534.1724 calcd for $C_{24}H_{28}N_3O_{11}$. For **72**: IR ($CHCl_3$) 3380, 3020, 1740, 1690 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.78 (s, 3 H, 5-CH_3), 2.00, 2.07 (2 s, 2 × 3 H, $OCOCH_3$), 3.63 (s, 3 H, CO_2CH_3), 3.74 (d, J = 5.0 Hz, 1 H, H-5′), 4.18 (t, J = 4.12 Hz, 1 H, H-4′), 5.37 (dd, J = 5.89 and 3.24 Hz, 1 H, H-3′), 5.44 (t, J = 6.3 Hz, 1 H, H-2′), 5.95 (d, J = 6.3 Hz, 1 H, H-1′), 7.83 (s, 1 H, H-6); ^{13}C NMR (acetone-d_6) δ 11.0 (q, –, 5-CH_3), 18.6, 18.9 (q, –, $OCOCH_3$), 50.9 (q, –, CO_2CH_3), 63.2 (d, –, C-5′), 70.2 (d, –, C-3′ or C-4′), 71.4 (d, –, C-4′ or C-2′), 82.8 (d, –, C-2′), 84.2 (d, –, C-1′), 109.8 (s, +, C-5), 134.3 (d, –, C-6), 149.8 (s, +, C-2), 162.2 (s, +, C-4), 167.7, 168.3 (s, +, 2 $OCOCH_3$), 170.9 (s, +, CO_2CH_3); HRMS (FAB/glycerol) m/e 400.1346, M + 1, 400.1356 calcd for $C_{16}H_{22}N_3O_9$.

5-Amino-1,5-dideoxy-1-(3,4-dihydro-5-methyl-2,4-dioxo-1(2*H*)-pyrimidinyl)-β-D-allofuranuronic Acid (Synthetic Thymine Polyoxin C) (4). To a 0 °C solution of **71** (88.7 mg, 0.166 mmol) in THF (8 mL) and H_2O (1.5 mL) was added solid $LiOH·H_2O$ (24 mg, 0.57 mmol). The resulting yellow solution was stirred at 0 °C for 1 h at which time the TLC in 5:4:1 $CHCl_3$–MeOH–H_2O showed the formation of **73**, R_f 0.59, at the expense of starting material, R_f 0.96 (char A). The reaction was diluted with H_2O (10 mL) and extracted with CH_2Cl_2 (3 × 20 mL) to remove any nonacidic material, and the resulting basic solution was cooled to 0 °C and acidified to pH = 2–3 with 1 N HCl. This mixture was extracted with EtOAc (6 × 20 mL), and all organic layers were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo to give **73** a yellow solid (49 mg). To a solution of this material (42.1 mg, 0.10 mmol) in MeOH (4.5 mL) was added 5% Pd/C (33 mg). The black suspension was stirred under H_2 atm for 4 h when the TLC in 5:4:1 $CHCl_3$–MeOH–H_2O showed the formation of thymine polyoxin C (**4**), R_f 0.21 (char A), at the expense of starting material at R_f 0.51. The reaction mixture was filtered through a pad of Celite + activated carbon eluting with hot H_2O (3 × 10 mL), and the filtrate was concentrated in vacuo to give synthetic **4** as a yellow solid (20.8 mg, 54% yield): mp 182–185 °C, (shr 145 °C) [authentic **4**: mp 190–194 °C (shr at 170 °C), lit.[1a] mp 240–244 °C, lit.[4b] mp 242–244 °C]; $[\alpha]_D$ +8.0° (c 0.37, H_2O) [lit.[1a] $[\alpha]_D$ +8.7° (c 0.208, H_2O), lit.[4b] $[\alpha]_D$ +8.2° (c 0.7, H_2O)]; ^1H NMR (400 MHz, D_2O + DCl, pD = 0.68) δ 1.72 (s, 3 H, 5-CH_3), 4.20 (dd, J = 6.9 and 2.6 Hz, 1 H, H-4′), 4.27 (dd, J = 6.1 and 4.0 Hz, 1 H, H-2′), 4.40 (d, J = 2.6 Hz, 1 H, H-5′), 4.53 (t, J = 6.5 Hz, 1 H, H-3′), 5.60 (d, J = 3.9 Hz, 1 H, H-1′), 7.17 (s, 1 H, H-6). This ^1H NMR spectrum was identical with one obtained with authentically derived thymine polyoxin C (vide supra). ^{13}C NMR (2:1 D_2O–DMSO-d_6) δ 11.8 (q, –, 5-CH_3), 55.7 (d, –, C-5′), 69.8 (d, –, C-3′), 72.6 (d, –, C-4′), 83.1 (d, –, C-2′), 89.2 (d, –, C-1′), 111.2 (s, +, C-5), 138.0 (d, –, C-6), 151.7 (s, +, C-2), 165.4 (s, +, C-4), 169.3 (s, +, CO_2H); HRMS (FAB/glycerol) m/e 302.0999, M + 1, 302.0988 calcd for $C_{11}H_{16}N_3O_7$.

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Synthesis of Cyclopentanobenz[*a*]anthracene Compounds Related to Carcinogenic Benz[*a*]anthracene and Cholanthrene Hydrocarbons

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Syntheses of benz[*e*]aceanthrylene (**4a**), 8-methylbenz[*e*]aceanthrylene (**4b**), and their 1,2-dihydro derivatives (**3a,b**), as well as 6-methylbenz[*j*]aceanthrylene (**5a**) and its 1,2-dihydro derivative (**2b**) from benz[*a*]anthracene-7,12-dione are described. Compounds **2b**, **3b**, **4b**, and **5b**, all of which contain a methyl group in nonbenzo bay region position, are predicted to be relatively potent carcinogens.

