organic solutions were washed with saturated sodium thiosulfate (2 × 30 mL) and sodium bicarbonate solutions (2 × 30 mL) prior to drying. Solvent evaporation afforded a pale yellow oil that crystallized upon cooling. This solid was dissolved in the minimum amount of dichloromethane and diluted with petroleum ether to yield 1.29 g (95.6%) of **6** as colorless crystals, mp 196.0–196.5 °C (from dichloromethane–petroleum ether): IR ($CHCl_3$) cm^{-1} 2980, 2960, 2150, 1390, 1360, 1250, 1105, 1075, 840; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.81 (m, 1 H), 4.20 (br s, 1 H), 3.62 (d, J = 0.98 Hz, 1 H), 3.48 (d, J = 0.98 Hz, 1 H), 3.03 (d, J = 8.6 Hz, 2 H), 2.87–2.72 (m, 2 H), 2.44 (m, 2 H), 2.07–2.02 (m, 1 H), 1.96 (d, J = 12.5 Hz, 1 H), 1.72 (dt, J = 12.0, 3.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$) ppm 118.69, 83.16, 79.24, 55.79, 54.39, 47.97, 45.84, 43.83, 41.65, 39.92, 38.61, 19.64; MS, m/z calcd (M^+) 203.0947, obsd 203.0891.

Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45. Found: C, 70.92, H, 6.42.

Decahydro-7-hydroxy-2,4,6-methenopentaleno[1,6-*bc*]-pyran-5-carbonitrile (7a). Epoxide **6** (35.7 mg, 0.176 mmol) in dry tetrahydrofuran (1 mL) was added to a slurry of potassium hydride (0.1 mL, 6.15 mmol/mL) in the same solvent (4 mL) under nitrogen. The reaction mixture was heated at reflux for 30 min, cooled, and quenched with saturated ammonium chloride solution. Water (20 mL) was added and the product was extracted into dichloromethane (3 × 25 mL). The combined organic layers were dried, filtered, and evaporated to give a yellow oil which was passed through a silica gel column to give 27.7 mg (78%) of **7a** as an oil that was tosylated directly: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.94–4.91 (m, 1 H), 4.70–4.67 (m, 1 H), 3.71 (s, 1 H), 3.33–3.32 (m, 1 H), 3.16 (s, 1 H), 3.02–2.99 (m, 1 H), 2.72–2.70 (m, 1 H), 2.39–2.34 (m, 2 H), 2.17 (br s, 1 H), 2.06 (br s, 1 H), 2.01 (d, J = 12.3 Hz, 1 H), 1.63 (dt, J = 12.3, 4.3 Hz, 1 H); ^{13}C NMR ($CDCl_3$) ppm 121.43, 86.14, 79.40, 54.05, 51.81, 51.02, 42.68, 41.01, 40.45, 40.24, 38.59, 36.61; MS, m/z calcd (M^+) 203.0945, obsd 203.0937.

This reaction proceeds in equally satisfactory yield on larger scale.

Decahydro-7-[[(4-methylphenyl)sulfonyl]oxy]-2,4,6-methenopentaleno[1,6-*bc*]pyran-5-carbonitrile (7b). Cyano alcohol **7a** (273 mg, 1.3 mmol) was dissolved in dry pyridine (2 mL) and treated with *p*-toluenesulfonyl chloride (256 mg, 1.3 mmol). The reaction mixture was stirred under nitrogen at room temperature for 68 h, poured into water, and extracted with dichloromethane (3×). The combined organic layers were twice washed with 6 N hydrochloric acid and once with water, saturated sodium bicarbonate solution, and brine. Drying, solvent removal, and MPLC on silica gel (elution with 42% ethyl acetate in petroleum ether) gave the tosylate as a colorless solid, mp 118–120 °C (from dichloromethane–petroleum ether) (407 mg, 85%): IR ($CHCl_3$) cm^{-1} 2950, 2860, 2240, 1600, 1490, 1445, 1360, 1165, 1080, 1070, 1030, 945, 820; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, J = 8.5 Hz, 2 H), 7.38 (d, J = 8.5 Hz, 2 H), 4.80 (t, J = 4.57 Hz, 1 H), 4.69 (t, J = 3.91 Hz, 1 H), 4.41 (s, 1 H), 3.37–3.32 (m, 1 H), 3.17 (s, 1 H), 3.02–2.96 (m, 1 H), 2.88 (d, J = 5.65 Hz, 1 H), 2.48 (s, 3 H), 2.40–2.39 (m, 1 H), 2.19–2.16 (m, 2 H), 1.98 (d, J = 12.49 Hz, 1 H), 1.64 (dt, J = 12.49, 3.83 Hz, 1 H); ^{13}C NMR ($CDCl_3$) ppm 145.32, 134.00, 130.12, 127.61, 119.57, 87.15, 84.41, 79.55, 53.91, 51.01, 49.97, 46.47, 43.52, 40.78, 40.18, 39.91, 21.65; MS, m/z calcd (M^+) 357.1036, obsd 357.1036.

