Synthesis of the Angular Ring Tetrahydro Epoxides of the Carcinogens 7- and 12-Methylbenz[*a*]anthracene and 7,12-Dimethylbenz[*a*]anthracene

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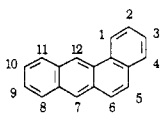
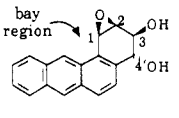
Received August 26, 1988

Tetrahydro epoxide derivatives at the 1,2- and 3,4-positions on the angular ring of the carcinogens 7- and 12-methylbenz[*a*]anthracene (7- and 12-MeBA) and 7,12-dimethylbenz[*a*]anthracene (7,12-DMBA) have been synthesized in order to probe the basis for the tumorigenicity-enhancing effects of methyl groups on polycyclic aromatic hydrocarbons (PAH). The epoxides were prepared from the corresponding dihydro PAH. For the 7-MeBA and 12-MeBA derivatives, access to the dihydro derivatives was achieved by acetoxylation at the 1- and 4-positions of the tetrahydro ring of 7- and 12-acetoxy-1,2,3,4-tetrahydrobenz[*a*]anthracene, respectively (Scheme II). For the 7,12-DMBA derivatives, oxidation of 1,2,3,4-tetrahydrobenz[*a*]anthracene-7,12-quinone afforded the 1- and 4-oxo derivatives, which were converted to the respective dihydro compounds (Scheme III). Alkenes **13** and **22**, both of which have a 12-methyl group and a C_1–C_2 double bond, were highly susceptible to endoperoxide formation. The dihydro compounds were converted to the epoxides via cyclization of the bromohydrin or bromoacetate derivatives (Scheme IV). The 1,2-bromohydrin and/or bromoacetate derivatives of 3,4-dihydro-12-methylbenz[*a*]anthracene and 3,4-dihydro-7,12-dimethylbenz[*a*]anthracene were highly labile and required special handling in order to be purified and converted into the epoxide derivatives.

The carcinogenic potency of a polycyclic aromatic hydrocarbon (PAH) can be profoundly altered by methyl substitution. A good example is provided by benz[*a*]anthracene (BA) and its methylated derivatives. BA is at best a weak carcinogen on mouse skin, but 7-methylbenz[*a*]anthracene (7-MeBA) is a potent carcinogen that is more than 10 times as tumorigenic as BA, and 7,12-dimethylbenz[*a*]anthracene (DMBA) is one of the most potent carcinogens, being approximately 1000 times as tumorigenic as BA.[1,2] 12-Methylbenz[*a*]anthracene (12-MeBA) is at least 10 times as tumorigenic as BA but is not as active as 7-MeBA.[2] Evidence accumulated to date indicates that the methylated derivatives are activated via bay-region 3,4-diol 1,2-epoxides, a pathway that appears to be general for alternant PAH.[3]

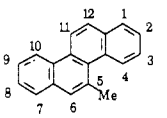


benz[a]anthracene (BA)



BA 3,4-diol-1,2-epoxide

Methyl groups can affect the carcinogenicity of PAH by influencing both the extent of metabolism to bay-region diol epoxides and the properties of the bay-region diol epoxides once they are formed. For example, substitution of a methyl group peri to the nonbay carbon atom of the angular ring may decrease the extent of metabolism to diol epoxide derivatives on that ring.[4] Substitution at other peri positions might enhance metabolism on the angular ring due to the same effect. At the same time, the intrinsic mutagenic and tumorigenic properties of the bay-region diol epoxides can be significantly influenced by methyl substitution. Hecht and colleagues have shown that the 1,2-diol 3,4-epoxide derivatives of 5-methylchrysene are



5-methylchrysene

much more mutagenic and tumorigenic than the 7,8-diol 9,10-epoxide derivatives.[5] Enhancement of tumorigenicity by a bay-region methyl group may be a general effect as numerous similarly substituted PAH (including 12-MeBA and DMBA) are more tumorigenic than the corresponding unsubstituted PAH.[4]

In addition to such a steric effect, a methyl group might enhance mutagenicity and tumorigenicity by increasing the electrophilicity of the diol epoxide derivative. For unsubstituted PAH, the relative electronic stabilization of the carbocation that would result from ring opening of the diol epoxide has been shown to be an important factor affecting the mutagenicity and tumorigenicity of diol epoxides.[6] Bay-region diol epoxide derivatives of 7-methyl- and 7,12-dimethylbenz[*a*]anthracene have been synthesized,[7,8] but there is at present insufficient data to enable a systematic assessment of the magnitude and source of the effects of methyl groups on mutagenicity and tumorigenicity.

The present work describes the syntheses of angular ring tetrahydro epoxides of 7-MeBA, 12-MeBA, and DMBA (Scheme IV). In previous studies, the use of tetrahydro epoxides as models for diol epoxides has been helpful in elucidating electronic and conformational factors affecting the biological activity of diol epoxides.[6] The mutagenic activity of the unsubstituted BA 1,2- and 3,4-dihydro epoxides has previously been studied.[9] Both epoxides are

(1) This work was supported, in part, by Grant CA 22985 from the National Cancer Institute to R.E.L.

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(4) Such an effect has been observed for 5,12-dimethylchrysene: Amin, S.; Camanzo, J.; Hecht, S. S. *Carcinogenesis* **1982**, *3*, 1159. For a general discussion of effects of methyl substitution on PAH carcinogenicity, see: Hecht, S. S.; Melikian, A. A.; Amin, S. In *Polycyclic Aromatic Hydrocarbon Carcinogenesis: Structure-Activity Relationships*; Yang, S. K., Silverman, B. D., Eds.; CRC Press, Inc.; Boca Raton, FL, 1988; Vol. I, pp 96–128.

(5) Hecht, S. S.; Radok, L.; Amin, S.; Huie, K.; Melikian, A. A.; Hoffmann, D.; Pataki, J.; Harvey, R. G. *Cancer Res.* **1985**, *45*, 1449–1452.

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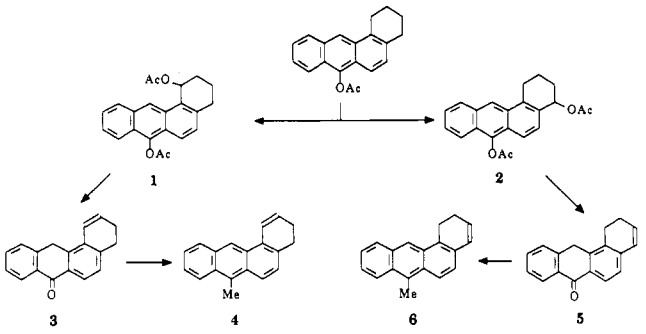
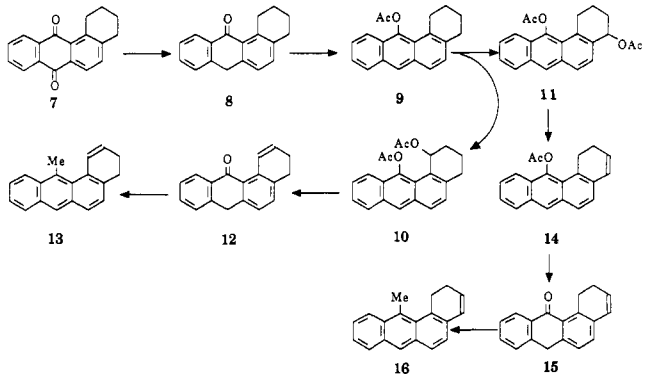
Scheme I



Scheme II



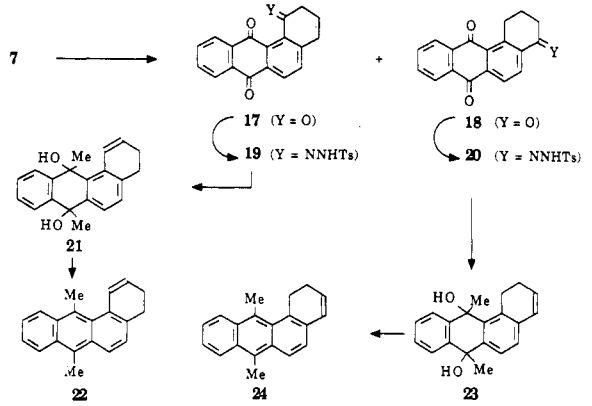
strong mutagens, with the bay-region (1,2-) derivative being 4–5 times as mutagenic as the nonbay (3,4-) epoxide in *S. typhimurium* strain TA 100. By studying these two series of epoxides, it should be possible to discern whether patterns of activation exist. For example, electronic stabilization of the carbocation formed at C_1 by ring opening of the 1,2-epoxide should be greater than that of the carbocation formed at C_4 by ring opening of the 3,4-epoxide.[10] If such stabilization were a significant factor in mutagenesis, the mutagenicity of the 1,2-epoxide should be enhanced more than that of the 3,4-epoxide. Tetrahydro epoxides **28–30** and **35–37** and their dihydro precursors **4**, **6**, **13**, **16**, **22**, and **24** have been submitted for biological studies, the results of which will be reported separately.