Methyl substitution in the 7- or 12-positions of benz[*a*]anthracene (BA) markedly enhances its carcinogenic activity,[1-5] and fusion of a cyclopentano ring in this same molecular region has a similar effect. Thus, while 7-methyl-BA (**1b**), 12-methyl-BA (**1c**), 7,12-dimethyl-BA (**1d**), cholanthrene[6] (**2a**), 6-methylcholanthrene (**2b**), 3-methylcholanthrene (**2c**), and 3,6-dimethylcholanthrene (**2d**) are relatively potent tumorigens, the parent hydrocarbon (**1a**) exhibits only weak borderline activity.[1,2]

In order to probe these structure–activity relationships further, we have undertaken the synthesis of several benz[*a*]anthracene derivatives that combine these structural features, i.e. a methyl group and a fused cyclopentano ring in the meso region. We now report the synthesis of 1,2-dihydrobenz[*e*]aceanthrylene (**3a**), 8-methyl-1,2-dihydrobenz[*e*]aceanthrylene (**3b**), **2b**, and the related fully unsaturated hydrocarbons benz[*e*]aceanthrylene (**4a**), 8-methylbenz[*e*]aceanthrylene (**4b**), and 6-methylbenz[*j*]aceanthrylene (**5b**). On the basis of current concepts concerning the mechanisms of metabolic activation and cancer induction by polycyclic hydrocarbons,[2,7] all of these hydrocarbons may be predicted to exhibit mutagenic and/or tumorigenic activity. In particular, compounds **2b**,

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(4) Hecht, S. S.; Amin, S.; Melikian, A. A.; LaVoie, E. J.; Hoffmann, D. In *Polycyclic Hydrocarbons and Carcinogenesis*; ACS Monograph No. 283; Harvey, R. G., Ed.; American Chemical Society: Washington, DC, 1985; p 85.
(5) Harvey, R. G.; Cortez, C.; Sugiyama, T.; Ito, Y.; Sawyer, T. W.; DiGiovanni, J. *J. Med. Chem.* **1987**, *31*, 154.
(6) According to CA rules, **2a** is named 1,2-dihydrobenz[*j*]aceanthrylene.
(7) Harvey, R. G. *Acc. Chem. Res.* **1981**, *14*, 218. (b) Conney, A. H. *Cancer Res.* **1977**, *37*, 3356. (c) Harvey, R. G. *Polycyclic Hydrocarbons and Carcinogenesis*; ACS Monograph No. 283; American Chemical Society: Washington, DC, 1985.

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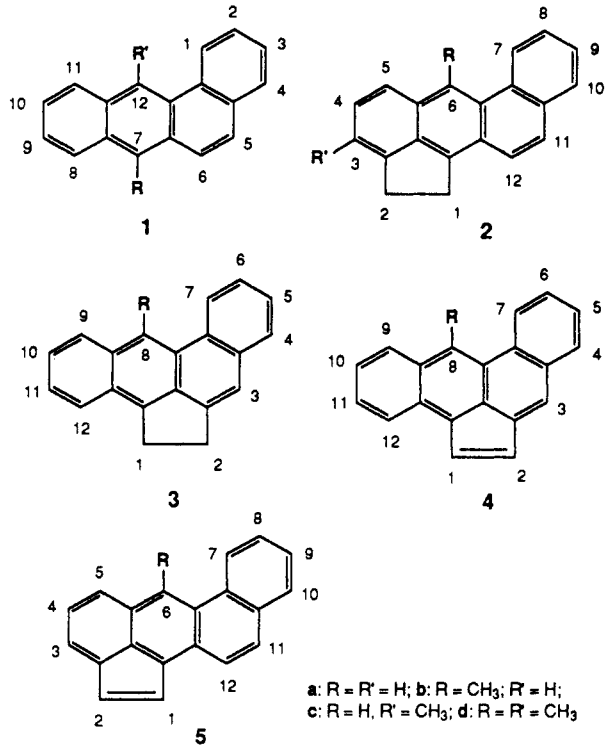

3b, **4b**, and **5b**, all of which contain a methyl group in nonbenzo bay region position, may be expected to be relatively potent carcinogens.[5]

Results

The synthetic approach to **3a** and **4a** is based upon the readily available benz[*a*]anthracene-7,12-dione (Chart I). Reformatski reaction of this quinone with ethyl bromoacetate and zinc in refluxing benzene took place smoothly and regiospecifically in the less crowded 7-position to furnish the adduct **6**. Reduction of the carbonyl group of the latter with sodium borohydride in methanol gave a mixture of ethyl *cis*- and *trans*-7,12-dihydroxy-7,12-dihydro-7-benz[*a*]anthracenylacetate (**7**). Treatment of **7** with $SnCl_2/HCl$[8] furnished the fully aromatic ethyl ester **8a**.

Cyclization of the free carboxylic acid **8b** in HF afforded a mixture of the products of cyclization to both the 6- and 8-positions,[9] with the latter predominating (1:3). In order to direct cyclization to the less favored 6-position, the terminal ring of **8a** was hydrogenated over a platinum catalyst[10] to give regioselectively **9a**, which was hydrolyzed to yield the partially saturated free acid **9b**. Cyclization of **9b** in polyphosphoric acid furnished the ketone **10** which on reduction by the Wolff–Kishner method provided 9,10,11,12-tetrahydrobenz[*e*]aceanthrylene (**11**). Dehydrogenation of **11** over a palladium/charcoal provided 1,2-dihydrobenz[*e*]aceanthrylene (**3a**). Further dehydrogenation of **3a** with DDQ in refluxing benzene yielded benz[*e*]aceanthrylene (**4a**). Dehydrogenation in two stages was necessary since five-membered rings are resistant to catalytic dehydrogenation.[11]

The synthesis of **3b** and **4b** was also based on BA-7,12-dione (Chart II). Addition of methyllithium to the quinone followed by treatment of the adduct with HCl in ethyl acetate[8] furnished 7-(chloromethyl)-12-methylbenz[*a*]anthracene (**12a**). Reaction of **12a** with KCN in dimethyl sulfoxide provided the corresponding nitrile (**12b**). Hydrolysis of **12b** in refluxing aqueous KOH and ethylene glycol under the usual conditions[12,13] (3 days) yielded the amide **12d** as the principal product. Conversion of **12d** to the free acid 12-methylbenz[*a*]anthracenylacetic acid (**12c**) required an additional 3 days under the same conditions. However, the time required could be shortened to a single day by drastically decreasing the ratio of water employed.