Octahydro-2,4,5-methenocyclo[3,4]pentaleno[1,6-*bc*]-pyran-4a(4*H*)-carbonitrile (8). A. Short Reaction Time. An excess of potassium hydride in mineral oil (27 mL of 24.6% by weight, 160 mmol) was washed under nitrogen 3 times with petroleum ether and dry tetrahydrofuran (5 mL). A solution of **7b** (1.20 g, 3.39 mmol) in dry tetrahydrofuran (4 mL) was added, and the mixture was heated at the reflux temperature for 30 min. Workup in the manner described below afforded 380 mg (60.7%) of **8**, identical in all respects with the material whose spectral properties are given in part B.

B. Longer Heating. An excess of potassium hydride in mineral oil (37 mL of 24.6% by weight, 225 mmol) was washed under nitrogen 3 times with petroleum ether and dry tetrahydrofuran (10 mL) was added. A solution of **7b** (1.61 g, 4.51 mmol) in the same solvent (20 mL) was introduced and the mixture was heated at reflux for 1 h. After cooling, saturated ammonium chloride solution was carefully added, to be followed by water (50 mL). The product was taken up in dichloromethane (3 × 75 mL), washed with brine, dried, and evaporated. The residue was chromatographed on silica gel (elution with 16% ethyl acetate in petroleum ether) to give 310 mg (37.2%) of **8** as a colorless solid, mp 116–118 °C: IR ($CHCl_3$) cm^{-1} 2970, 2840, 2220, 1445, 1340, 1100, 1065, 1055, 1000, 900; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.59–4.55 (m, 1 H), 4.45–4.42 (m, 1 H), 3.53–3.47 (m, 1 H), 2.96–2.87 (m, 3 H), 2.63–2.53 (m, 2 H), 2.47–2.44 (m, 1 H), 2.05 (d, J = 12.5 Hz, 1 H), 1.55 (dt, J = 12.5, 3.60 Hz, 1 H); ^{13}C NMR ($CDCl_3$) ppm 119.85, 90.46, 80.18, 61.69, 56.82, 56.62, 53.39, 45.13, 40.72, 39.19, 36.44, 30.64; MS, m/z calcd (M^+) 185.0840, obsd 185.0806.

Anal. Calcd for $C_{12}H_{11}NO$: C, 77.81; H, 5.99; N, 7.56. Found: C, 77.26; H, 5.89; N, 7.45.

Also isolated was 80 mg (11.1%) of **9**, a volatile colorless solid, mp 173.5–174.5 °C (following sublimation): IR ($CHCl_3$) cm^{-1} 3050, 2960, 2860, 1440, 1330, 1320, 1230, 1040; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.46 (t, J = 5.3 Hz, 1 H), 4.34–4.31 (m, 1 H), 3.24–3.18 (m, 1 H), 2.73–2.65 (m, 1 H), 2.63–2.60 (m, 1 H), 2.56–2.50 (m, 1 H), 2.23–2.17 (m, 1 H), 2.09–1.95 (m, 2 H), 1.93–1.72 (m, 2 H), 1.45 (dt, J = 11.9, 3.7 Hz, 1 H); ^{13}C NMR ($CDCl_3$) ppm 91.23, 80.43, 62.04, 57.05, 54.18, 53.86, 40.89, 37.25, 35.01, 34.50, 29.29; MS, m/z calcd (M^+) 160.0888, obsd 160.0921.

Anal. Calcd for $C_{11}H_{12}O$: C, 82.46; H, 7.55. Found: C, 82.47; H, 7.83.