Results and Discussion

Synthesis of tetrahydro epoxides required successful approaches to the corresponding dihydro derivatives. For the monomethyl derivatives, acetoxylation at the benzylic positions of 7(or 12)-acetoxy-1,2,3,4-tetrahydrobenz[*a*]anthracene provided access to the dihydro angular ring. The aromatic acetates were then converted to the aromatic methyl derivatives **4**, **6**, **13**, and **16** via the corresponding anthrones (Schemes I and II). For the dihydro derivatives in the angular ring of 7,12-dimethylbenz[*a*]anthracene, chromic acid oxidation of tetrahydro quinone **7** afforded the 1- and 4-keto derivatives, which could be converted to the desired dihydro derivatives (Scheme III).

Dihydro Derivatives. 1,2- and 3,4-Dihydro-7-methylbenz[*a*]anthracene. Acetoxylation of 1.9 g of 7-acetoxy-1,2,3,4-tetrahydrobenz[*a*]anthracene[11] at room temperature with DDQ in HOAc gave a mixture of the 1- and 4-acetoxy derivatives, which were isolated in 24% and 38% yields, respectively, by flash chromatography on silica gel (Scheme I). Dihydro anthrones **3** and **5** were produced in almost quantitative yield by heating **1** and **2** in glacial HOAc containing concentrated HCl. Reaction of the dihydro anthrones with methyllithium afforded dihydroalkenes **4** and **6** in yields of 54% and 35%, respectively, after workup and chromatography on silica gel.

Scheme III



1,2- and 3,4-Dihydro-12-methylbenz[*a*]anthracene. For the analogous 12-methyl derivatives, 1,2,3,4-tetrahydrobenz[*a*]anthracene-7,12-dione (**7**) was the key starting material. It was prepared by cyclization of 2-(5,6,7,8-tetrahydro-1-naphthoyl)benzoic acid, which itself is prepared by reaction of the Grignard reagent of 1-bromo-5,6,7,8-tetrahydronaphthalene with phthalic anhydride.[12] Two modifications of literature procedures were found useful. In the first, 1-bromo-5,6,7,8-tetrahydronaphthalene was prepared from commercially available 1-amino-5,6,7,8-tetrahydronaphthalene by isolating the diazonium tetrafluoroborate produced by its reaction with tetrafluoroboric acid and sodium nitrite and adding it to a suspension of $CuBr_2$ in DMSO.[13] The bromo derivative was formed in good yield (79%), and the procedure is much easier to effect than that described in the literature.[14] In the second, the cyclization of 2-(5,6,7,8-tetrahydro-1-naphthoyl)benzoic acid to **7** was found to proceed in good yield (81%) in warm $MeSO_3H$. A second procedure using fused $ZnCl_2$, Ac_2O, and glacial HOAc cyclization was found to proceed in high yield (94%), but the procedure and workup are less straightforward. The literature procedure[15] involves cyclization with a boric acid/sulfuric acid mixture and is reported to proceed in 85% yield.

Quinone **7** was selectively reduced to anthrone **8** in good yield (85%) with hydrazine and acid in ethylene glycol at reflux. Reaction of **8** with Ac_2O and pyridine gave aromatic acetate **9** in 74% yield. Acetoxylation of **9** with DDQ in HOAc at 30 °C gave equal amounts (32% each) of 1- and 4-acetoxy derivatives **10** and **11**, after flash chromatography of the crude reaction products on silica gel. The NMR spectrum of the 4-acetoxy derivative **11** at room temperature gave four very broad peaks centered at δ 3.00, 3.19, 3.60, and 3.82 for the two hydrogen atoms at C_1, due to slow interconversion of two conformers at that tempera-

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ture. Similarly, the C_1 hydrogens in **9** appear as two broad peaks centered at δ 3.05 and 3.65 at room temperature. These peaks coalesce to a single broad peak centered at δ 3.35 when the NMR sample is heated to 50 °C.

Diacetate **10** was converted to anthrone **12** in quantitative yield with HOAc, HCl, and H_2O at 80–85 °C. Similar treatment of **11** led to 89% yield of aromatic acetate **14**, which was converted to anthrone **15** with CH_3Li in 96% yield. Anthrones **12** and **15** were converted to 3,4-dihydro- and 1,2-dihydro-12-methylbenz[*a*]anthracene in 61% and 76% yields, respectively, by treatment with MeLi and chromatography on silica gel. Alkene **13** was highly susceptible to endoperoxide formation during workup and purification. Consequently, solvents used in reactions involving and producing **13** and in workup of the reactions were degassed with N_2 or Ar, and solutions containing **13** were protected from light.

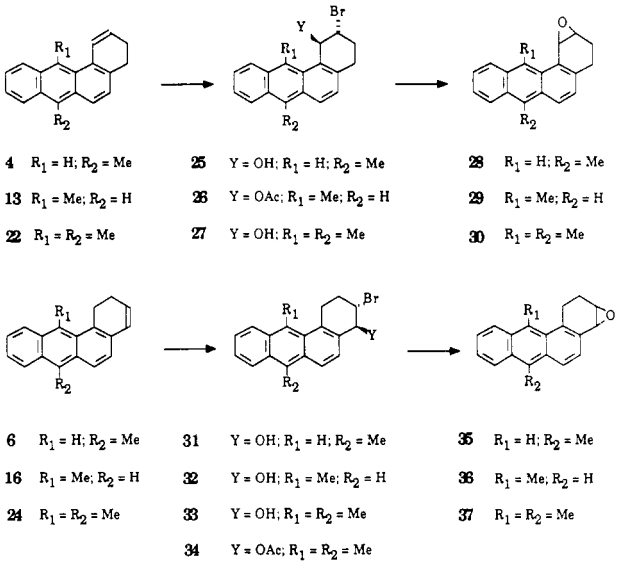
1,2- and 3,4-Dihydro-7,12-dimethylbenz[*a*]anthracene. Quinone **7** was oxidized with CrO_3 in HOAc, Ac_2O, and CH_2Cl_2 to a 2:3 mixture of triones **17** and **18**. The triones were not readily separated on large scale, and the crude mixture was converted to the tosylhydrazones **19** and **20**. These were isolated in yields of 26% and 38%, respectively. The tosylhydrazones were converted to dihydro, dihydroxy derivatives **21** and **23** in 63% and 61% yields, respectively, by reaction with MeLi first in PhH, then in PhH/THF. Use of THF as the only solvent led to complex mixtures that included dimers and reduced species. The diols were cleaved to the desired alkenes **22** and **24** in good yield (74% and 72%, respectively) with $TiCl_3$/LAH (2:1) in THF.

Alkene **22**, like the analogous 12-Me derivative **13**, readily formed an endoperoxide under normal workup procedures. Thus, light and oxygen were excluded during reactions and workup procedures, as for **13**. The endoperoxides were not isolated, but their presence was inferred through NMR spectral characteristics of reactions in which they were produced. For the endoperoxide of **13**, the vinyl hydrogen H_2 was shifted slightly downfield (to δ 6.22) from the corresponding hydrogen atom in **13**, the methyl peak appeared as a singlet at δ 2.31 and H_7 appeared as a singlet at δ 5.86. For the endoperoxide of **22**, H_2 was centered at δ 6.20 and the C_7 and C_{12} methyl hydrogens appeared at δ 2.11 and 2.31, respectively. Interestingly, **13** and **22** appear to be exceptionally susceptible to endoperoxide formation. We did not observe endoperoxide formation for the alkenes **16** and **24**, which have the 12-methyl group, but a C_3–C_4 double bond. Also, endoperoxide formation was not observed for dihydro-7-methylbenz[*a*]anthracenes **4** and **6**. Endoperoxide formation has been reported for *trans*-3,4-dihydroxy-3,4-dihydro-DMBA.[8]

Tetrahydro Epoxides. The dihydro aromatic compounds were converted to *trans*-bromohydrin or bromoacetate derivatives, which were then cyclized to the tetrahydro epoxides with Amberlite IRA-400 (–OH) (Scheme IV). Yields obtained via this route are generally much higher for reactive tetrahydro epoxides than when *m*-CPBA is used.

Tetrahydro 1,2-Epoxides 28–30. 3,4-Dihydro-7-methylbenz[*a*]anthracene was converted, without special precautions, to bromohydrin **25**, which was isolated in 58% yield after flash chromatography on silica gel. However, conversion of both 3,4-dihydro-12-methylbenz[*a*]anthracene (**13**) and 3,4-dihydro-7,12-dimethylbenz[*a*]anthracene (**22**) to the corresponding bromohydrins was exceedingly difficult to achieve. For alkene **13**, ^1H NMR analysis of the crude reaction product with NBA in THF/H_2O indicated the presence of substantial bromohydrin. However, attempted purification of the bromohydrin by column chromatography on silica gel, even at ~0 °C, led to decomposition. The bromoacetate derivative **26** proved to be more stable, and could be isolated in 79% yield by cold column chromatography on silica gel. In the latter reaction, it was important to use less than 1 molar equiv of NBA relative to alkene **13**, otherwise small amounts of bromoacetate containing an additional bromine atom on an aromatic ring were formed.