Hydrogenation of the methyl ester derivative **12e** over PtO_2 furnished a mixture of the products of hydrogen addition to the terminal ring (**13**) and to the 5,6-bond (**14**). Cyclization of this mixture in liquid HF yielded a mixture of the two ketones (**15** and **16**) which were readily separated by chromatography on Florisil. Since the yields of **15** and **16** were only moderate (31% and 23%, respectively), alternative hydrogenation catalysts were also investigated. The most satisfactory of these was a two-phase catalyst system consisting of $RhCl_3 \cdot 3H_2O$, Aliquat 336, and tri-*n*-octylamine in water and 1,2-dichloroethane.[14] Hydrogenation of **12e** with this catalyst afforded a mixture of **13** and **14** free of 7,12-dihydro-**12e** in 86% yield. Cyclodehydration of this mixture in liquid HF furnished smoothly **15** and **16** (48% and 37% isolated yields, respectively), readily separated by column chromatography. Wolff–Kishner reduction of **15** gave **17**, which underwent dehydrogenation over a 10% Pd/charcoal catalyst to yield **3b**. Treatment of **3b** with DDQ in refluxing benzene furnished 8-methylbenz[*e*]aceanthrylene (**4b**). Dehydrogenation of **16** over Pd/charcoal furnished the fully aromatic ketone derivative **18** in good yield.

The direct cyclization of **12e** in HF was also investigated.[15] There was obtained a mixture of the products of cyclization in both directions (**18** and **19**) in 2:1 ratio. However, the yield was low, and only **18** (16%) could be isolated pure. Wolff–Kishner reduction of **18** gave 6-methyl-1,2-dihydrobenz[*j*]aceanthrylene (**2b**), also known as 6-methylcholanthrene, identical in its properties with an authentic sample.[16] Dehydrogenation of **2b** with DDQ gave 6-methylbenz[*j*]aceanthrylene (**5b**).

Discussion

The syntheses described provide relatively convenient access to benz[*e*]aceanthrylene (**4a**), its dihydro derivative (**3a**), and their methyl-substituted derivatives in the nonbenzo bay region positions (**3b**, **4b**) as well as the corresponding methyl-substituted derivatives of benz[*j*]aceanthrylene (**2b**, **5b**).

In the synthesis of **4a** (Chart I), the observed remarkable regiospecificity of attack at the 7-position of benz[*a*]anthracene-7,12-dione in the Reformatski reaction is apparently largely a consequence of the steric bulk of the reagent, since addition of methyllithium was observed to show only a slight preference for attack at the 7-position of this quinone. The most significant feature of this synthetic approach is the use of selective hydrogenation in the terminal ring[10] to direct subsequent acid-catalyzed cyclodehydrogenation to the otherwise less favorable 6-position of the benz[*a*]anthracene ring system. This route provides **3a** and **4a** in higher overall yield than the alternative approach[9] involving cyclization without prior hydrogenation.

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(9) Sangaiah, R.; Gold, A.; Toney, G. E. *J. Org. Chem.* **1983**, *48*, 1632.
(10) Fu, P. P.; Lee, H. M.; Harvey, R. G. *J. Org. Chem.* **1980**, *45*, 2797.
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(12) Konieczny, M.; Harvey, R. G. *J. Org. Chem.* **1979**, *44*, 2158.
(13) Fu, P. P.; Harvey, R. G. *Org. Prep. Proc. Internat.* **1981**, *13*, 152.
(14) Amer, I.; Amer, H.; Ascher, R.; Blum, J.; Sasson, Y.; Vollhardt, K. P. *J. Mol. Catal.* **1987**, 185.
(15) It was reported by Russian investigators that heating **11d** with $ZnCl_2$ failed to afford cyclized products but instead gave 7,12-dimethylbenz[*a*]anthracene as the only isolable compound: Chernova, N. G.; Milkhailov, B. M. *J. Gen. Chem. (U.S.S.R.)* **1939**, *9*, 2168.
(16) Harvey, R. G.; Cortez, C. *J. Org. Chem.* **1987**, *52*, 283.