Independent Decyanation of 8. A solution of **8** (30 mg, 0.162 mmol) in dry tetrahydrofuran (2 mL) was added to a slurry of petroleum ether–washed potassium hydride (approximately 8 mmol) in the same solvent (5 mL). The reaction mixture was heated at reflux for 8 h, cooled, quenched with saturated ammonium chloride solution (20 mL), and extracted with dichloromethane (3 × 20 mL). The combined organic extracts were washed with brine (20 mL), dried, and evaporated. The residual yellow oil was purified by MPLC (silica gel, elution with 7% ethyl acetate in petroleum ether) to give 2.2 mg (8.5%) of **9** as a colorless solid, spectroscopically identical with the substance described above.

Octahydro-2,4,5-methanocyclopropa[3,4]pentaleno[1,6-*bc*]pyran-4a(4*H*)-carboxaldehyde (10). A solution of **8** (40 mg, 0.22 mmol) in dry benzene (2 mL) was added to a solution of diisobutylaluminum hydride (0.26 mmol, hexane solution) in dry benzene (1 mL). The reaction mixture was stirred at room temperature for 48 h, during which time additional aliquots of

the reducing agent were introduced. Saturated Rochelle salt solution was added, and after 1 h of stirring the product was extracted into dichloromethane (3 × 30 mL). The combined organic layers were washed with brine (30 mL), dried, and evaporated. The residue was purified by medium pressure liquid chromatography on silica gel (elution with 20% ethyl acetate in petroleum ether) to give **10** as a clear, colorless solid (23 mg, 57.5%), mp >225 °C (from dichloromethane–petroleum ether): IR ($CHCl_3$) cm^{-1} 2970, 2880, 2740, 1700, 1465, 1345, 1235, 1125, 1100, 1070, 1060, 1010, 945, 835; ^1H NMR (300 MHz, $CDCl_3$) δ 8.98 (s, 1 H), 4.55 (t, J = 5.2 Hz, 1 H), 4.40–4.39 (m, 1 H), 3.39–3.35 (m, 1 H), 3.14–2.72 (m, 4 H), 2.23 (br s, 1 H), 1.99 (d, J = 12.6 Hz, 1 H), 1.96 (br s, 1 H), 1.60–1.47 (m, 1 H); ^{13}C NMR ($CDCl_3$) ppm 196.95, 90.52, 80.48, 60.68, 56.49, 53.01, 50.41, 46.85, 40.85, 40.40, 36.80 (quaternary carbon not observed); MS, m/z calcd (M^+) 188.0837, obsd 188.0830.

Octahydro-2,4,5-methenocyclopropa[3,4]pentaleno[1,6-*bc*]pyran-4a(4*H*)-carboxylic Acid (11). When the benzene-d_6 solution of **10** was allowed to stand open to the air, quantitative oxidation to the carboxylic acid occurred, mp 208–209 °C (from ethyl acetate–petroleum ether): IR ($CHCl_3$) cm^{-1} 3300–2900, 2980, 1735, 1695, 1345, 1250, 1100, 1075, 1060, 1005, 995, 900; ^1H NMR (300 MHz, $CDCl_3$) δ 10.1–9.6 (br, 1 H), 4.63–4.57 (m, 1 H), 4.57–4.44 (m, 1 H), 3.47–3.37 (m, 1 H), 3.09–3.05 (m, 1 H), 2.88–2.61 (m, 4 H), 2.45–2.40 (m, 1 H), 2.06 (dd, J = 8.46, 12.5 Hz, 1 H), 1.56 (dt, J = 12.5, 3.9 Hz, 1 H); ^{13}C NMR ($CDCl_3$) ppm 177.27, 90.71, 80.68, 60.75, 56.47, 53.72, 53.08, 48.17, 41.59, 41.33, 36.92, 29.77; MS, m/z calcd (M^+) 204.0798, obsd 204.0792.

Anal. Calcd for $C_{12}H_{12}O_3$: C, 70.58; H, 5.92. Found: C, 70.69; H, 5.88.

