Synthesis of Isomeric *cis*-Dihydrodiols and Phenols of Highly Mutagenic Dibenz[*a*,*c*]anthracene

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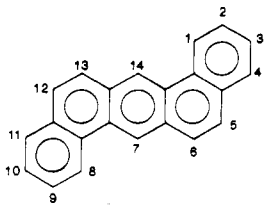
Received August 30, 1988

The isomeric benzo-ring *cis*-dihydrodiols and phenols of dibenz[*a*,*c*]anthracene (DB[a,c]A) have been synthesized. The appropriate dihydro-DB[a,c]A was treated with osmium tetraoxide to produce the corresponding *cis*-tetrahydrodiols of DB[a,c]A. These *cis*-tetrahydrodiols were converted to the corresponding *cis*-dihydrodiols by the synthetic routes useful in the preparation of *trans*-dihydrodiols of the polynuclear aromatic hydrocarbons. Essentially two synthetic routes were followed for the preparation of the phenolic derivatives of DB[a,c]A. 1-Hydroxy-, 2-hydroxy-, 3-hydroxy-, 4-hydroxy-, and 10-hydroxy-DB[a,c]A were obtained by a catalytic dehydrogenation of the corresponding aryl ketones. These aryl ketones were obtained either by Jones oxidation of the appropriate alcohol or by acid-catalyzed debenzoylation of the appropriate tetrahydro diesters of DB[a,c]A. Alternatively, *trans*-1,2-bis(benzoyloxy)-1,2,3,4-tetrahydro-DB[a,c]A and *trans*-10,11-bis(benzoyloxy)-10,11,12,13-tetrahydro-DB[a,c]A were treated with a catalytic amount of *p*-toluenesulfonic acid to produce the corresponding enol benzoate, which on dehydrogenation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) followed by acid- or base-catalyzed hydrolysis produced 2-hydroxy- and 11-hydroxy-DB[a,c]A, respectively. UV and fluorescence data for the *cis*-dihydrodiols and phenols of DB[a,c]A have also been recorded.

Polynuclear aromatic hydrocarbons (PAHs) are ubiquitous environmental contaminants. It is well established that these chemicals require metabolic activation to exhibit their mutagenic and carcinogenic activities. It is now generally accepted that the bay-region diol epoxides[3,4] are the ultimate mutagenic and carcinogenic metabolits of a number of alternant PAHs including dibenz[*a*,*h*]-anthracene (DB[a,h]A) (1). In our earlier communication



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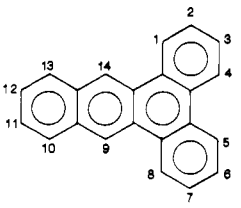

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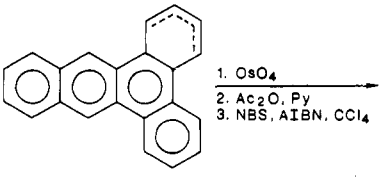
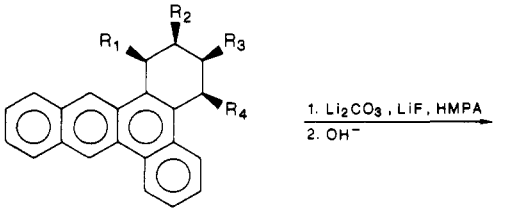
we propsed that, in contrast to DB[a,h]A, the isomeric dibenz[*a*,*c*]anthracene (DB[a,c]A) (2) is not likely to be activated via the bay-region diol epoxide pathway.[5] Since DB[a,c]A, a weak tumor initiator,[6,7] is more mutagenic than DB[a,h]A,[8,9] it is likely that DB[a,c]A is metabolically activated to mutagenic products structurally different from its bay-region diol epoxides.

While clearcut evidence on the structure of biologically active metabolite(s) of DB[a,c]A is lacking, the most probable candidates appear to be DB[a,c]A-1,2-oxide and/or DB[a,c]A-3,4-oxide. Like bay-region diol epoxides of PAHs, these arene oxides may be more effective as electrophilic intermediates capable of alkylating nucleic acid (DNA) due to the following reasons: (i) they are sterically hindered arene oxides, and there is sufficient evidence[10–12] that sterically hindered arene oxides are relatively poorer substrates for microsomal epoxide hydrolase than are sterically unhindered arene oxides; and

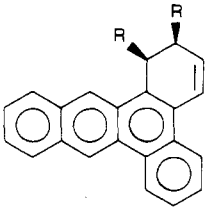
Scheme I



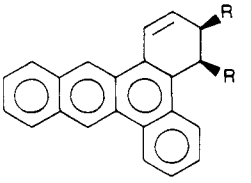
12: 3,4-dihydro-
13: 1,2-dihydro-



15: $R_1 = R_2 = OH$, $R_3 = R_4 = H$
16: $R_1 = R_2 = H$, $R_3 = R_4 = OH$
18: $R_1 = R_2 = OAc$, $R_3 = R_4 = H$
19: $R_1 = R_2 = H$, $R_3 = R_4 = OAc$
22: $R_1 = R_2 = OAc$, $R_3 = H$, $R_4 = Br$
23: $R_1 = Br$, $R_2 = H$, $R_3 = R_4 = OAc$