Chart I

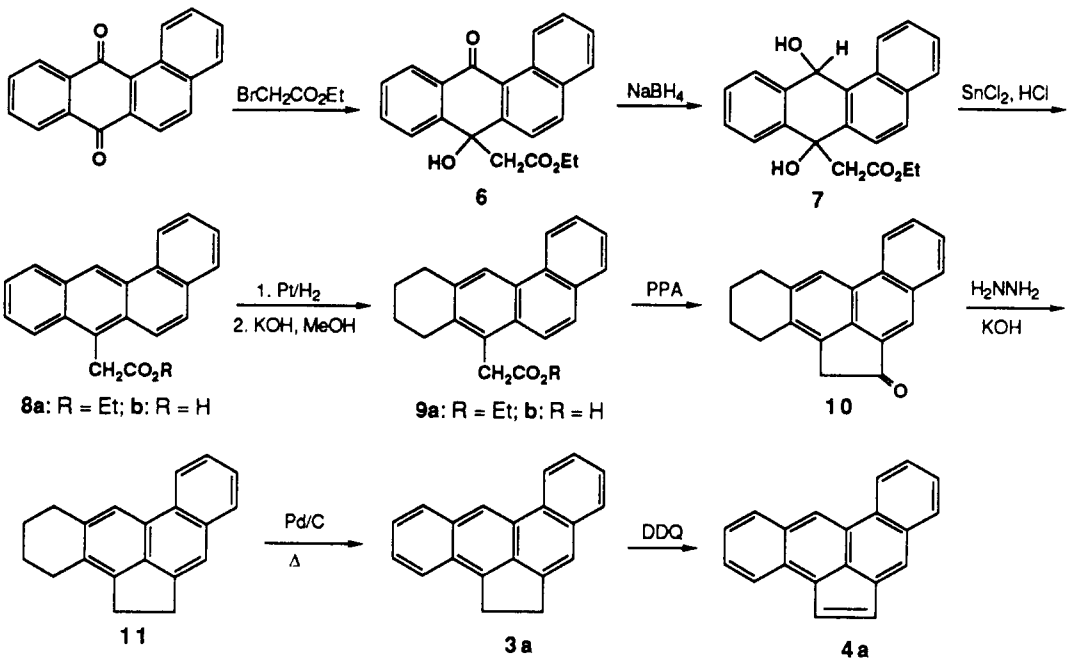
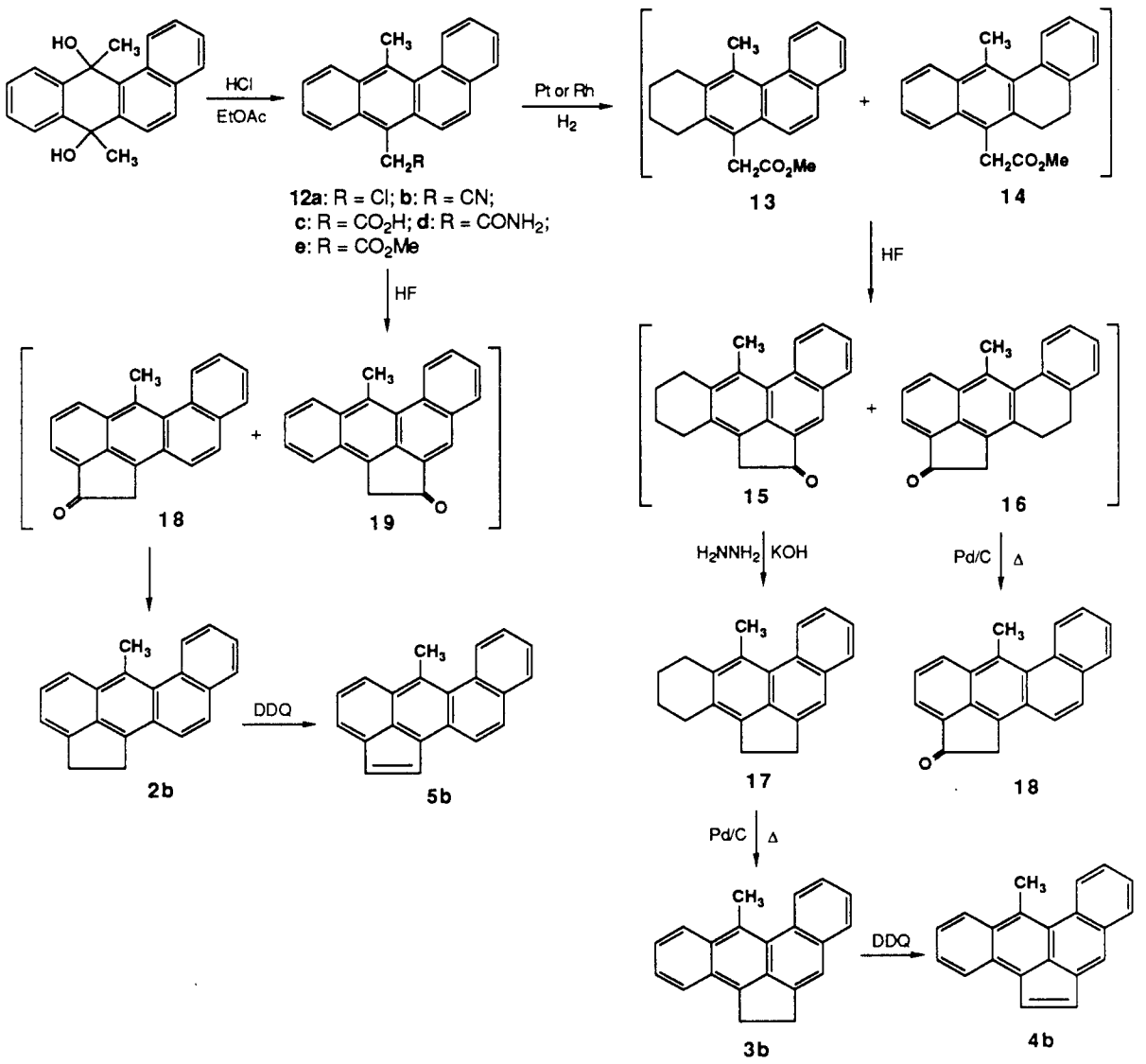


Chart II



For the conversion of the ketone **10** to products, Wolff–Kishner reduction followed by DDQ dehydrogenation was employed in preference to the alternative method involving reduction with $NaBH_4$ followed by acidic dehydration.[9,17] This route offers the twin advantages of providing the desired saturated compound **3a** and avoiding secondary loss of **4a** by acid-catalyzed dimerization and polymerization.[17] For the synthesis of the methyl-substituted compounds **2b**, **3b**, **4b**, and **5b**, it was initially attempted to employ the keto ester **6** as the starting compound. However, reaction of **6** with excess methyllithium took place preferentially on the carbonyl group of the ester function rather than on the 12-keto group.