Decahydro-7-iodo-2,4,6-methanocyclopropa[3,4]pentaleno[1,6-*bc*]pyran-5-carbonitrile (12). A. Elevated Temperature. A mixture of hexamethyldisilane (300 mg, 2.0 mmol) and iodine (500 mg, 2.0 mmol) was warmed at 65 °C until homogeneous and then heated at reflux for 1.5 h. To the cooled black mixture was added 5 mL of carbon tetrachloride. Cyano ether **8** (55.7 mg, 0.30 mmol) was next introduced and this solution was heated at the reflux temperature for 17 h. Water was added and the product was extracted into dichloromethane (3 × 30 mL). The combined organic layers were washed once each with saturated sodium thiosulfate and sodium chloride solutions, dried, and evaporated. The residue was purified by silica gel chromatography (dichloromethane elution) to give 38.3 mg (40.8%) of **12** as a pale yellow oil: IR ($CHCl_3$) cm^{-1} 2995, 2960, 2870, 2250, 1450, 1365, 1340, 1330, 1270, 1230, 1160, 1110, 1070, 1020, 820; ^1H NMR (300 MHz, $CDCl_3$) δ 5.33 (t, J = 4.28 Hz, 1 H), 4.72 (s, 1 H), 4.65–4.62 (m, 1 H), 3.11–3.10 (m, 2 H), 2.99–2.91 (m, 2 H), 2.60 (br s, 1 H), 2.51–2.50 (m, 1 H), 2.31 (br s, 1 H), 1.95 (d, J = 12.5 Hz, 1 H), 1.46 (dt, J = 12.5, 3.9 Hz, 1 H); ^{13}C NMR ($CDCl_3$) ppm 118.92, 86.96, 79.55, 53.59, 50.40, 50.08, 49.19, 46.96, 41.36, 40.88, 39.43, 28.66; MS, m/z calcd (M^+) 312.9965, obsd 312.9964.

B. Room Temperature. A mixture of hexamethyldisilane (300 mg, 2.0 mmol) and iodine (500 mg, 2.0 mmol) was warmed at 65 °C until homogeneous and then heated at reflux for 1.5 h. To the cooled black mixture was added 5 mL of carbon tetrachloride and 1.1 g of potassium carbonate. Cyano ether **8** (20 mg, 0.108 mmol) was added and stirring was maintained at room temperature for 36 h. Water was added and the product was extracted into dichloromethane (3 × 30 mL). The combined organic layers were washed with sodium thiosulfate (30 mL) and sodium chloride solutions (30 mL), dried, and evaporated. The resulting yellow oil was purified by silica gel chromatography (silica gel elution) to give 29.4 mg (87%) of **12**, identical with the material described in part A.

Recyclization of 12. Potassium hydride in mineral oil (5 mL of 24.6%, 0.8 mmol) was washed 3 times with petroleum ether, and dry tetrahydrofuran (5 mL) was added. A solution of **12** (50 mg) in the same solvent (5 mL) was added, and the reaction mixture was heated at reflux for 2 h and stirred at room temperature for 36 h. Saturated ammonium chloride solution was carefully added and the product was taken up in dichloromethane (3 × 25 mL). The combined organic layers were washed with brine, dried, and evaporated to leave a colorless solid shown to be **8** by IR and ^1H NMR spectroscopy.

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Absolute Configuration of Benzo[*c*]phenanthrene 5,6-Oxide and Other K-Region Derivatives

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Synthesis of enantiomerically pure benzo[*c*]phenanthrene (+)-(5*S*,6*R*)- and (−)-(5*R*,6*S*)-oxides is described from diastereomerically pure (−)-(5*R*,6*R*)-*trans*-5-bromo-6-[(menthyloxy)acetyl]- and (+)-(5*S*,6*S*)-*trans*-5-bromo-6-[(menthyloxy)acetyl]-5,6-dihydrobenzo[*c*]phenanthrene derived from (−)-(menthyloxy)acetic acid. Configurational assignment of the enantiomeric arene oxides is based on correlation of the CD spectra of their *trans*-*N*-acetyl-L-cysteine adducts as methyl esters with the bis((−)-α-methoxy(trifluoromethyl)phenylacetate) of (+)-(5*R*,6*R*)-*trans*-5,6-dihydroxy-5,6-dihydrobenzo[*c*]phenanthrene of known absolute configuration. Separable major and minor S adducts were obtained from each arene oxide enantiomer. Structures of the major (attack at C-6) and minor (attack at C-5) adducts were established through the use of 5-deuterated arene oxide. Predominant attack (3:1) of the thiolate at C-6 of the arene oxide is consistent with PMO calculations.

The polycyclic aromatic hydrocarbon benzo[*c*]-phenanthrene (**1**) is a weakly carcinogenic environmental contaminant.[1,2] Although the tumorigenicity of the hydrocarbon can be accounted for by formation of bay-region[3] diol epoxides on the benzo ring,[4] most of the in vitro

(1) Lunde, G.; Bjorseth, A. *Nature (London)* **1977**, *268*, 518–519.

(2) Stevenson, J. L.; Von Haam, E. *Am. Ind. Hyg. Assoc. J.* **1965**, *26*, 475–478.