Scheme IV



Similarly, bromohydrin **27** produced from 3,4-dihydro-7,12-dimethylbenz[*a*]anthracene (**22**) was very unstable. NMR spectra of chromatographed or concentrated samples of **27** often indicated the presence of substantial 2-bromo-3,4-dihydro-DMBA, as shown by a singlet for H_1 at δ 7.44, new methyl signals at δ 3.13 and 3.04, and two pseudotriplets (2 H each) centered at δ 3.04 and 2.89. In attempts to prepare the bromohydrin of **13** (vide supra), similar peaks (H_1 at δ 7.54, 12-Me at 3.17, and pseudotriplets centered at 3.04 and 2.88) indicated the presence of 2-bromo-3,4-dihydro-12-methylbenz[*a*]anthracene. In order to avoid decomposition of bromohydrin **27**, evaporation of solvent in the initial workup was done at –15 °C (in the presence of $NaHCO_3$), and column chromatography on silica gel was effected at 0 °C. Since evaporation of solvent from the pooled chromatography fractions occasionally resulted in almost total decomposition, presumably because a small amount of HBr is generated that catalyzes further reaction, Amberlite IRA 400 (–OH) was added directly to the pooled chromatography fractions, the solvent was removed under vacuum at –15 °C, and dry THF was added. This gave epoxide **30** in 36% yield, based on alkene **22**. Epoxides **28** and **29** were produced from the corresponding bromohydrin **25** and bromoacetate **26** in greater than 90% yield with Amberlite IRA 400 (–OH), although 3 days were required to complete the cyclization of bromoacetate **26** to the epoxide. Tetrahydro epoxides **28–30** each appeared as a single spot on silica gel TLC (10% ether in hexane was used as eluting solvent).

Tetrahydro 3,4-Epoxides 35–37. Conversion of alkenes **6**, **16**, and **24** to the bromohydrins **31–33** proceeded in modest yields (41–48%), and the bromohydrins were cyclized to the corresponding tetrahydro epoxides in high yield (>90%).

The chemical shifts of selected hydrogen atoms in the tetrahydro epoxides are shown in Table I. Several interesting effects can be noted. First, a 12-methyl group

Table I. Chemical Shifts of Selected Hydrogen Atoms in Tetrahydro Epoxides 28–30 and 35–37

compd	H_1	H_4	H_5	H_7	H_{12}	7-Me	12-Me
28	4.90		7.27		8.79	3.10	
29	4.63		7.15	8.25			3.36
30	4.56		7.19			3.06	3.32
35		4.03	7.43		8.54	3.11	
36		4.04	7.40	8.25			3.18
37		4.06	7.45			3.06	3.13

causes a modest upfield chemical shift ($\delta \sim 0.3$) of the oxirane atom H_1 in the H_4 1,2-epoxides (cf. H_1 in **28** vs. **29** and **30**). This contrasts with the downfield shifts that are observed for H_5, H_{12}, and the 12-Me when the oxirane ring is proximal (cf. H_5 in **28–30** vs **35–37**; H_{12} in **28** vs **35**; 12-Me in **29** and **30** vs **36** and **37**).

Experimental Section

Melting points were obtained on a Kofler melting point apparatus and are uncorrected. Nominal mass spectra were recorded on a Hewlett-Packard 5985 quadrupole mass spectrometer. Spectra were recorded at 70 eV, unless noted otherwise. High-resolution mass spectra were recorded on a Kratos MS25 RF mass spectrometer. ^1H NMR spectra were recorded on a Varian XL-300 spectrometer in $CDCl_3$. Chemical shifts are reported in δ units, and coupling constants are reported in hertz. For workup procedures, Na_2SO_4 was used as a drying agent, and solvents were evaporated under reduced pressure (rotovap). N_2 was bubbled through solvents used in the preparations and purifications of dihydrobenz[*a*]anthracenes and their bromohydrin and epoxide derivatives. For the bromohydrins and epoxides, solvents were evaporated at −15 °C under vacuum (oil pump). Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, TN.

1,7- and 4,7-Diacetoxy-1,2,3,4-tetrahydrobenz[*a*]anthracene (1 and 2). To a stirred suspension of 7-acetoxy-1,2,3,4-tetrahydrobenz[*a*]anthracene[11] (1.9 g, 6.5 mmol) in freshly distilled glacial HOAc (75 mL) was added DDQ (1.8 g, 7.9 mmol). The mixture was stirred, under Ar, at room temperature for 96 h. EtOAc was added, and the mixture was extracted with brine, H_2O, and aqueous NaOH. The EtOAc phase was dried ($MgSO_4$), filtered, and evaporated to leave a brown oil, which was purified by flash chromatography on silica gel with petroleum ether, 1:1 petroleum ether/PhH, and PhH as eluting solvents. This gave, sequentially, unreacted starting material and its aromatized derivative (220 mg), 1,7-diacetoxy-1,2,3,4-tetrahydrobenz[*a*]anthracene (**1**, 563 mg, 24%), 4,7-diacetoxy-1,2,3,4-tetrahydrobenz[*a*]anthracene (**2**, 883 mg, 38%), and a mixture of more polar products (110 mg). Compound **1** is a white solid of mp 156–157 °C (resolidifies and melts at 168–170 °C) after recrystallization from EtOH and has the following: ^1H NMR δ 1.91–2.08 (m, 3 H), 2.09 (s, 3 $H_{1\text{-OAc}}$), 2.32–2.40 (m, 1 H), 2.63 (s, 3 $H_{12\text{-OAc}}$), 2.91–3.02 (m, 2 H), 6.79 (br s, 1 H_1), 7.25 (d, 1 H_5, $J_{5,6}$ = 8.9), 7.46–7.52 (m, 2 $H_{9,10}$), 7.85–7.94 (m, 2 H), 8.01–8.05 (m, 1 H), 8.31 (s, H_{12}). Compound **2** is a pale yellow solid of mp 160–162 °C after recrystallization from EtOH and has the following: ^1H NMR δ 2.00–2.20 (m, 2 H), 2.14 (s, 3 $H_{4\text{-OAc}}$), 3.08–3.16 (m, 2 H), 3.36–3.45 (m, 2 H), 6.15 (br s, 1 H_4), 7.37 (d, 1 H_5, $J_{5,6}$ = 9.0), 7.46–7.56 (m, 2 $H_{9,10}$), 7.80 (d, 1 H, J = 9.0), 7.93 (d, 1 H, J = 7.9), 8.03 (d, 1 H, J = 8.0), 8.48 (s, 1 H_{12}).

3,4-Dihydrobenz[*a*]anthracen-7(12*H*)-one (3). 1,7-Diacetoxy-1,2,3,4-tetrahydrobenz[*a*]anthracene (**1**, 175 mg) was dissolved in glacial HOAc (22 mL), and concentrated HCl (1.1 mL) was added. The flask was flushed with Ar, and the mixture was heated at 80–85 °C for 1 h. Benzene (250 mL) was added, and the organic layer was washed with H_2O (2 × 250 mL), 10% aqueous $NaHCO_3$ (2 × 250 mL), and H_2O (2 × 200 mL). The benzene phase was dried ($MgSO_4$), filtered, and evaporated to give 3,4-dihydrobenz[*a*]anthracen-7(12*H*)-one as a yellow solid (123 mg, 99%): ^1H NMR δ 2.36 (m, 2 H), 2.90 (t, 2 H, J_{app} = 8.3), 4.29 (s, 2 H), 6.29 (m, 1 H_2), 6.85 (d, 1 H_1), 7.25 (d, 1 H, J = 7.9), 7.44–7.62 (m, 3 H), 8.22 (d, 1 H, J = 8.0), 8.37 (d, 1 H, J = 7.9), $J_{1,2}$ = 8.9, $J_{2,3}$ = 4.7.