The regioselectivity of hydrogenation of the BA ring system was found to depend upon the presence of substituents. While addition of hydrogen to unsubstituted BA was regiospecific, hydrogenation of the methyl ester **12e** over PtO_2 was less regioselective, affording a mixture of the 8,9,10,11-tetrahydro-BA and 5,6-dihydro-BA (3:2) along with a small amount of the 7,12-dihydro product. The use of the soluble rhodium catalyst in place of PtO_2 afforded a higher yield of a cleaner product but did not improve regioselectivity. Decreased regioselectivity is apparently due to the distortion of the aromatic ring system of **12e** from planarity caused by the steric effect of the methyl group in the bay region.[18] This distortion confers greater olefinic character on the K-region 5,6-bond, making it more susceptible to addition of hydrogen.[10] Nevertheless, hydrogenation prior to cyclization was advantageous since a considerably higher yield of cyclized products was obtained by this route, and compound **3b** was only accessible from **15** obtained via the hydrogenation route.

Experimental Section

General. 7-(Chloromethyl)-12-methylbenz[*a*]anthracene (**12a**), mp 137–38 °C (lit.[8] mp 138–40 °C); NMR δ 3.2 (s, 3, CH_3), 5.2 (s, 2, CH_2), 8.5 (m, 10 Ar), was synthesized by the published method.[8] Benz[*a*]anthracene-7,12-dione and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) were purchased from the Aldrich Chemical Co.; DDQ was recrystallized from benzene. Ether was dried over sodium, and triglyme was dried over molecular sieves, 4A. The NMR spectra were obtained on a Varian EM360 or the University of Chicago 500-MHz NMR spectrometer in $CDCl_3$ with tetramethylsilane as internal standard unless stated otherwise. Integration was consistent with all structural assignments. All new compounds gave satisfactory microanalysis for C, H within ±0.3% and/or mass spectra consistent with assigned structures.

Ethyl (7-Hydroxy-12-oxo-7-benz[*a*]anthracenyl)acetate (6). Zinc powder (3.27 g, 50 mmol), preactivated by washing with 2% HCl, H_2O, ethanol, acetone, and ether and heated under vacuum at 80 °C for 1 h, was placed in a flask equipped with an addition funnel and a condenser. A few crystals of iodine were added, and benz[*a*]anthracene-7,12-dione (10.32 g, 40 mmol) in a solution of ethyl bromoacetate (8.35 g, 50 mmol) in benzene (200 mL) was added portionwise over a period of 1 h. The mixture was refluxed overnight. The usual workup followed by chromatography on a column of Florisil afforded on elution with CH_2Cl_2 **6** (12.2 g, 86%): mp 169–70 °C; NMR δ 1.85 (t, 3, CH_3), 2.82 (s, 2, CH_2CO_2Et), 3.80 (q, 2, $CH_3CH_2O_2C$), 5.00 (br s, 1, OH), 7.30–8.21 (m, 10, Ar); HRMS calcd for $C_{22}H_{18}O_4$ 258.0678, *m/e* 258.0688, M^+ ($H^+CH_2CO_2Et$).

Ethyl (7-benz[*a*]anthracenyl)acetate (8a). To a cooled solution of **6** (12.18 g, 34 mmol) in 300 mL of THF and 400 mL of methanol was added $NaBH_4$ (5 g) portionwise. The mixture was stirred at room temperature under N_2 for 2.5 h. The usual workup followed by chromatography on Florisil (CH_2Cl_2) furnished a mixture of *cis*- and *trans*-**7** (10.24 g, 84%). To a stirred suspension of $SnCl_2$ (50 g) in ether (800 mL) was added concentrated HCl (30 mL), and the clear solution that resulted was added to **7**. After 10 min, 100 mL of water was added slowly, and the product was isolated by partition between ether and water and evaporated to dryness. Chromatography on Florisil gave on elution with benzene–hexane (1:1) **8a** (5.86 g, 63%) as a white solid: mp 85–86 °C (EtOAc); NMR δ 1.15 (t, 3, CH_3), 4.15 (q, 2, CH_2), 4.58 (s, 2, CH_2CO_2Et), 7.2–8.5 (m, 9, Ar), 8.80 (m, 1, H_1), 9.2 (s, 1, H_{12}). Anal. Calcd for $C_{22}H_{18}O_2$: C, 84.05; H, 5.77. Found: C, 84.33; H, 5.86.

(8,9,10,11-Tetrahydro-7-benz[*a*]anthracenyl)acetic Acid (9b). A mixture of **8a** (1 g) and PtO_2 (100 mg) in ethyl acetate (100 mL) was hydrogenated at 20 psig for 2 h. The catalyst was removed by filtration, and the solvent was evaporated to yield **9a** (950 mg, 95%): NMR δ 1.28 (t, 3, CH_3), 1.98 (m, 4, $H_{9,10}$), 3.10 (m, 4, $H_{8,11}$), 4.15 (s, 2, CH_2CO_2Et), 4.20 (q, 2, CH_2), 7.55–8.10 (m, 5, Ar), 8.45 (s, 1, H_{12}), 8.70 (m, 1, H_1).