3: R = OH
24: R = OAc



4: R = OH
25: R = OAc

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Scheme II

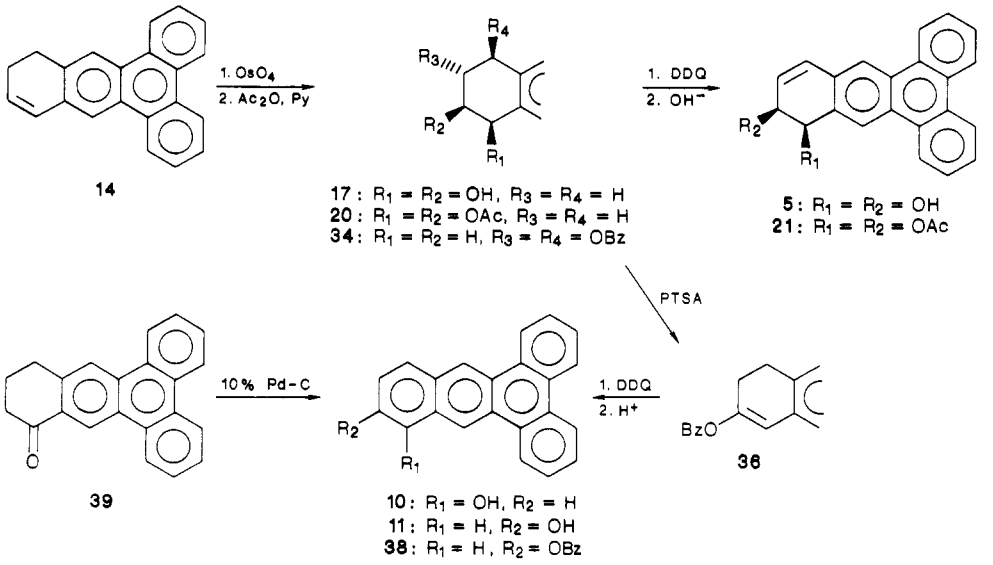

Table I. ^{1}H NMR Spectral Data of Dihydrodiol Diesters and Dihydrodiols[a]

compd	carbinol ester/carbinol hydrogens: benzylic	carbinol ester/carbinol hydrogens: nonbenzylic	vinyl hydrogens: benzylic	vinyl hydrogens: nonbenzylic	acetyl hydrogens	aromatic hydrogens
24	H_1 7.14 (d)	H_2 6.09 (m)	H_4 7.44 (dd)	H_3 6.26 (dt)	2.08, 2.25	7.00–8.44 (7 H), 8.63 (H_{14}), 8.93 (H_8), 9.23 (H_9)
	($J_{1,2}$ = 5.3; $J_{1,3}$ = $J_{2,3}$ = 1.2; $J_{2,4}$ = 2.9; $J_{3,4}$ = 10.1; $J_{7,8}$ = 7.3 Hz)					
25	H_4 6.93 (m)	H_3 6.03 (m)	H_1[b]	H_2 6.25 (m)	2.07, 2.20	7.50–8.20 (8 H), 8.72 (H_{14}), 8.87 (H_8), 9.22 (H_9)
	($J_{1,2}$ = 9.9; $J_{2,3}$ = $J_{2,4}$ = 1.3; $J_{3,4}$ = 5.6 Hz)					
21	H_{10} 6.35 (d)	H_{11} 5.84 (m)	H_{13} 6.91 (dd)	H_{12} 6.09 (dd)	2.10, 2.16	7.50–9.08 (10 H)
	($J_{10,11}$ = 4.5; $J_{11,12}$ = 3.8; $J_{11,13}$ = 1.0; $J_{12,13}$ = 9.8 Hz)					
3	H_1 5.37 (d)	H_2 4.66 (m)	H_4 7.18 (dd)	H_3 6.18 (d)	–	7.45–8.32 (7 H), 8.83 (H_{14}), 8.94 (H_8), 9.33 (H_9)
	($J_{1,2}$ = 4.7; $J_{2,3}$ = 1.0; $J_{2,4}$ = 2.3; $J_{3,4}$ = 9.9 Hz)					
4	H_1 5.31 (d)	H_3 4.74 (m)	H_1 7.47 (dd)	H_2 6.30 (d)	–	7.53–8.45 (7 H), 8.92 (H_{14}), 9.04 (H_8), 9.45 (H_9)
	($J_{1,2}$ = 10.1; $J_{1,3}$ = 2.8; $J_{2,3}$ = $J_{2,4}$ = 1; $J_{3,4}$ = 5 Hz)					
5	H_{10} 4.74 (d)	H_{11} 4.29 (m)	H_{13} 6.82 (d)	H_{12} 6.16 (dd)	–	7.72–8.81 (m, 10 H)
	($J_{10,11}$ = 4.3; $J_{11,12}$ = 4.4; $J_{12,13}$ = 9.7 Hz)					

[a] Spectra were recorded in acetone-d_6 and CD_3OD, with Me_4Si as internal standard. [b] The resonance of the indicated bay-region hydrogens occurs within the aromatic absorption region.

(ii) these arene oxides are calculated[13,14] to be fairly stable to rearrangement to phenols. In order to prove our hypothesis and to elucidate the mechanism by which DB[a,c]A is metabolized to mutagenic and possibly carcinogenic metabolites, we require authentic samples of isomeric *cis*-dihydrodiols, *trans*-dihydrodiols, and benzo-ring phenols which are the spontaneous hydration and isomerization products of the arene oxide metabolites of DB[a,c]A. In the previous communication[5] we reported the synthesis and the UV spectrum of *trans*-1,2-dihydroxy-1,2-dihydro- and *trans*-3,4-dihydroxy-3,4-dihydro-DB[a,c]A. The present paper describes herein the synthesis and spectral properties of isomeric *cis*-dihydrodiols **3–5** and benzo-ring phenols **6–11**.