3,4-Dihydro-7-methylbenz[*a*]anthracene (4). Dihydroanthrone **3** (80 mg, 0.32 mmol) was dissolved in dry Et_2O (15 mL), the solution was cooled to 0 °C, and MeLi (2.3 mL, 1.4 M in Et_2O, 0.32 mmol) was added. The mixture was stirred at room temperature for 1.5 h under Ar and protected from light. The solution was cooled to 0–5 °C and cold 5% aqueous HCl (25 mL) was added. The aqueous layer was separated, and the Et_2O layer was washed with 5% aqueous $NaHCO_3$ (2 × 25 mL) and H_2O (1 × 25 mL). The ether phase was dried ($MgSO_4$), filtered, and evaporated to afford 80 mg of crude product, which was purified by flash chromatography on silica gel, with petroleum ether as eluting solvent, to give 43 mg (54%) of 3,4-dihydro-7-methylbenz[*a*]anthracene (**4**) of mp 73–75 °C after recrystallization from EtOH: ^1H NMR δ 2.44 (m, 2 H_3), 2.95 (t, 2 H_4, J_{app} = 8.8), 3.09 (s, 3 H), 6.32 (m, 1 H_2), 7.34 (d, 1 H_5, $J_{5,6}$ = 9.0), 7.42–7.51 (m, 3 $H_{1,9,10}$), 8.00 (d, 1 $H_{6,8,11}$, J = 9.5), 8.14 (d, 1 $H_{6,8,11}$, J = 9.0), 8.25 (d, 1 $H_{6,8,11}$, J = 8.3), 8.58 (s, 1 H_{12}), $J_{1,2}$ = 10.0, $J_{2,3}$ = 4.7; mass spectrum (70 eV), m/e (relative intensity) 244 (100), 229 (63), 228 (52). Anal. Calcd for $C_{19}H_{16}$: C, 93.40; H, 6.60. Found: C, 93.49; H, 6.82.

1,2-Dihydrobenz[*a*]anthracen-7(12*H*)-one (5). 4,7-Diacetoxy-1,2,3,4-tetrahydrobenz[*a*]anthracene (**2**, 500 mg, 1.4 mmol) was added to a solution of glacial HOAc (60 mL) and concentrated HCl (3 mL). The mixture was heated, under Ar, at 80–85 °C for 1.5 h, PhH (150 mL) was added, and the organic phase was washed with H_2O (2 × 100 mL), 10% aqueous $NaHCO_3$ (3 × 70 mL), and H_2O (2 × 100 mL). The PhH phase was dried ($MgSO_4$), filtered, and evaporated to give 1,2-dihydrobenz[*a*]anthracen-7(12*H*)-one (**5**, 350 mg, 99%), which was used without further purification: ^1H NMR δ 2.47 (m, 2 H_2), 2.94 (t, 2 H_1, J_{app} = 8.5), 4.23 (s, 2 H_{12}), 6.24 (m, 1 H_3), 6.55 (m, 1 H_4), 7.18 (d, 1 H_5, J = 8.0), 7.46–7.62 (m, 3 H), 8.25 (d, 1 H, J = 7.9), 8.36 (d, 1 H, J = 7.8), $J_{3,4}$ = 9.6, $J_{2,3} \sim 4.8$, $J_{2,4} \sim 1.9$.

1,2-Dihydro-7-methylbenz[*a*]anthracene (6). Dihydroanthrone **5** (370 mg, 1.5 mmol) was dissolved in dry Et_2O (75 mL). The mixture was cooled to 0–5 °C and MeLi (11 mL, 1.4 M in Et_2O, 15 mmol) was added. The mixture was stirred at room temperature for 2 h, cooled to 0–5 °C, and treated with 5% aqueous HCl. The aqueous layer was separated, and the Et_2O layer was washed with 5% aqueous $NaHCO_3$ (2 × 50 mL) and H_2O (1 × 50 mL). The Et_2O phase was dried ($MgSO_4$), filtered, and evaporated to give 376 mg of a brown oil, which was subjected to flash chromatography on silica gel, with use of petroleum ether as eluting solvent. This gave 1,2-dihydro-7-methylbenz[*a*]anthracene (**6**, 130 mg, 35%) as a solid of mp 101.5–104.5 °C after recrystallization from EtOH: ^1H NMR δ 2.55 (m, 2 H_3), 3.09 (s, 3 H), 3.38 (t, 2 H_1, J_{app} = 9.0), 6.17 (m, 1 H_3), 6.60 (d, 1 H_4), 7.28 (d, 1 H_5), 7.40–7.52 (m, 2 $H_{9,10}$), 7.99 (d, 1 $H_{6,8,11}$, $J \sim 8.5$), 8.15 (d, 1 $H_{6,8,11}$, J = 9.1), 8.25 (d, 1 $H_{6,8,11}$, J = 8.0), 8.52 (s, 1 H_{12}); mass spectrum, m/z (relative intensity) 244 (100), 229 (68), 228 (59).

1,2,3,4-Tetrahydrobenz[*a*]anthracene-7,12-dione (7). In the first procedure, a mixture of 2-(5,6,7,8-tetrahydronaphthoyl)benzoic acid (5.0 g), fused $ZnCl_2$ (5.0 g), Ac_2O (25 mL), and glacial HOAc (25 mL) was refluxed for 30 min and then poured into 500 mL of cold H_2O. A solid separated, was collected, and then was dissolved in EtOAc. The EtOAc solution was extracted with dilute $NaHCO_3$ and H_2O, dried (Na_2SO_4), filtered, and evaporated to give 4.9 g of solid, which was purified by column chromatography on silica gel with 1:3 $CHCl_3$–petroleum ether. This gave 4.4 g (94%) of **7** as a solid of mp 152–153 °C. However, the following procedure under cyclization in $MeSO_3H$ is more convenient and also proceeds in high yield.

A mixture of $MeSO_3H$ (85 mL) and 2-(α-tetraloyl)benzoic acid (10.2 g) were stirred at 60 °C for 4 h. The reaction mixture was poured over ice, and the mixture was stirred for 10 min, diluted with H_2O (900 mL), and extracted with EtOAc (2 × 300 mL). The combined organic phase was washed successively with H_2O, 5% NaOH (100 mL), and brine to neutrality. The organic solvent

was dried and evaporated to leave a solid that was chromatographed on Florisil with CH_2Cl_2 as eluant. Solvent removal furnished 7.7 g (81%) of pure yellow product. A portion crystallized from EtOAc had mp 152–154 °C (lit.[12] mp 152–153 °C): ^{1}H NMR δ 1.86 (m, 4 H), 2.93 (m, 2 H), 3.40 (m, 2 H), 7.47 (d, 1 H, J = 8.0), 7.70–7.80 (m, 2 H), 8.14 (d, 1 H, J = 8.0), 8.20–8.25 (m, 2 H).

The 2-(5,6,7,8-tetrahydro-1-naphthoyl)benzoic acid was prepared according to the literature,[12] but the 1-bromo-5,6,7,8-tetrahydronaphthalene used in its preparation was synthesized by the following method, which was a more convenient and higher yield process than that described in the literature.[14]

To fluoroboric acid (48%, 90 mL), placed in a 1-L beaker, was slowly added 5,6,7,8-tetrahydro-1-naphthylamine (29.4 g). The mixture was cooled in an ice bath with mechanical stirring. When the mixture had attained a temperature of −3 °C, an ice-cold solution of sodium nitrite (16 g) in H_2O (50 mL) was added dropwise so that the temperature did not rise above −3 °C. The diazonium tetrafluoroborate was collected by filtration under suction and washed quickly with HBF_4 (5%, 50 mL) and ice-cold H_2O (3 × 100 mL). The wet diazonium tetrafluoroborate cake was added in parts to a suspension of $CuBr_2$ (56 g) in DMSO (500 mL)[13] with vigorous mechanical stirring. The mixture was stirred an additional 30 min, diluted with H_2O (1500 mL), and extracted with EtOAc (2 × 500 mL). The organic phase was dried, filtered, and evaporated. The residual oil was purified by chromatography on Florisil with petroleum ether as eluting solvent. This gave pure 1-bromo-5,6,7,8-tetrahydronaphthalene (33.3 g, 79%).

1,2,3,4-Tetrahydrobenz[*a*]anthracen-12(7*H*)-one (8). A mixture of 1,2,3,4-tetrahydrobenz[*a*]anthracene-7,12-dione (7, 5.25 g), ethylene glycol (50 mL), 95% hydrazine (51 mL), and concentrated H_2SO_4 (2.0 mL) were refluxed under Ar for 4–5 h. The mixture was cooled and extracted with EtOAc. The EtOAc phase was washed with H_2O, dried (Na_2SO_4), filtered, and evaporated to give 6.0 g of residue. Column chromatography on silica gel with 30% $CHCl_3$/hexane gave, successively, 1,2,3,4-tetrahydrobenz[*a*]anthracen-12(7*H*)-one (**8**, 3.0 g, 85% based on quantity of **7** reacted) and 1,2,3,4-tetrahydrobenz[*a*]anthracene-7,12-dione (**7**, 1.5 g). After recrystallization from EtOH, **8** had mp 108–109 °C (lit.[16] mp 109–109.7 °C).