Hydrolysis of the partially saturated ester with KOH (20 g) in water (20 mL) and methanol (50 mL) at reflux for 2 h provided the free acid **9b** (855 mg, 95%): mp >246 °C (EtOAc); NMR (acetone-d_6) δ 2.00 (m, 4, $H_{9,10}$), 3.05 (m, 4, $H_{8,11}$), 4.10 (s, 2, CH_2CO_2H), 7.4–8.1 (m, 5, Ar), 8.5 (s, 1, H_{12}), 8.7 (m, 1, H_1); HRMS calcd for $C_{20}H_{18}O_2$ 290.1302, *m/e* 290.1309.

2-Oxo-1,2,9,10,11,12-hexahydrobenz[*e*]aceanthrylene (10). Liquid HF (100 mL) was added to **9a** (1.5 g, 4.6 mmol), and the mixture was stirred overnight. The HF was evaporated, and the residue was taken up in ether, washed with aqueous sodium bicarbonate and water, dried over $MgSO_4$, and evaporated to dryness. Purification of the residue by chromatography on Florisil eluted with benzene afforded **10** (774 mg, 76%): mp 194–95 °C (benzene); NMR δ 1.90 (m, 4, $H_{10,11}$), 3.00 (m, 4, $H_{9,12}$), 3.60 (s, 2, CH_2CO), 7.5–8.2 (m, 5, Ar), 8.6 (m, 1, H_7). Anal. Calcd for $C_{20}H_{16}O$: C, 88.20; H, 5.92. Found: C, 88.06; H, 5.95.

1,2,9,10,11,12-Hexahydrobenz[*e*]aceanthrylene (11). A mixture of **10** (2.2 g, 8 mmol), H_2NNH_2 (2.5 mL), and KOH (2.1 g) in ethylene glycol (200 mL) was heated at reflux overnight. The product was worked up conventionally and chromatographed on Florisil to yield on elution with hexane **11** (1.51 g, 73%): mp 110–11 °C; NMR δ 1.85 (m, 4, $H_{10,11}$), 2.5–3.3 (m, 4, $H_{9,12}$), 3.20 (s, 4, CH_2), 7.10–7.90 (m, 4, Ar), 7.95 (s, 1, H_8), 8.42 (m, 1, H_7). Anal. Calcd for $C_{20}H_{18}$: C, 92.98; H, 7.02. Found: C, 92.94; H, 7.06.

1,2-Dihydrobenz[*e*]aceanthrylene (3a). A solution of **11** (1.06 g, 4.1 mmol) in triglyme (50 mL) in the presence of 10% Pd/C (530 mg) was heated at reflux for 2 h under N_2. The usual workup followed by crystallization from hexane–benzene gave **3a** (991 mg, 95%): mp 147–48 °C; NMR (500 MHz) δ 3.44 (m, 2, H_2), 3.66 (m, 2, H_1), 7.29 (s, 1, H_3), 7.50–7.54 (m, 4, $H_{5,6,10,11}$), 7.73 (m, 1, H_{12}), 7.95 (m, 1 H_4), 8.10 (m, 1 H_9), 8.63 (m, 1 H_7), 8.71 (s, 1, H_8); UV λ_{max} (EtOH), 222.8 nm (35 200), 263.4 (38 300), 273.3 (40 280), 284.0 (76 900), 294.5 (99 900). Anal. Calcd for $C_{20}H_{14}$: C, 94.45; H, 5.55. Found: C, 94.37; H, 5.60.

Benz[*e*]aceanthrylene (4a). A solution of **3a** (151 mg, 0.59 mmol) and DDQ (140 mg, 0.62 mmol) in benzene (130 mL) was stirred at ambient temperature under N_2. The reaction was monitored by HPLC and found to be complete in 2 h. The mixture was passed through a column of neutral alumina. Elution with benzene afforded **4a** (82 mg, 55%) as an orange solid, mp 136–37 °C (lit.[9] mp 138 °C).

7-(Cyanomethyl)-12-methylbenz[*a*]anthracene (12b). A solution of **12a** (1.77 g, 6.1 mmol) in DMSO (15 mL) was added over 10 min to a rapidly stirred suspension of KCN (595 mg, 9.2 mmol) in DMSO (30 mL) at 70 °C under N_2. The mixture was stirred for an additional 40 min, cooled to room temperature, and diluted with water. The aqueous layer was saturated with sodium chloride and then extracted several times with ether. The combined extracts were washed with water, dried ($MgSO_4$), filtered, and concentrated to give crude **12b**, which was purified by chromatography on Florisil. Elution with benzene furnished pure **12b** (1.37 g, 79%): mp 140–41 °C; NMR δ 3.00 (s, 3, CH_3), 4.12 (s, 2 CH_2), 7.2–8.3 (m, 10, Ar). Anal. Calcd for $C_{21}H_{15}N$: C, 89.65; H, 5.37; N, 4.98. Found: C, 89.55; H, 5.38; N, 4.96.

(17) Becker, H.-D.; Hansen, L.; Andersson, K. *J. Org. Chem.* **1985**, *50*, 277.

(18) The effect of methyl substitution in the bay region of benz[*a*]anthracene on planarity is dramatic. X-ray analyses of 7,12-dimethylbenz[*a*]anthracene indicate that the angle between the planes of the two outer rings is approximately 24°. Review: Glusker, J. P. In *Polycyclic Hydrocarbons and Carcinogenesis*; Harvey, R. G., Ed.; ACS Monograph No. 283. American Chemistry Society: Washington, DC, 1985; p 125.

7-(12-Methylbenz[*a*]anthryl)acetic Acid (12c). To a suspension of **12b** (1.40 g, 4.9 mmol) in ethylene glycol (50 mL) was added KOH (1.12 g) in 5 mL of H_2O. The mixture was heated at reflux for 24 h until all the solid was completely dissolved. The hot solution was filtered, and the filtrate was acidified with dilute aqueous HCl. The white solid precipitate of **12c** (1.25 g, 85%), melted at 237–38 °C (EtOAc): NMR δ 3.3 (s, 3, CH_3), 4.5 (s, 2, CH_2), 7.3–8.5 (m, 10, Ar). Anal. Calcd for $C_{21}H_{16}O_2$: C, 83.98; H, 5.36. Found: C, 83.74; H, 5.43.