Results and Discussion

***cis*-Dihydrodiols of DB[a,c]A.** The general approach for synthesizing *cis*-dihydrodiol derivatives of DB[a,c]A is outlined in Schemes I and II. The appropriate dihydro-DB[a,c]A, namely, 3,4-dihydro- (**12**), 1,2-dihydro- (**13**), and 10,11-dihydro-DB[a,c]A (**14**), were prepared as described earlier[5,15] and treated with osmium tetraoxide[16] in pyridine to produce tetrahydro-*cis*-diols **15–17**, respectively, in 59–98% yields. These tetrahydro-*cis*-diols **15–17** were acetylated (Ac_2O–pyridine) to the corresponding tetrahydro-*cis*-diol diacetates **18–20** in nearly quantitative yields. The dehydrogenation of *cis*-10,11-diacetoxy-10,11,12,13-tetrahydro-DB[a,c]A (**20**) with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) proceeded smoothly in refluxing dioxane to produce **21** (see Scheme II). An alternate procedure, which requires radical bromination followed by base-catalyzed dehydrobromination, converted **18** and **19** to **24** and **25**, respectively, in moderate yield. Finally, *cis*-dihydrodiol diacetates **24**, **25**, and **21** were saponified in a 1:1 mixture of THF and MeOH to produce the corresponding *cis*-dihydrodiols **3–5**. The high-resolution NMR spectrum of *cis*-dihydrodiols **3–5** and their precursors were consistent with their structural assignments. The UV spectra of *cis*-dihydrodiols **3–5** of DB[a,c]A were nearly identical with those for the corresponding *trans*-dihydrodiols[5] of DB[a,c]A (EtOH). The ^{1}H NMR spectra of *cis*-dihydrodiols **3–5** were very informative in assigning the relative conformation of carbinol protons. The values of the coupling constants between the

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Table II. Ultraviolet Absorption Data for the *cis*-Dihydrodiols and Phenols of DB[a,c]A[a]

compd	absorption maxima (molar extinction coefficients), nm ($10^{-4}\epsilon_{max}$)
3	228 (5.71), 254 (sh, 3.83), 263 (4.67), 280 (2.15), 290 (2.97), 303 (4.36), 316 (5.08), 351 (0.51), 368 (0.73), 387 (0.56)
4	227 (3.79), 263 (5.44), 272 (9.09), 289 (2.01), 300 (1.96), 314 (1.91), 348 (0.48), 365 (0.70), 384 (0.47)
5	203 (2.78), 240 (sh, 2.63), 255 (sh, 4.51), 264 (7.12), 274 (9.05), 293 (1.93), 305 (1.68), 319 (1.64)
6	209 (4.0), 240 (2.14), 265 (4.67), 275 (6.80), 285 (7.71), 321 (1.19), 334 (1.10), 349 (0.45), 361 (0.26), 380 (0.19)
7	211 (4.14), 244 (3.11), 264 (4.71), 274 (7.16), 283 (8.58), 311 (2.0), 324 (0.96), 350 (0.48)
8	207 (3.75), 250 (3.73), 256 (3.71), 264 (4.20), 281 (6.80), 291 (8.21), 319 (1.03), 333 (0.93), 363 (0.22), 383 (0.18)
9	212 (3.40), 263 (3.95), 279 (5.38), 289 (7.29), 337 (0.59), 351 (0.38), 363 (0.33), 382 (0.27)
10	205 (2.74), 221 (2.74), 242 (sh, 3.79), 250 (4.89), 261 (3.44), 271 (3.50), 283 (5.80), 294 (6.98), 334 (1.01), 360 (0.56), 380 (0.37)
11	206 (3.07), 250 (2.83), 279 (6.16), 289 (8.12), 367 (0.26), 387 (0.24)

[a] Spectra were measured in 1% THF-EtOH.

carbinol hydrogens (J_{diol}) of the synthetic *cis*-dihydrodiols **3–5** were very similar ($J_{diol} \sim 4.30$–5.0 Hz) (see Table I) but were markedly different in the trans isomers.[5] Since, unlike for *trans*-dihydrodiol isomers, the relative conformation of the carbinol protons for all three *cis*-dihydrodiol isomers **3–5** remains the same, pseudoaxial-equatorial, J_{diol} values do not change from one isomer to another isomer. Further, the significant coupling constant (*W* coupling) between the allylic carbinol hydrogen and the benzylic vinyl hydrogen indicates that, in *cis*-1,2-dihydrodiol **3** ($J_{2,4}$ = 3 Hz) and *cis*-3,4-dihydrodiol **4** ($J_{1,3}$ = 3 Hz), the allylic hydroxyl group prefers the pseudoequatorial conformation. This was expected because the benzylic hydroxyl group in these compounds prefers the pseudoaxial conformation due to steric strain in the bay region. The fact that the *W* coupling was not observed in *cis*-10,11-dihydrodiol **5** ($J_{11,13}$ = 0 Hz) suggests that the allylic hydroxyl group in **5** prefers the pseudoaxial conformation.[16] Furthermore, the relatively large value for $J_{11,12}$ in **5** compared to those of $J_{2,3}$ in **3** and **4**, respectively, is consistent with the expected conformations of the vicinal carbinol protons of the *cis*-dihydrodiols.[16]

Hydroxydibenz[*a*,*c*]anthracenes 6–11. Synthesis of 1-hydroxy-DB[a,c]A (**6**) and 4-hydroxy-DB[a,c]A (**9**) was conveniently achieved by catalytic dehydrogenation of 1-oxo- and 4-oxo-1,2,3,4-tetrahydro-DB[a,c]A, **28** and **31**, respectively, with 10% Pd–C in refluxing 1-methylnaphthalene (Scheme III). The desired ketones **28** and **31** were obtained by the Jones oxidation of the corresponding hydroxy derivatives **26** and **27** prepared according to the reported procedures.[5] The catalytic dehydrogenation of 10-oxo-10,11,12,13-tetrahydro-DB[a,c]A (**39**)[17] with 10% Pd–C/1-methylnaphthalene (Scheme II) provided pure 10-hydroxy-DB[a,c]A (**10**).