12-Acetoxy-1,2,3,4-tetrahydrobenz[*a*]anthracene (9). A mixture of 1,2,3,4-tetrahydrobenz[*a*]anthracen-12(7*H*)-one (6.6 g), acetic anhydride (160 mL), and pyridine (16 mL, dried over KOH) was heated at 50 °C for 3 h, under Ar. The mixture was cooled and poured into H_2O. The mixture was extracted with EtOAc, and the EtOAc phase was washed with H_2O, dried (Na_2SO_4), filtered, and evaporated. Flash chromatography of the residue on silica gel, using 20% $CHCl_3$ in petroleum ether, gave 5.7 g (74%) of **9** of mp 103–104 °C: ^{1}H NMR δ 1.75–2.05 (m, 4 H), 2.57 (s, 3 H), 2.93 (br s, 2 H), 2.95–3.15 (br s, 1 H), 3.55–3.75 (br s, 1 H), 7.12 (d, 1 H_5, $J_{5,6}$ = 8.7), 7.43–7.51 (m, 2 H), 7.73 (d, 1 H_6, $J_{5,6}$ = 8.7), 7.84 (d, 1 H, J = 7.7), 7.96 (m, 1 H), 8.27 (s, H_{10}); mass spectrum (12 eV), m/z (relative intensity) 290 (43), 248 (100).

1,12- and 4,12-Diacetoxy-1,2,3,4-tetrahydrobenz[*a*]anthracene (10 and 11). A mixture of 12-acetoxy-1,2,3,4-tetrahydrobenz[*a*]anthracene (**9**) (2.9 g, 10 mmol), DDQ (2.71 g, 12 mmol), and glacial HOAc (50 mL) were stirred at 30 °C, under Ar, for 7 h. The mixture was poured into H_2O, and the aqueous phase was extracted with EtOAc. The organic phase was extracted with cold 5% NaOH and H_2O, dried, filtered, and evaporated to give 3.5 g of crude product, which was purified by flash chromatography on silica gel, using 2–3% acetone in hexane as eluting solvent. This gave, consecutively, 1.12 g (32%) of 1,12-diacetoxy-1,2,3,4-tetrahydrobenz[*a*]anthracene, **10**, mp 201–205 °C (from EtOH), and 1.10 g (32%) of 4,12-diacetoxy-1,2,3,4-tetrahydrobenz[*a*]anthracene, **11**, mp 124–125 °C, as well as 290 mg of a fraction containing a ca. 1:1 mixture of the two isomers: ^{1}H NMR of **10** δ 1.80–2.20 (m, 3 H), 2.35–2.42 (m, 1 H), 2.04 (s, 3 $H_{1\text{-OAc}}$), 2.61 (s, 3 $H_{12\text{-OAc}}$), 2.95–3.01 (m, 2 H), 6.57 (br s, 1 H_1), 7.16 (d, 1 H_5, $J_{5,6}$ = 8.6), 7.49 (m, 2 H), 7.81 (d, 1 H, J = 7.8), 7.88 (d, 1 H_6, $J_{5,6}$ = 8.7), 7.99 (d, 1 H, J = 7.5), 8.31 (s, 1 H_7); ^{1}H NMR of **11** δ 1.95–2.10 (m, 4 H), 2.13 (s, 3 $H_{4\text{-OAc}}$), 2.58 (s, 3 $H_{12\text{-OAc}}$), 2.90–3.95 (m, 2 H_1, broad peaks centered at 3.00, 3.19, 3.60, and 3.82), 6.11 (br s, 1 H_1), 7.24 (d, 1 H_5, J = 8.8), 7.45–7.55 (m, 2 $H_{9,10}$), 7.81 (d, 1 H, J = 8.8), 7.84–7.88 (m, 1 H), 7.96–8.02 (m, 1 H), 8.30 (s, 1 H_7).

3,4-Dihydrobenz[*a*]anthracen-12(7*H*)-one (12). A mixture of 1,12-diacetoxy-1,2,3,4-tetrahydrobenz[*a*]anthracene (**10**, 525 mg), glacial HOAc (53 mL), H_2O (0.42 mL), and concentrated HCl (0.22 mL) was stirred at 80–85 °C, under Ar, for 20–25 min. The mixture was poured into ice water and extracted with EtOAc. The EtOAc phase was washed with H_2O, aqueous $NaHCO_3$, and H_2O, dried ($MgSO_4$), filtered, and evaporated, leaving crude 3,4-dihydrobenz[*a*]anthracen-12(7*H*)-one (**12**, 370 mg), which was used without further purification: ^{1}H NMR spectrum of **12** δ 2.30 (m, 2 H_3), 2.82 (t, 2 H_4, J_{app} = 8.1), 4.29 (s, 2 H_7), 6.34 (m, 1 H_2), 7.22–7.7 (m, 5 H), 7.99 (d, 1 H_1), 8.22 (d, 1 H_{11}), $J_{1,2}$ = 9.9, $J_{2,3}$ = 5.0, $J_{10,11}$ = 7.8.

3,4-Dihydro-12-methylbenz[*a*]anthracene (13). Crude **12** (370 mg) was dissolved in dry Et_2O (25 mL), and the solution was cooled to 0 °C. The reaction mixture was protected from light with Al foil, and MeLi (43 mL of a 1.4 M solution in ether) was added, under Ar. The mixture was stirred at 0 °C for 2 h and at room temperature for 7 h, and then H_2O was added dropwise to the cooled mixture to decompose excess MeLi. The mixture was extracted with H_2O, dried (Na_2SO_4), filtered, and evaporated. The residue was purified by flash chromatography on silica gel, with use of Ar-flushed petroleum ether and then 5% ether in petroleum ether as eluting solvents. The alkene **13** (200 mg) was eluted by the petroleum ether. A more polar fraction (50 mg) contained mostly the intermediate alcohol 12-hydroxy-3,4,7,12-tetrahydrobenz[*a*]anthracene (as shown by the appearance of the 12-Me signal as a singlet at δ 1.70 in the NMR spectrum) and some **12**. This fraction was reacted with MeLi, as above, and then dehydrated with *p*-TsOH/benzene at room temperature. The residue from workup was purified by chromatography, as above, to give an additional 26 mg of **13** (total yield, 226 mg, 61%). Recrystallization from EtOH gave **13** of mp 88–89 °C: ^{1}H NMR of **13** δ 2.40 (m, 2 H_3), 2.87 (t, 2 H_4, J_{app} = 8.5), 3.18 (s, 3 $H_{12\text{-Me}}$), 6.15 (m, 1 H_2), 7.15–7.25 (m, 2 $H_{1,5}$), 7.40–7.50 (m, 2 $H_{9,10}$), 7.75 (d, 1 H_6, J = 8.4), 7.95 (d, 1 H_8, J = 7.9), 8.21 (s, 1 H_7), 8.22 (d, 1 H_{11}, J ~ 7.0); mass spectrum (12 eV), m/z (relative intensity) 244 (100), 229 (31). Anal. Calcd for $C_{19}H_{16}$: C, 93.40; H, 6.60. Found: C, 93.32; H, 6.65.

12-Acetoxy-1,2-dihydrobenz[*a*]anthracene (14). A mixture of 4,12-diacetoxy-1,2,3,4-tetrahydrobenz[*a*]anthracene (200 mg), glacial HOAc (20 mL), H_2O (0.2 mL), and concentrated HCl (0.08 mL) were stirred at 80–85 °C for 0.5 h, under Ar, with protection from light. The mixture was poured onto cold H_2O and extracted with ether. The ether phase was extracted with H_2O, aqueous $NaHCO_3$, and H_2O, dried (Na_2SO_4), filtered, and evaporated. The residue was purified by flash chromatography on silica gel with petroleum ether and 3% EtOAc in petroleum ether as eluting solvents. This gave 147 mg (89%) of **14**, which was used without further purification: ^{1}H NMR of **14** δ 2.2–2.5 (m, 2 H_2), 2.55 (s, 3 $H_{12\text{-OAc}}$), 3.12 (v br s, 2.9–3.3, 1 H_1), 3.96 (v br s, 3.7–4.1, 1 H_1), 6.16 (m, 1 H_3), 6.55 (d, 1 H_4), 7.19 (d, 1 H_5), 7.38–7.52 (m, 2 $H_{9,10}$), 7.74–8.00 (m, 3 H), 8.28 (s, 1 H_7), $J_{3,4}$ = 9.8, $J_{2,3}$ = 4.5, $J_{5,6}$ = 8.5.

1,2-Dihydro-12-methylbenz[*a*]anthracene (16). MeLi (7 mL, 1.4 M in Et_2O) was added dropwise to 12-acetoxy-1,2-dihydrobenz[*a*]anthracene (**14**, 207 mg) in cold, dry ether (30 mL) at 0 °C, under Ar. After 20 min, H_2O was added dropwise to destroy excess MeLi, and the mixture was acidified with cold 5% aqueous HCl and extracted with ether. The ether phase was dried ($MgSO_4$), filtered, and evaporated to give 170 mg of crude 1,2-dihydrobenz[*a*]anthracen-12(7*H*)-one (**15**), which was used without further purification: ^{1}H NMR of **15** δ 2.25–2.36 (m, 2 H_2), 3.56 (m, 2 H_1, J_{app} = 8.4), 4.31 (s, 2 H_7), 6.13 (m, 1 H_3), 6.50 (m, 1 H_4), 7.1–7.6 (m, 5 H), 8.20 (d, 1 H_{11}), $J_{2,3}$ = 4.8, $J_{3,4}$ = 9.5, $J_{10,11}$ ~ 8.5.