Methyl 7-(12-Methylbenz[*a*]anthryl)acetate (12e). A solution of **12c** (500 mg, 1.66 mmol) and 5 drops of concentrated HCl in methanol (150 mL) was stirred overnight at room temperature. Conventional workup provided the crude **12e**, which was purified by chromatography on Florisil eluted with benzene. Crystallization from EtOAc afforded **12e** as a white solid (470 mg, 90%): mp 140–42 °C; NMR δ 3.4 (s, 3, CH_3), 3.6 (s, 3, CH_3O), 4.5 (s, 2, CH_2), 7.3–8.5 (m, 10, Ar). Anal. Calcd for $C_{22}H_{18}O_2$: C, 84.05; H, 5.77. Found: C, 83.95; H, 5.77.

2-Oxo-1,2,9,10,11,12-hexahydro-8-methylbenz[*e*]aceanthrylene (15) and 2-Oxo-1,2,11,12-tetrahydro-6-methylbenz[*j*]aceanthrylene (16). (a) PtO_2 Catalyst. A mixture of **12e** (370 mg, 1.18 mmol) and PtO_2 (37 mg) in EtOAc (30 mL) was hydrogenated at 30 psig for 8 h. After removal of the catalyst by filtration, the solvent was evaporated, and the residue was chromatographed on Florisil. Elution with benzene gave a mixture (350 mg) of **13** and **14**. The mixture was stirred in liquid HF (100 mL) at room temperature overnight. Following evaporation of the HF, the residue was taken up in ether, washed with water and aqueous $NaHCO_3$, and chromatographed on Florisil. Elution with benzene afforded **16** (100 mg, 23%): mp 203–4 °C (EtOAc); NMR δ 2.81–2.90 (m, 4, $H_{11,12}$), 2.9 (s, 3, CH_3), 3.73 (s, 2, CH_2), 7.22–8.22 (m, 7, Ar). Anal. Calcd for $C_{21}H_{16}O$: C, 88.70; H, 5.67. Found: C, 88.43; H, 5.72. Further elution with benzene furnished pure **15** (137 mg, 31%): mp 209–210 °C (EtOAc); NMR δ 1.86 (m, 2, H_{10or11}), 1.94 (m, 2, H_{10or11}), 2.81 (t, 2, H_{9or12}), 2.94 (t, 2, H_{12or9}), 3.52 (s, 2, H_2), 7.56 (t, 1, H_{6or5}), 7.66 (t, 1, H_{5or6}), 7.99 (d, 1, H_4, $J_{4,5}$ = 5.8 Hz), 8.00 (s, 1, H_3), 8.77 (d, 1, H_7, $J_{6,7}$ = 8.5 Hz). Anal. Calcd for $C_{21}H_{18}O$: C, 88.08; H, 6.34. Found: C, 87.98; H, 6.35. In addition, there was obtained a small amount of the 7,12-dihydro product (by NMR).

(b) Rhodium Catalyst. Hydrogen gas was bubbled through a solution of **12e** (1.5 g, 4.8 mmol) in 1,2-dichloroethane (50 mL) and 1 mL of distilled water, 5 drops of trioctylamine, and 5 drops of Aliquot 336 in the presence of $RhCl_3 \cdot 3H_2O$ (50 mg) at 20 psig for 24 h at room temperture. The reaction was monitored by TLC. After the usual workup, the product was purified by chromatography on Florisil (benzene) to provide a mixture of **13** and **14** (1.3 g, 86%). The mixture (1.06 g, 3.3 mmol) was stirred in liquid HF (100 mL) at ambient temperature overnight and worked up conventionally. Chromatography on a Florisil column gave on initial elution with benzene **16** (365 mg, 37%) followed by **15** (470 mg, 48%); these products were identical by NMR with the samples obtained from hydrogenation of **12e** over PtO_2.

1,2,9,10,11,12-Hexahydro-8-methylbenz[*e*]aceanthrylene (17). A mixture of **15** (470 mg, 1.59 mmol), H_2NNH_2 (0.6 mL), and KOH (500 mg) in ethylene glycol (50 mL) was refluxed overnight. The usual workup followed by chromatography on Florisil (hexane) afforded **17** (264 mg, 59%) as a white solid: mp 134–5 °C (EtOAc); NMR δ 1.88 (m, 2, H_{10or11}), 1.94 (m, 2, H_{10or11}), 2.85 (t, 2, H_{1or2}), 2.90 (s, 3, CH_3), 2.97 (t, 2, H_{1or2}), 3.22 (t, 2, H_{12or9}), 3.34 (m, 2, H_{9or12}), 7.37 (s, 1, H_3), 7.46 (m, 2 $H_{5,6}$), 7.78 (m, 1, H_4), 8.75 (m, 1, H_7). Anal. Calcd for $C_{21}H_{20}$: C, 92.60; H, 7.40. Found: C, 92.66; H, 7.45.