2-Oxo-1,2,3,4-tetrahydro-[DB[a,c]A (**29**) and 3-oxo-1,2,3,4-tetrahydro-DB[a,c]A (**30**), key intermediates for the synthesis of 2-hydroxy-DB[a,c]A (**7**) and 3-hydroxy-DB[a,c]A (**8**), were synthesized from *trans*-1,2-bis(benzoyloxy)-1,2,3,4-tetrahydro-DB[a,c]A (**32**)[5] and *trans*-3,4-bis(benzoyloxy)-1,2,3,4-tetrahydro-DB[a,c]A (**33**),[5] respectively, as shown in Scheme III. The refluxing of **32** and **33** with an excess of *p*-toluenesulfonic acid (PTSA) in dry benzene produced almost quantiative yields of ketones **29** and **30**, respectively. The use of a catalytic amount of *p*-toluenesulfonic acid converted **32** and **34** to 2-(benzoyloxy)-3,4-dihydro-DB[a,c]A (**35**) and 11-(benzoyloxy)-12,13-dihydro-DB[a,c]A (**36**) in 36% yield (Schemes II and III). The latter reaction failed to proceed with **33** as evident from the total recovery of the starting material. The catalytic dehydrogenation of ketones **29** and **30** with 10% Pd–C in refluxing 1-methylnaphthalene produced the desired 2-hydroxy-DB[a,c]A (**7**) and 3-hydroxy-DB[a,c,]A (**8**). Alternatively, the dehydrogenation of dihydro esters **35** and **36** with DDQ gave 2-(benzoyloxy)-DB[a,c]A (**37**) and 11-(benzoyloxy)-DB[a,c]A (**38**), respectively. Base- and/or acid-catalyzed hydrolysis of these esters provided the free phenols 2-hydroxy-DB[a,h]A (**7**) and 11-hydroxy-DB[a,h]A (**11**).

Scheme III

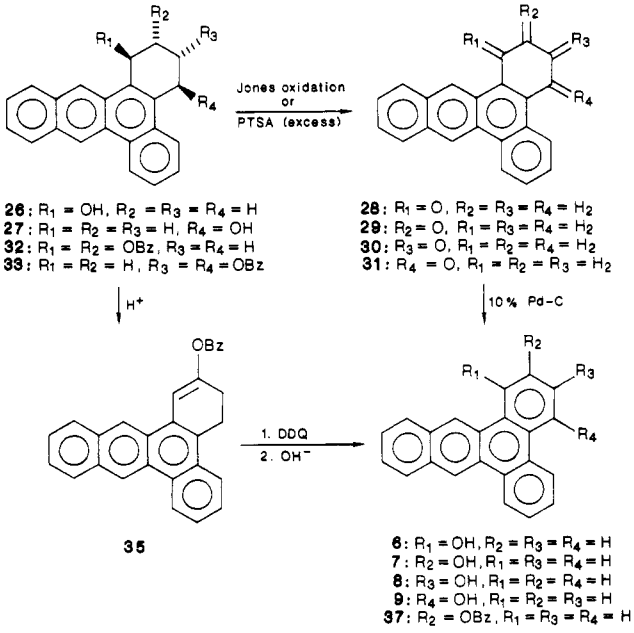

Table III. Fluorescence Spectral Data for the *cis*-Dihydrodiols and Phenols of DB[a,c]A[a]

compd	maxima, nm	relative intensity
3	412, 436	13, 14
4	410, 429	20, 22
5	372, 382, 405	1, 1, 1
6	385, 406	16, 16
7	422	10
8	400, 416	22, 23
9	386, 408	25, 25
10	427	6
11	403, 418	18, 20

[a] Spectra were measured in 1% THF–EtOH at an excitation wavelength of 337 nm with a slit width of 3 nm.

The ^{1}H NMR spectra of six isomeric benzo-ring phenols of DB[a,c,]A are consistent with their structures. The bay-region protons (H_1, H_4, H_5, H_8, H_9, and/or H_{14}) of phenols appear at the lowest field due to their steric interaction.[18,19] The protons ortho to the hydroxyl group in the ^{1}H NMR spectra of the isomeric phenols appear relatively upfield with respect to other aromatic protons. This observation is consistent with those reported earlier[20,21] for phenolic derivatives of other PAHs. In order to

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facilitate the identification of the phenolic and dihydrodiol metabolites of DB[a,c]A, UV and fluorescence spectral data on these derivatives have also been recorded and given in Table II and Table III, respectively.

Experimental Section

^{1}H NMR spectra were recorded on a JEOL-270 FX spectrometer in the Department of Biochemistry, the State University of New York, Buffalo, NY. Unless noted otherwise, $CDCl_3$ was used as the solvent with tetramethylsilane as an internal standard. Ultraviolet and fluorescence spectra were recorded on Perkin-Elmer Model Lambda-4B and LS-5B spectrophotometers, respectively. Mass spectra were obtained on a KRATOS MS80RFA spectrometer in the Department of Biophysics, State University of New York, Buffalo, NY. Elemental microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, TN. Dry column-grade silica gel was purchased from E. Merck. Melting points were uncorrected.