Crude **15** (170 mg) in dry ether was reacted with MeLi (6 mL of a 1.4 M solution) under essentially the same procedure as described for **13**. This gave 160 mg of a mixture of 12-hydroxy-12-methyl-1,2,7,12-tetrahydrobenz[*a*]anthracene (^{1}H NMR spectrum shows 12-Me as singlet at δ 1.71) and alkene **16**. The mixture was dissoved in dry PhH (20 mL), *p*-TsOH (15 mg) was added, and the mixture was stirred at room temperature for 5.5 h, under Ar, with protection from light. The mixture was poured into H_2O, and the ether phase was extracted with aqueous $NaHCO_3$ and H_2O, dried ($MgSO_4$), filtered, and evaporated. The

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residue (150 mg) was purified by flash chromatography on silica gel with petroleum ether as eluting solvent. This gave 133 mg (76%) of **16**, mp 89–90 °C after recrystallization from EtOH: ^{1}H NMR δ 2.23–2.33 (m, 2 H_2), 3.16 (s, 3 $H_{12\text{-}Me}$), 3.46 (t, 2 H_1, J_{app} = 8.5), 6.15 (m, 1 H_3), 6.61 (d, 1 H_4), 7.16 (d, 1 H_5), 7.39–7.49 (m, 2 $H_{9,10}$), 7.76 (d, 1 H_6), 7.92 (d, 1 H_8), 8.19 (s, 1 H_7), 8.21 (d, 1 H_{11}), $J_{3,4}$ = 9.3, $J_{5,6}$ = 8.5, $J_{8,9}$ = 7.9, $J_{10,11}$ = 9.3; mass spectrum (12 eV), m/z (relative intensity) 244 (100), 229 (22).

1,2,3,4-Tetrahydrobenz[*a*]anthracene-4,7,12-trione (18) and 1,2,3,4-Tetrahydrobenz[*a*]anthracene-1,7,12-trione (17). To the solution of quinone **7** (2.65 g, 10.1 mmol) in a mixture of CH_2Cl_2 (40 mL), AcOH (50 mL), and Ac_2O (10 mL) was added over a 6-h period a solution of CrO_3 (2 g, 19 mmol) in a mixture of Ac_2O (10 mL) and AcOH (25 mL). The reaction mixture was stirred for an additional 10 h at room temperature. 2-Propanol (20 mL) and then H_2O (800 mL) were added. The mixture was extracted successively with EtOAc (300 mL) and CH_2Cl_2 (2 × 300 mL). The combined organic extract was washed with H_2O (300 mL), NaOH (10%, 200 mL), and finally with brine to neutrality. Drying and evaporating the solvent furnished 2.67 g of a crude mixture of **17** and **18** in the ratio of (2:3). A portion was separated by chromatography on silica gel, and the remaining material was used in the next step, which results in more easily separated products. **18**: crystallized from EtOAc; mp 196–198 °C (lit.[17] mp 198–199 °C); ^{1}H NMR δ 2.19 (quintet, 2 H_2, J_{app} = 6.4), 2.75 (t, 2 H_3, J_{app} = 6.6), 3.65 (t, 2 H_1, J_{app} = 6.1), 7.78–7.82 (m, 2 $H_{9,10}$), 8.25 (d, 1 H_8 or H_{11}, J = 6.6), 8.26 (d, 1 H_8 or H_{11}, J = 7.2), 8.33 (d, 1 H_5 or H_6, J = 8.1), 8.47 (d, 1 H_5 or H_6, J = 8.1); mass spectrum, m/z (relative intensity) 276 (100), 248 (23), 247 (32), 234 (23), 233 (78), 220 (27). **17**: crystallized from EtOAc–*n*-hexane; mp 199–202 °C; ^{1}H NMR δ 2.23 (quintet, 2 H_3, J_{app} = 6.4), 2.92 (t, 4 $H_{2,4}$, J_{app} = 6.8), 7.55 (d, 1 H_5), 7.76–7.79 (m, 2 $H_{9,10}$), 8.16–8.19 (m, 1 H_8 or H_{11}), 8.22–8.25 (m, 1 H_8 or H_{11}), 8.28 (d, 1 H_6), $J_{5,6}$ = 8.0; mass spectrum, m/z (relative intensity) 276 (100), 248 (22), 247 (31), 234 (17), 233 (76), 220 (27).

Tosylhydrazones 19 and 20. A mixture of **17** and **18** (1.52 g, 5.5 mmol) was dissolved in $CHCl_3$ (70 mL), *p*-TsNHNH$_2$ (2.4 g, 12.8 mmol) was added, and the mixture was stirred at room temperature for 16 h followed by reflux for 5 h. Most of $CHCl_3$ was removed, and the residue was diluted with MeOH and centrifuged. The supernatant was decanted. Washing of the solid with cold MeOH by centrifugation and decantation was repeated five times to remove most of the *p*-TsNHNH$_2$. The residue was purified on a dry column of silica gel with a $CHCl_3$ and EtOAc/$CHCl_3$ (1:9) mixture as eluting solvent. This gave first **20** (0.972 g) and then **19** (0.648 g) in 38% and 26% yields, respectively, after two steps. **20**: crystallized from $CHCl_3$/MeOH; mp 237–240 °C dec (lit.[17] mp 239–241 °C dec); ^{1}H NMR δ 1.92 (quintet, 2 H_2, J_{app} = 6.3), 2.42 (s, 3 $H_{Ts\text{-}4'Me}$), 2.49 (t, 2 H_3, J_{app} = 6.6), 3.43 (t, 2 H_1, J_{app} = 6.1), 7.35 (d, 2 $H_{Ts\text{-}3'}$, J = 8.2), 7.69 (s, 1 H_{NH}), 7.75–7.79 (m, 2 $H_{9,10}$), 7.93 (d, 2 $H_{Ts\text{-}2'}$, J = 7.9), 8.19–8.25 (m, 3 H_5 or H_6, $H_{8,11}$), 8.43 (d, 1 H_5 or H_6), $J_{5,6}$ = 8.2; mass spectrum, m/z (relative intensity) 444 (0.1), 261 (100), 260 (63), 231 (39), 202 (46). **19**: crystallized from $CHCl_3$/MeOH; mp 190–192 °C; ^{1}H NMR δ 1.99 (quintet, 2 H_3, J_{app} = 6.02), 2.54 (s, 3 $H_{Ts\text{-}4'Me}$), 2.74 (t, 4 $H_{2,4}$, J_{app} = 6.7), 7.29 (d, 2 $H_{Ts\text{-}3'}$, J = 8.3), 7.44 (d, 1 H_5), 7.46 (dd, 1 H_8 or H_{11}, J = 6.9, 1.9), 7.66–7.76 (m, 2 $H_{9,10}$), 7.79 (d, J = 8.2, 2 $H_{Ts\text{-}2'}$), 7.87 (s, 1 H_{NH}), 8.18 (d, 1 H_6), 8.21 (dd, 1 H_8 or H_{11}, J = 7.2, 1.9), $J_{5,6}$ = 8.0; mass spectrum, m/z (relative intensity) 272 (100), 213 (19).

3,4-Dihydro-7,12-dihydroxy-7,12-dimethylbenz[*a*]anthracene (21). Into a dry two-necked 250-mL round-bottomed flask containing a magnetic stir bar was placed tosylhydrazone **19** (0.530 g, 1.1 mmol) followed by PhH (20 mL). The mixture was cooled to 0 °C for 10 min with stirring under N_2, and then MeLi (1.4 M, 12 mL, 8.6 mmol) was added dropwise. The mixture was stirred at 0–5 °C for 1 h, dry THF (40 mL) was added, and the reaction mixture was stirred further at room temperature for 2 h. Afterwards, the reaction mixture was cooled to 0 °C and was decomposed with ice-cold water. The organic layer was separated, and the aqueous layer was extracted with EtOAc (80 mL). The combined organic extract was washed with brine (3 × 100 mL) to neutrality. The solvent was dried and evaporated, and the residue was purified by chromatography on silica gel (35 g) using $CHCl_3$ (400 mL), which furnished diol **21** (0.220 g, 63%). A portion crystallized from $CHCl_3$–*n*-hexane had mp 198–202 °C: ^{1}H NMR δ 1.55 (s, 3 $H_{7\text{-}Me}$), 1.76 (s, 3 $H_{12\text{-}Me}$), 2.07 (s, 1 H_{OH}), 2.11 (s, 1 H_{OH}), 2.2–2.3 (m, 2 H_3), 2.81 (t, 2 H_4, J_{app} = 8.9), 6.16 (quintet, 1 H_2), 7.18 (d, 1 H_5), 7.37–7.40 (m, 2 $H_{9,10}$), 7.69 (d, 1 H_6), 7.75–7.86 (m, 3 $H_{1,8,11}$), $J_{1,2}$ = 9.9, $J_{2,3}$ = 4.8, $J_{5,6}$ = 8.0; mass spectrum, m/z (relative intensity) 292 (30), 277 (100), 262 (74), 259 (13), 256 (1); exact mass calcd for $C_{20}H_{20}O_2$ 292.1458, obsd 292.1464.