1,2-Dihydro-8-methylbenz[*e*]aceanthrylene (3b). A solution of **17** (43 mg, 0.16 mmol) in triglyme (20 mL) in the presence of 10% Pd/C (25 mg) was refluxed for 5 h under N_2. The usual workup followed by chromatography on Florisil (hexane) afforded **3b** (42 mg, 99%): mp 143–44 °C (EtOAc); NMR δ 3.49 (s, 3, CH_3), 3.56 (m, 2, H_2), 3.83 (m, 2, H_1), 7.44 (s, 1, H_3), 7.64–7.77 (m, 4, $H_{5,6,10,11}$), 7.90 (m, 1, H_4), 8.16 (m, 1, H_{12}), 8.56 (m, 1, H_9), 8.87 (m, 1, H_7); UV λ_{max} (EtOH) 204.7 nm (18200), 222.0 (25400), 261.9 (23350), 271.4 (26900), 282.0 (56330), 293.4 (81510). Anal. Calcd for $C_{21}H_{16}$: C, 93.99; H, 6.01. Found: C, 93.95; H, 6.05.

8-Methylbenz[*e*]aceanthrylene (4b). A solution of **3b** (42 mg, 0.12 mmol) and DDQ (39 mg, 0.17 mmol) in benzene (20 mL) was stirred at room temperature for 30 min under N_2. Filtration through a short column of neutral alumina (benzene) yielded **4b** (26 mg, 63%) as a white solid: mp 88–90 °C; NMR δ 3.47 (s, 3, CH_3), 7.02 (d, 1, H_2, $J_{1,2}$ = 5.2 Hz), 7.54–7.60 (m, 4, $H_{5,6,10,11}$), 7.66 (d, 1, H_1), 7.98 (s, 1, H_3), 7.99 (d, 1, H_4, $J_{4,5}$ = 10.1 Hz), 8.27 (d, 1, H_{12}, $J_{11,12}$ = 8.0 Hz), 8.41 (d, 1, H_9, $J_{8,9}$ = 8.6 Hz), 8.86 (d, 1, H_7, $J_{6,7}$ = 8.2 Hz); UV λ_{max} (EtOH) 230.8 nm (31400), 264.9 (42200), 281.8 (37600), 292.8 (43600), 293.3 (44700); HRMS calcd for $C_{21}H_{14}$ 266.1092, *m/e* 266.1059 (M^+).

2-Oxo-1,2-dihydro-6-methylbenz[*j*]aceanthrylene (18). (a) From 12c. The acid **12c** (300 mg, 1 mmol) was stirred in liquid HF (100 mL) at room temperature overnight. The usual workup followed by chromatography on Florisil afforded on elution with benzene–ether (9:1) a mixture of **18** and **19**. Crystallization from benzene afforded pure **18** (45 mg, 16%) as a white solid: mp 186–87 °C (EtOAc); NMR δ 3.38 (s, 3, CH_3), 4.06 (s, 2, H_1), 7.62–7.70 (m, 4, $H_{8,9,11,12}$), 7.82–7.88 (m, 2, $H_{4,10}$), 8.03 (d, 1, H_3, $J_{3,4}$ = 6.8 Hz), 8.48 (d, 1, H_5, $J_{4,5}$ = 8.3 Hz), 8.64 (m, 1, H_7); HRMS calcd for $C_{21}H_{14}O$ 282.1044, *m/e* 282.1086 (M^+).

(b) From 16. N_2 was bubbled through a solution of **16** (30 mg, 0.10 mmol) in triglyme (30 mL) and 10% Pd/C (40 mg) in a flask equipped with a condenser, and the mixture was maintained at reflux for 24 h. The usual workup followed by column chromatography on Florisil provided **18** (25 mg, 83%) as a white solid, mp 186–187 °C. The NMR spectrum matched that of an authentic sample.

6-Methyl-1,2-dihydrobenz[*j*]aceanthrylene (2b). Wolff–Kishner reduction of the carbonyl group of **18** (45 mg, 0.15 mmol) with KOH (100 mg) and H_2NNH_2 (0.5 mL) in diethylene glycol (20 mL) by the procedure employed for the preparation of **17** provided **2b** (20 mg, 46%) as a white solid: mp 143–44 °C (lit.[14] mp 143–144 °C); NMR δ 3.44 (s, 3, CH_3), 3.65 (m, 1, H_2), 3.84 (m, 1, H_1), 7.46 (d, 1, H_3, $J_{3,4}$ = 6.7 Hz), 7.65–7.72 (m, 4, $H_{4,8,9,12}$), 7.82 (d, 2, H_{11}, $J_{11,12}$ = 9.0 Hz), 7.95 (m, 1, H_{10}), 8.09 (d, 1, H_5), 8.78 (m, 1, H_7); UV λ_{max} (EtOH) 200.9 nm (7400), 221.5 (9500), 366.5 (3800) 285.6 (25000), 296.0 (26000).

6-Methylbenz[*j*]aceanthrylene (5b). A solution of **2b** (9 mg, 0.033 mmol) and DDQ (8.2 mg, 0.036 mmol) in benzene (5 mL) was stirred at room tempertaure for 30 min under N_2. Filtration through a short column of neutral alumina (benzene) yielded **5b** (8 mg, 88%) as an orange solid: mp 133–134 °C; NMR δ 3.48 (s, 3, CH_3), 7.06 (d, 1, H_2, $J_{1,2}$ = 5.1 Hz), 7.50 (d, 1, H_1), 7.55–7.62 (m, 3, $H_{4,8,9}$), 7.63 (d, 1, H_{11}, $J_{11,12}$ = 8.97 Hz), 7.63 (d, 1, H_{3or10}), 7.81 (d, 1, H_{3or10}), 7.97 (d, 1, H_{12}), 8.23 (d, 1, H_5, $J_{4,5}$ = 8.52 Hz), 8.60 (d, 1, H_7, $J_{7,8}$ = 7.94 Hz); UV λ_{max} (EtOH) 201.7 nm (19800), 221.0 (19600), 269.2 (22000), 306.0 (15000); HRMS calcd for $C_{21}H_{14}$ 266.1092, *m/e* 266.1055 (M^+).

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