***cis*-1,2-Diacetoxy-1,2,3,4-tetrahydrodibenz[*a*,*c*]anthracene (18).** To a stirred solution of OsO_4 (375 mg, 1.47 mmol) in dry pyridine (8.5 mL) at 0 °C under argon was added 3,4-dihydrodibenz[*a*,*c*]anthracene (**12**)[5] (413 mg, 1.474 mmol). The resultant mixture was stirred at room temperature for 30 min, and then a solution of sodium bisulfite (760 mg) in water (11 mL) and methanol (22 mL) was added to it. This reaction mixture was stirred further for 52 h at room temperature, after which it was poured into water (250 mL). The solid thus obtained was filtered, washed with water, and dried to yield 455 mg (98%) of **15**. Recrystallization from ethyl acetate yielded a colorless crystalline solid, mp 242–243 °C.

A mixture of **15** (410 mg, 1.306 mmol), pyridine (10 mL), and acetic anhydride (25 mL) was stirred for 24 h at room temperature. The reaction mixture was poured into water (125 mL) and stirred. The solid that separated out was filtered, washed with water, and dried to yield a crystalline solid. Recrystallization of the solid yielded 486 mg (93%) of pure **18**: mp 273–275 °C; ^{1}H NMR (270 MHz) δ 2.11 (s, 3 H), 2.15 (s, 3 H), 1.80–2.60 (m, 2 H_3), 3.00–3.75 (m, 2 H_4), 5.38 (m, H_2), 7.10 (br s, H_1), 7.40–8.21 (m, 7 H), 8.46 (s, H_{14}), 8.86 (d, H_8), 9.17 (s, H_9), $J_{7,8}$ = 7.8 Hz; high-resolution mass spectrum mass obsd 398.1542, calcd 398.1517.

***cis*-1,2-Diacetoxy-1,2-dihydrodibenz[*a*,*c*]anthracene (24).** A mixture of **18** (100 mg, 0.25 mmol), *N*-bromosuccinimide (50 mg, 0.28 mmol), and α,α'-azobis(isobutyronitrile) (AIBN, 10 mg) in dry CCl_4 (25 mL) was stirred at 70–75 °C for 15 min under argon. After cooling to room temperature, the mixture was filtered, and the filtrate was evaporated under reduced pressure to yield 117 mg (98%) of **22** as a yellow aerosol, which on trituration with ether–hexane gave a crystalline solid, mp 131–132 °C dec.

A solution of **22** (110 mg, 0.23 mmol) in HMPA (2.5 mL) was stirred with LiF (225 mg) and Li_2CO_3 (350 mg) at 70–75 °C for 3 h in an Ar atmosphere. After cooling, the reaction mixture was extracted with EtOAc (4 × 25 mL). The combined EtOAc extracts were washed repeatedly with water (5 × 25 mL), dried (Na_2SO_4), and evaporated. The residue was chromatographed on preparative TLC (silica gel, uniplates) using 5% EtOAc–benzene as developing solvent. Compound **24** was recrystallized from EtOAc as light yellow crystals: 34 mg (37%); mp 212–213 °C; ^{1}H NMR (270 MHz) (see Table I); high-resolution mass spectrum mass obsd 396.137 680 1, calcd 396.136 159.

***cis*-1,2-Dihydroxy-1,2-dihydrodibenz[*a*,*c*]anthracene (3).** A solution of **24** (20 mg, 0.051 mmol) and sodium hydroxide (40%, 0.1 mL) in THF (1 mL) and MeOH (1 mL) was stirred under argon at room temperature for 5 min. Ethyl acetate (20 mL) was added, and the solution was washed with water, dried (Na_2SO_4), filtered, and evaporated under reduced pressure to yield a solid residue. Recrystallization of the solid from ethanol–ethyl acetate yielded pure **3** as pale yellow crystals (11 mg, 70%): mp 280–281 °C dec; ^{1}H NMR (270 MHz) (see Table I); mass spectrum, *m*/*e* 294 ($M^+ - H_2O$).

***cis*-3,4-Diacetoxy-1,2,3,4-tetrahydrodibenz[*a*,*c*]anthracene (19).** 1,2-Dihydrodibenz[*a*,*c*]anthracene (**13**)[5] (415 mg, 1.48 mmol) was added to a stirred solution of OsO_4 (378 mg, 1.48 mmol) in dry pyridine (7.0 mL) at 0 °C under argon. The mixture was stirred at room temperature for 30 min, and then a solution of sodium bisulfite (760 mg) in 33 mL of 1:2 water and methanol was added to it. After the reaction mixture was stirred for 52 h, it was worked up as described for the preparation of **15** to yield **16** (450 mg, 96.7%); mp 238–240 °C.

In the manner described for **18**, tetrahydrodiol **16** (425 mg, 1.354 mmol) was treated with dry pyridine (10 mL) and acetic anhydride (25 mL) to give 535 mg (99%) of **19**. Recrystallization of **19** from ethyl acetate yielded a colorless crystalline solid: mp 215–216 °C; ^{1}H NMR (270 MHz) δ 2.14 (s, 6 H), 2.20–2.47 (m, 2 H_2), 3.30–3.65 (m, 2 H_1), 5.35 (m, H_3), 6.91 (d, H_4), 7.50–8.10 (m, 7 H), 8.53 (s, H_{14}), 8.82 (d, H_8), 9.15 (s, H_9), $J_{2,3}$ = 3.4, $J_{2,3'}$ = 13.0, $J_{3,4}$ = 2.6, $J_{7,8}$ = 7.6 Hz; high-resolution mass spectrum mass obsd 398.1531, calcd 398.1517.