3,4-Dihydro-7,12-dimethylbenz[*a*]anthracene (22). In a dry two-necked 100-mL round-bottomed flask equipped with a magnetic stir bar and a reflux condenser was placed 1.4 g of a $TiCl_3$/LAH (2:1) mixture, and the flask was cooled to 0 °C under N_2. Dry THF (60 mL) was added slowly, and the mixture was stirred for 30 min at 0 °C and afterwards refluxed for 1 h. The mixture was cooled to 0 °C, and a solution of diol **21** (0.200 g, 0.68 mmol) in dry THF (20 mL) was added dropwise. The reaction mixture was stirred at 0 °C for 15 min and then refluxed for 3 h. Afterwards, the reaction mixture was cooled to 0 °C, HCl (2 N, 20 mL) was added, and the mixture was stirred for 5 min. The reaction mixture was extracted with PhH (200 mL). The PhH extract was washed successively with saturated $NaHCO_3$ solution and brine to neutrality. The solvent was dried and evaporated, and the residue was chromatographed on Florisil (15 g) with *n*-hexane (100 mL), which gave the alkene **22** (0.130 g, 74%). A portion crystallized from *n*-hexane–THF had mp 75–78 °C: ^{1}H NMR δ 2.35–2.45 (m, 2 H_3), 2.87 (t, 2 H_4, J_{app} = 8.5), 3.04 (s, 3 $H_{7\text{-}Me}$), 3.13 (s, 3 $H_{12\text{-}Me}$), 6.13 (quintet, 1 H_2), 7.09 (d, 1 H_1), 7.27 (d, 1 H_5), 7.48–7.52 (m, 2 $H_{9,10}$), 8.08 (d, 1 H_6), 8.23–8.30 (m, 2 $H_{8,11}$), $J_{1,2}$ = 9.8, $J_{2,3}$ = 4.9, $J_{5,6}$ = 8.9; mass spectrum, m/z (relative intensity) 258 (100), 243 (71), 228 (57); exact mass calcd for $C_{20}H_{18}$ 258.1404, obsd 258.1409.

1,2-Dihydro-7,12-dihydroxy-7,12-dimethylbenz[*a*]anthracene (23). Into a dry two-necked 250-mL round-bottomed flask containing a magnetic stir bar was placed tosylhydrazone **20** (0.5 g, 1.1 mmol). To this, dry PhH (50 mL) was added, and the mixture was cooled to 0 °C for 10 min with stirring under N_2 atmosphere. MeLi (1.4 M, 12 mL, 8.6 mmol) was added slowly. The mixture was stirred at 0–5 °C for 1 h, and then dry THF (50 mL) was added and the mixture was stirred for 2 h at room temperature. After being cooled to 0 °C, the mixture was decomposed with ice-cold water. The organic layer was separated, and the aqueous layer was extracted with EtOAc (50 mL). The combined organic extracts were washed with brine (3 × 100 mL) to neutrality. The solvent was dried and evaporated; the crude product was chromatographed on silica gel, employing $CHCl_3$ as eluting solvent, which furnished the desired diol **23** (0.202 g, 61%). A portion crystallized from EtOAc–*n*-hexane had mp 153–156 °C: ^{1}H NMR δ 1.54 (s, 3 $H_{7\text{-}Me}$), 1.76 (s, 3 $H_{12\text{-}Me}$), 2.05 (s, 1 H_{OH}), 2.08 (s, 1 H_{OH}), 2.25–2.35 (m, 2 H_2), 3.36 (t, 2 H_1, J_{app} = 7.9), 6.14 (quintet, 1 H_3), 6.5 (d, 1 H_4), 7.08 (d, 1 H_5), 7.36 (t, 2 $H_{9,10}$), 7.37 (d, 1 H_6), 7.76–7.82 (m, 2 $H_{8,11}$), $J_{2,3}$ = 4.5, $J_{3,4}$ = 9.3, $J_{5,6}$ = 8.0; mass spectrum, m/z (relative intensity) 292 (12), 277 (76), 274 (44), 262 (100), 259 (77), 256 (52); exact mass calcd for $C_{20}H_{20}O_2$ 292.1458, obsd 292.1463.

1,2-Dihydro-7,12-dimethylbenz[*a*]anthracene (24). In a dry two-necked 100-mL round-bottomed flask equipped with a magnetic stir bar and a reflux condenser was placed 0.6 g of $TiCl_3$/LAH (2:1) mixture. The flask was cooled to 0 °C under N_2, and dry THF (30 mL) was added slowly. The mixture was stirred for 30 min at 0 °C, refluxed for 1 h, and then cooled to 0 °C. A solution of diol **23** (0.0940 g, 0.32 mmol) in dry THF (15 mL) was added dropwise. The mixture was stirred at 0 °C for 15 min and then refluxed for 3 h. The reaction mixture was cooled to 0 °C, HCl (2 N, 10 mL) was added, and the mixture was stirred for 5 min. The reaction mixture was extracted with benzene (100 mL) and washed successively with saturated $NaHCO_3$ solution and brine to neutrality. The solvent was dried and evaporated and was rapidly chromatographed on Florisil (15 g) with *n*-hexane (100 mL) as eluting solvent, which gave the alkene **24** (0.060 g, 72%). A portion crystallized from THF–*n*-hexane had mp 123–127 °C (lit.[17] mp 123–124 °C): ^{1}H NMR δ 2.2–2.3 (m, 2 H_2), 3.04 (s, 3 $H_{7\text{-}Me}$), 3.11 (s, 3 $H_{12\text{-}Me}$), 3.41 (t, 2 H_1, J_{app} = 8.4), 6.15 (quintet, 1 H_3), 6.63 (br d, 1 H_4), 7.21 (d, 1 H_5), 7.46–7.49 (m, 2 $H_{9,10}$), 8.11 (d, 1 H_6), 8.22–8.27 (m, 2 $H_{8,11}$), $J_{2,3}$ = 4.9, $J_{3,4}$ = 9.8, $J_{5,6}$ = 8.9; mass spectrum, m/z (relative intensity) 258 (100), 243

(17) Inbasekaran, M. N.; Witiak, D. T. *J. Med. Chem.* **1980**, *23*, 278–281.

(28), 228 (38); exact mass calcd for $C_{20}H_{18}$ 258.1404, obsd 258.1409.

***trans*-2-Bromo-1-hydroxy-7-methyl-1,2,3,4-tetrahydrobenz[*a*]anthracene (25).** *N*-Bromoacetamide (20 mg, 0.14 mmol) was added to a cold (−5 to 0 °C) solution of alkene **4** (35 mg, 0.14 mmol) in freshly distilled THF (6 mL) and acidic H_2O (1.4 mL of a solution prepared from 4 mL of H_2O and 1 drop of concentrated HCl). The solution was stirred at −5 to 0 °C for 35 min, Et_2O (20 mL) was added, and the organic phase was washed with 10% aqueous $NaHCO_3$ (2 × 20 mL) and H_2O (1 × 20 mL), dried ($MgSO_4$), filtered, and evaporated, to give a yellow oil that was purified by flash chromatography on silica gel, with use of petroleum ether, 20% petroleum ether/PhH, and PhH successively as eluting solvents. This gave 28 mg (58%) of bromohydrin **25** as a solid, mp 135–137 °C after crystallization from ether–petroleum ether: ^{1}H NMR δ 2.18–2.32 (m, 1 H), 2.40 (d, 1 H_{OH}), 2.46–2.60 (m, 1 H), 2.85–2.94 (m, 1 H), 3.07 (s, 3 $H_{7\text{-Me}}$), 3.23–3.35 (m, 1 H), 4.75 (br s, 1 H_2), 5.72 (br s, 1 H_1), 7.23 (d, 1 H_5), 7.42–7.56 (m, 2 $H_{9,10}$), 8.03 (d, 1 H, J = 9.3), 8.21 (d, 1 H, J = 9.2), 8.26 (d, 1 H, J = 8.0), 8.63 (s, 1 H_{12}), $J_{1,OH}$ = 5.5, $J_{5,6}$ = 9.1; mass spectrum (12 eV), m/z (relative intensity) 340 (97), 342 (100), 322 (25), 324 (22).