***cis*-3,4-Diacetoxy-3,4-dihydrodibenz[a,c]anthracene (25).** To a solution of tetrahydrodiol diacetate **19** (99.5 mg, 0.25 mmol) in dry CCl_4 (10 mL) were added NBS (47.7 mg, 0.26 mmol) and α,α'-azobis(isobutyronitrile) (AIBN, 15 mg). The mixture was stirred under argon at 70 °C for 15 min, cooled to room temperature and filtered. The filtrate was evaporated, and the residue was triturated with ether–petroleum ether to give 118 mg (99%) of **23** as a light yellow crystalline solid, mp 132–133 °C dec.

The 1-bromo derivative **23** (91 mg, 0.19 mmol) was treated with LiF (225 mg) and Li_2CO_3 (340 mg) in HMPA (2 mL), and the product was isolated as described for the preparation of **24**. The crude product was chromatographed on preparative TLC (silica gel, uniplates) using 5% EtOAc–benzene as developing solvent and then recrystallized from EtOAc to yield 25 mg (33%) of pure **25**: mp 170–171 °C; ^{1}H NMR (see Table I); high-resolution mass spectrum mass obsd 336.1152, calcd 336.1146 (for $M^+ - CH_3COOH$).

***cis*-3,4-Dihydroxy-3,4-dihydrodibenz[*a*,*c*]anthracene (4).** To a solution of dihydrodiol diacetate **25** (15 mg, 0.038 mmol) in THF (1 mL) and MeOH (1 mL) was added 40% sodium hydroxide (0.1 mL). The reaction was completed in 5 min. The mixture was diluted with EtOAc (25 mL), and the organic layer was washed with water (2 × 10 mL), dried (Na_2SO_4), and evaporated under reduced pressure. The residue was recrystallized from ether to yield **4** (10 mg, 84%) in pure form: mp 235–237 °C; ^{1}H NMR (270 MHz) (see Table I); mass spectrum, *m*/*e* 294.3 ($M^+ - H_2O$).

***cis*-10,11-Diacetoxy-10,11,12,13-tetrahydrodibenz[*a*,*c*]-anthracene (20).** A mixture of 10,11-dihydrobenz[*a*,*c*]anthracene (**14**)[15] (585 mg, 2.09 mmol) and OsO_4 (540 mg, 2.1 mmol) in dry pyridine (10 mL) was stirred for 30 min at 0 °C under argon. Sodium bisulfite (110 mg) in 15 mL of water and 30 mL of methanol was added to it at the end of 30 min. After an additional stirring for 50 h, the reaction mixture was worked up as described for **15** to yield 390 mg (59%) of **17**.

The treatment of **17** (350 mg, 1.1 mmol) with pyridine (15 mL) and acetic anhydride (5 mL) as described for **18** yielded **20** (260 mg, 58%). Recrystallization of a small sample of **20** from ether yielded pure **20** as colorless crystals: mp 225–226 °C; ^{1}H NMR (270 MHz) δ 2.10 (s, 3 H), 2.15 (s, 3 H), 1.90–2.48 (m, H_{12}), 3.05–3.40 (m, H_{13}), 5.39 (m, H_{11}), 6.40 (d, H_{10}), 7.48–9.06 (m, 10 H), $J_{10,11}$ = 2.3 Hz.

***cis*-10,11-Diacetoxy-10,11-dihydrodibenz[*a*,*c*]anthracene (21).** A solution of **20** (100 mg, 0.25 mmol) and DDQ (100 mg) in dry dioxane (10.1 mL) was refluxed for 72 h under argon. After cooling, the reaction mixture was passed through a small column of silica gel. Elution of the column with benzene yielded 52 mg (52%) of **21**; mp 195–196 °C; ^{1}H NMR (see Table I). Anal. Calcd for $C_{26}H_{20}O_4$: C, 78.78; H, 5.05. Found: C, 79.16; H, 5.19.

***cis*-10,11-Dihydroxy-10,11-dihydrodibenz[*a*,*c*]anthracene (5).** To a solution of dihydrodiol diacetate **21** (21 mg, 0.053 mmol) in THF (2 mL) and MeOH (1 mL) was added 5% NaOH (1 mL). The mixture was stirred for 10 min under argon and worked up as described for the preparation of **3**. The solid residue thus obtained was recrystallized from benzene–ether to yield 6.0 mg (36%) of **5** as a light yellow crystalline solid: mp 185–187 °C; ^{1}H NMR (see Table I); mass spectrum, *m*/*e* 312 (M^+), 294 ($M^+ - H_2O$).

1-Hydroxydibenz[*a*,*c*]anthracene (6). A mixture of 1-oxo-1,2,3,4-tetrahydrodibenz[*a*,*c*]anthracene (**28**)[5] (100 mg, 0.338

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mmol) and 25 mg of 10% Pd–C in 1-methylnaphthalene (5 mL) was refluxed for 2 h under argon. The reaction mixture was cooled, diluted with CH_2Cl_2 (25 mL), and filtered to remove the catalyst. After evaporation of CH_2Cl_2, the residue was diluted with petroleum ether (25 mL) and left overnight in an ice chest. The solid that crystallized out was filtered and recrystallized from benzene to give 50 mg (50%) of **6** as colorless crystals: mp 210–211 °C; ^{1}H NMR (270 MHz) δ 5.76 (s, 1 H, exchangeable with D_2O), 7.01 (d, H_2), 7.36–8.12 (m, 7 H)), 8.21 (d, 1 H, J = 8.2), 8.52 (d, 1 H, J = 8.6), 8.73 (d, 1 H, J = 7.2), 9.06 (s, H_9), 10.35 (s, H_{14}), $J_{2,3}$ = 8.0 Hz; high-resolution mass spectrum mass obsd 294.1071, calcd 294.1041.

2-Hydroxydibenz[*a*,*c*]anthracene (7). Method A. A solution of *trans*-1,2-bis(benzoyloxy)-1,2,3,4-tetrahydrodibenz[*a*,*c*]anthracene (**32**)[5] (315 mg, 0.6 mmol) and *p*-toluenesulfonic acid (560 mg) in 50 mL of anhydrous benzene (CaH_2) was refluxed for 30 min under argon. The solution was cooled, washed with water (3 × 20 mL), dried (Na_2SO_4), and evaporated to yield a solid. The solid was recrystallized from EtOAc–hexane to produce 160 mg (90%) of 2-oxo-1,2,3,4-tetrahydrodibenz[*a*,*c*]anthracene (**29**) as brownish yellow crystals: mp 185–189 °C dec; ^{1}H NMR (270 MHz) δ 2.90 (t, 2 H_3), 3.58 (t, 2 H_4), 4.06 (s, 2 H_1), 7.40–8.20 (m, 7 H), 8.31 (s, H_{14}), 8.87 (m, H_8), 9.19 (s, H_9), $J_{3,4}$ = 6.9 Hz.

A mixture of ketone **29** (10 mg, 0.034 mmol) and 40 mg of 10% Pd–C in 3 mL of 1-methylnaphthalene was heated under reflux for 15 min. The usual workup of the reaction mixture as described for **6** produced 5 mg (50%) of **7**: mp 287–288 °C (ether); ^{1}H NMR (270 MHz) δ 5.13 (s, 1 H, exchangeable with D_2O), 7.18 (dd, H_3), 7.30–9.10 (m, 12 H), $J_{1,3}$ = 2, $J_{3,4}$ = 10 Hz; high-resolution mass spectrum mass obsd 294.0951, calcd 294.1041.

Method B. A solution of *trans*-1,2-bis(benzoyloxy)-1,2,3,4-tetrahydrodibenz[*a*,*c*]anthracene (**32**)[5] (174 mg, 0.33 mmol) was refluxed with a catalytic amount of *p*-toluenesulfonic acid (10 mg) in dry benzene (15 mL) for 6 h under argon. The reaction mixture was diluted with benzene (50 mL), washed with water (2 × 15 mL), dried (Na_2SO_4), and evaporated in vacuo. The residual solid was chromatographed over dry column grade silica gel, with benzene as eluant, to give pure **35** (60 mg, 36%) as light yellow crystals: mp 210–211 °C; ^{1}H NMR (270 MHz) δ 2.89 (t, 2 H_3), 3.53 (t, 2 H_4), 7.35 (d, H_1), 7.50–8,09 (m, 12 H), 8.56 (s, H_{14}), 8.87 (m, H_8), 9.21 (s, H_9), $J_{1,3}$ = 7.2, $J_{3,4}$ = 9.0 Hz.

A solution of the above ester **35** (50 mg, 0.125 mmol) and DDQ (60 mg, 0.26 mmol) was refluxed in dry benzene (10 mL) under argon for 15 min. The reaction mixture was passed through a short column of neutral alumina. The column was eluted with benzene to yield 46 mg (92%) of **37**: ^{1}H NMR (270 MHz) δ 7.50–8.70 (m, 16 H)), 8.97 (s, 1 H), 9.07 (s, 1 H). **37** (42 mg) was saponified with 40% NaOH (0.2 mL) in 20 mL of 1:1 THF and MeOH at room temperature for 30 min to produce 31 mg (84%) of pure **7** identical with that obtained as described in method A.

3-Hydroxydibenz[*a*,*c*]anthracene (8). 3-Oxo-1,2,3,4-tetrahydrodibenz[*a*,*c*]anthracene (**30**), mp 217–221 °C (EtOAc), was obtained in 72% yield by treating *trans*-3,4-bis(dibenzoyloxy)-1,2,3,4-tetrahydrodibenz[*a*,*c*]anthracene (**33**)[5] (195 mg, 0.3745 mmol) with *p*-toluenesulfonic acid (200 mg) in dry benzene (15 mL) as described for **29** in method A for the synthesis of 2-hydroxydibenz[*a*,*c*]anthracene (**7**): ^{1}H NMR (**30**, 270 MHz) δ 2.95 (t, 2 H_2), 3.67 (t, 2 H_1), 3.93 (s, 2 H_4), 7.50–8.0 (m, 7 H), 8.50 (s, H_{14}), 8.85 (m, H_8), 9.17 (s, H_9), $J_{1,2}$ = 7.0 Hz.

The ketone **30** (90 mg, 0.305 mmol) was dehydrogenated with 10% Pd–C in refluxing 1-methylnaphthalene as described for **29** (method A) to give 34 mg (60%) of **8** as light gray crystals: mp 252–253 °C (ether); ^{1}H NMR (270 MHz) δ 5.21 (s, 1 H, exchangeable with D_2O), 7.20 (dd, H_2), 7.50–9.10 (m, 12 H), $J_{1,2}$ = 8.6, $J_{2,4}$ = 2.4 Hz; high-resolution mass spectrum mass obsd 294.0939, calcd 294.1041.

4-Hydroxydibenz[*a*,*c*]anthracene (9). To a solution of 4-hydroxy-1,2,3,4-tetrahydrodibenz[*a*,*c*]anthracene (**27**)[5] (110.0 mg, 0.37 mmol) in acetone (15 mL) was added a 0.1 M solution of chromic acid (2.0 mL) in 5 min at 0 °C with stirring. The reaction mixture was stirred for an additional 10 min and then neutralized ($NaHCO_3$). After evaporation of most of the acetone, the residue was extracted with EtOAc (2 × 15 mL). The EtOAc layer was washed with water (2 × 5 mL), dried (Na_2SO_4), and evaporated to dryness. The residue (109 mg) was chromatographed over silica gel, with benzene as eluant, to furnish 97 mg (87%) of ketone **31**: mp 145–147 °C; ^{1}H NMR (270 MHz) δ 2.34 (t, 2 H_2), 2.85 (m, 2 H_3), 3.51 (t, 2 H_4), 7.50–8.08 (m, 6 H), 8.69 (s, H_{14}), 8.77 (m, H_8), 9.11 (s, H_9), 9.16 (m, H_5), $J_{1,2}$ = $J_{2,3}$ = 7 Hz.

A mixture of the ketone **31** (82.0 mg, 0.277 mmol) and 10% Pd–C (25 mg) in 1-methylnaphthalene (5 mL) was refluxed for 2 h. The product was isolated as described for **6** (method A) and then recrystallized from benzene to produce 64 mg (78.6%) of **9** as colorless crystals: mp 266–267 °C; ^{1}H NMR (270 MHz) δ 5.67 (s, OH, exchangeable with D_2O), 7.01 (d, H_3), 7.42–9.53 (m, 12 H), $J_{2,3}$ = 7.9 Hz; high-resolution mass spectrum mass obsd 294.0929, calcd 294.1041.

10-Hydroxydibenz[*a*,*c*]anthracene (10). A mixture of 10-oxo-10,11,12,13-tetrahydrodibenz[*a*,*c*]anthracene (**39**)[15] (57 mg, 0.193 mmol) and 10% Pd–C (90 mg) in 1-methylnaphthalene (2 mL) was refluxed for 0.5 h under argon. The crude **10** that was isolated as described for **6** was recrystallized from ether–hexane to yield 23 mg (40%) of pure **10**: mp 239–241 °C; ^{1}H NMR (200 MHz) δ 5.5 (br s, OH, exchangeable with D_2O), 6.86 (d, H_{11}), 7.15–9.50 (m, 12 H), $J_{11,12}$ = 7.3 Hz. 10-Acetoxy-DBA: mp 199–200 °C; ^{1}H NMR (270 MHz) δ 2.62 (s, 3 H), 7.32–9.45 (m, 13 H); high-resolution mass spectrum mass obsd 336.1129, calcd 336.1146.

11-Hydroxydibenz[*a*,*c*]anthracene (11). A solution of *trans*-10,11-bis(benzoyloxy)-10,11,12,13-tetrahydrodibenz[*a*,*c*]-anthracene (**34**)[15] (250 mg, 0.48 mmol) and *p*-toluenesulfonic acid (50 mg) in dry benzene (60 mL) was heated under reflux under argon for 6 h. After cooling to room temperature, the benzene solution was washed with 5% $NaHCO_3$ (2 × 20 mL) and then with water (2 × 20 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The residual solid was further purified by chromatography on preparative TLC using benzene as the developing solvent to yield 88 mg (46%) of pure 11-(benzoyloxy)-12,13-dihydrodibenz[*a*,*c*]anthracene (**36**): mp 189–190 °C; ^{1}H NMR (270 MHz) δ 2.77 (t, 2 H_{12}), 3.27 (t, 2 H_{13}), 6.6 (s, H_{10}), 7.50 (m, 5 H), 8.1 (m, H_8), 8.2 (s, 1 H), 8.37 (s, 1 H), $J_{12,13}$ = 8.0 Hz.

A solution of the ester **36** (80 mg, 10.2 mmol) and DDQ (80 mg) in dry benzene (30 mL) was refluxed under an argon atmosphere for 6 h. The reaction mixture was passed through a small column of neutral alumina using benzene as eluant to yield 20 mg (25%) of pure 11-(benzoyloxy)dibenz[*a*,*c*]anthracene (**38**): mp 219–220 °C (benzene); ^{1}H NMR (270 MHz) δ 7.90–8.60 (m, 13 H), 9.08 (s, 1 H), 9.13 (s, 1 H); mass spectrum, m/e 398.2 (M^+). Repetition of the same reaction without purification of the ester yielded 36.8% of **38** based on *trans*-10,11-bis(benzoyloxy)-10,11,12,13-tetrahydro-DB[a,c]A (**34**).

A mixture of the above ester **38** (50 mg, 0.123 mmol), glacial acetic acid (50 mL), and concentrated HCl (20 mL) was refluxed for 16 h under argon. The reaction mixture was diluted with H_2O (100 mL) and extracted with EtOAc (2 × 50 mL). The EtOAc layer was washed with water, dried (Na_2SO_4), and concentrated in vacuo to yield a residue, which was further purified by column chromatography using benzene as an eluant to produce 22 mg (57.9%) of pure **11**: mp 200–201 °C; ^{1}H NMR (270 MHz) δ 7.23 (dd, H_{12}), 7.41 (d, H_{13}), 7.60–9.30 (m, 11 H), $J_{10,12}$ = 2.3, $J_{12,13}$ = 8.9 Hz); mass spectrum, m/e 294.2 (M^+).

Acknowledgment. These investigations were supported by Grant No. ES03788 awarded to S.K. by the National Institute of Environmental Sciences, DHHS.