***trans*-1-Acetoxy-2-bromo-12-methylbenz[*a*]anthracene (26).** Alkene **13** (75 mg, 0.31 mmol) was dissolved in a minimum volume (15 drops) of CH_2Cl_2 and added to degassed glacial HOAc (8.5 mL). The mixture was cooled to 12 °C and protected from light. NBA (36 mg, 0.26 mmol) was added, and the solution was stirred for 5 min. The mixture was poured into cold H_2O and extracted with CH_2Cl_2. The organic phase was washed with H_2O, dried ($MgSO_4$), filtered, and evaporated at 0 °C. The residue was purified by dry column chromatography on silica gel, with external cooling of the column with water at ~0 °C, and 10% EtOAc in petroleum ether as eluting solvent. This gave 86 mg of solid, which after recrystallization from THF–petroleum ether afforded 80 mg (79%, based on the limiting reagent, NBA) of **26**, mp 76–77 °C: ^{1}H NMR δ 2.01 (s, 3 $H_{1\text{-OAc}}$), 2.2–2.3 (m, 1 H), 2.6–2.7 (m, 1 H), 3.05–3.2 (m, 1 H), 3.17 (s, 3 $H_{12\text{-Me}}$), 3.3–3.4 (m, 1 H), 4.88 (m, 1 H_2), 7.1 (d, 1 H_1), 7.17 (d, 1 H_5), 7.86–8.25 (m, 6 H), $J_{1,2}$ = 3.6, $J_{5,6}$ = 8.7; mass spectrum (12 eV), m/z (relative intensity) 324 (40), 322 (40), 242 (100).

***trans*-2-Bromo-1-hydroxy-7,12-dimethyl-1,2,3,4-tetrahydrobenz[*a*]anthracene (27).** A two-necked 100-mL round-bottomed flask containing a magnetic stir bar was evacuated with a vacuum pump and filled with N_2. The process was repeated five times. Into this reaction flask was placed alkene **22** (0.060 g, 0.2 mmol), AcOH (1.0 mL), THF (8.0 mL), and distilled water (5.0 mL). The mixture was stirred at 8 °C for 10 min under N_2. Then NBA (0.030 g, 0.2 mmol) was added, and the reaction mixture was further stirred at 8 °C for 15 min. The reaction mixture was poured into ice-cold water containing $NaHCO_3$ and extracted with EtOAc (2 × 50 mL). The combined organic extract was washed with saturated $NaHCO_3$ solution and brine to neutrality. The solvent was dried, $NaHCO_3$ was added, and the solvent was evaporated under oil pump vacuum at −15 °C. The residue was chromatographed on silica gel at 0 °C with *n*-hexane (125 mL) and *n*-hexane–THF (19:1, 150 mL, 17:3, 150 mL) as eluting solvents, which gave the pure bromohydrin **27**. This was used in the next step without evaporating the solvent as it decomposed during concentration even at low temperature. A small portion was concentrated in the presence of $NaHCO_3$ for obtaining the NMR spectrum: ^{1}H NMR δ 2.28 (d, 1 H_{OH}), 2.30–2.42 (m, 1 H_3), 2.60–2.74 (m, 1 H_3), 3.04 (s, 3 $H_{7\text{-Me}}$), 3.08–3.29 (m, 2 H_4), 3.32 (s, 3 $H_{12\text{-Me}}$), 4.42–4.49 (m, 1 H_2), 5.92 (t, 1 H_1), 7.14 (d, 1 H_5), 7.45–7.58 (m, 2 $H_{9,10}$), 8.25–8.36 (m, 2 $H_{8,11}$), 8.19 (d, 1 H_6), $J_{1,OH}$ = 5.6, $J_{1,2}$ = 5.4, $J_{5,6}$ = 9.2.

1,2-Epoxy-7-methyl-1,2,3,4-tetrahydrobenz[*a*]anthracene (28). A mixture of bromohydrin **25** (58 mg), Amberlite IRA 400 (−OH) (12 g), and dry THF (12 mL) were stirred for 45 min, under Ar, with exclusion of light. The mixture was filtered, and the resin was washed four times with dry CH_2Cl_2. The organic solvents were evaporated at 0 °C to give 44 mg (100%) of **28**: ^{1}H NMR δ 1.87–2.00 (dt, 1 H), 2.50–2.59 (dd, 1 H), 2.73–2.81 (dd, 1 H), 2.90–3.02 (m, 1 H), 3.10 (s, 3 $H_{7\text{-Me}}$), 3.94 (br s, 1 H_2), 4.90 (d, 1 H_1), 7.27 (d, 1 H_5), 7.47–7.54 (m, 2 $H_{9,10}$), 8.04 (d, 1 H_{11}), 8.23 (d, 1 $H_{6,8}$, J = 9.0), 8.28 (d, 1 $H_{6,8}$, J = 8.8), 8.79 (s, 1 H_{12}), $J_{1,2}$ = 4.3, $J_{5,6}$ = 9.1, $J_{10,11}$ = 7.6; exact mass calcd for $C_{19}H_{16}O$ 260.1201, obsd 260.1184.

1,2-Epoxy-12-methyl-1,2,3,4-tetrahydrobenz[*a*]anthracene (29). Bromoacetate **26** (25 mg) in dry THF (10 mL) was added to Amberlite IRA 400 (−OH) (8 g), which had been washed with dry THF, and covered with 2 mL of dry THF. The mixture was stirred for 75 h, under Ar, protected from light, and filtered under N_2. The resin was washed with dry CH_2Cl_2, and the solvents were combined and evaporated at 0 °C. This gave 16 mg (94%) of **29** as a semisolid: ^{1}H NMR δ 1.84–2.00 (m, 1 H), 2.43–2.56 (m, 1 H), 2.77–2.87 (m, 1 H), 2.91–3.04 (m, 1 H), 3.36 (s, 3 $H_{12\text{-Me}}$), 3.83 (m, 1 H_2), 4.63 (d, 1 H_1), 7.15 (d, 1 H_5), 7.49 (t, 1 $H_{9,10}$, J_{app} = 7.6), 7.52 (t, 1 $H_{9,10}$, J_{app} = 8.7), 7.84 (d, 1 $H_{6,8}$, J = 8.7), 7.97 (d, 1 $H_{6,8}$, J = 8.8), 8.25 (s, 1 H_7), 8.27 (d, 1 H_{11}), $J_{1,2}$ = 4.1, $J_{5,6}$ = 8.6, $J_{10,11}$ = 7.6; mass spectrum (12 eV), m/z (relative intensity) 260 (100), 232 (14); exact mass calcd for $C_{19}H_{16}O$ 260.1201, found 260.1199.

7,12-Dimethyl-1,2-epoxy-1,2,3,4-tetrahydrobenz[*a*]anthracene (30). Into a dry 250-mL round-bottomed flask, containing a magnetic stir bar, was placed the bromohydrin solution obtained in the preparation of **27** (vide supra). To this was added Amberlite IRA-400 (−OH) (20 g), and the mixture was concentrated at −15 °C under oil pump vacuum. The resin was just covered with dry THF, and the mixture was stirred, with protection from light, at 12 °C for 3 h under N_2. The mixture was filtered under suction, and the resin was washed with dry CH_2Cl_2 (3 × 15 mL). The filtrate was evaporated at −10 °C under oil pump vacuum to give the epoxide **30** (20 mg), mp 115–118 °C, in 36% yield based on alkene **22**: ^{1}H NMR δ 1.75–1.90 (m, 1 H_3), 2.45–2.56 (m, 1 H_3), 2.73–2.86 (m, 1 H_4), 2.90–3.03 (m, 1 H_4), 3.06 (s, 3 $H_{7\text{-Me}}$), 3.32 (s, 3 $H_{12\text{-Me}}$), 3.82 (m, 1 H_2), 4.56 (d, 1 H_1), 7.19 (d, 1 H_5), 7.48–7.56 (m, 2 $H_{9,10}$), 8.17 (d, 1 H_6), 8.27–8.31 (m, 2 $H_{8,11}$), $J_{1,2}$ = 4.4, $J_{5,6}$ = 8.9; mass spectrum, m/z (relative intensity) 274 (100), 259 (14), 258 (5); exact mass calcd for $C_{20}H_{18}O$ 274.1353, obsd 274.1358.

***trans*-3-Bromo-4-hydroxy-7-methyl-1,2,3,4-tetrahydrobenz[*a*]anthracene (31).** *N*-Bromoacetamide (28 mg, 0.2 mmol) was added to a cold (−5 to 0 °C) solution of alkene **6** (50 mg, 0.2 mmol) in freshly distilled THF (9 mL) and acidic H_2O (2 mL of a solution prepared from 4 mL of H_2O and one drop of concentrated HCl). The solution was stirred for 3 min, and then Et_2O (20 mL) was added. The ether phase was washed with 10% aqueous $NaHCO_3$ (2 × 20 mL) and H_2O (1 × 20 mL), dried ($MgSO_4$), filtered, and evaporated to give a yellow oil that was purified by flash chromatography on silica gel, with use of petroleum ether, 1:1 petroleum ether–PhH, and PhH sequentially as eluting solvents. This gave bromohydrin **31** (29 mg, 41%) as a solid of mp 165–167 °C, after crystallization from ether–petroleum ether at −10 °C: ^{1}H NMR δ 2.46–2.55 (m, 1 H), 2.67 (d, 1 H_{OH}), 2.70–2.80 (m, 1 H), 3.10 (s, 3 $H_{7\text{-Me}}$), 3.36–3.57 (m, 2 H), 4.48–4.55 (m, 1 H_3), 5.07–5.12 (m, 1 H_4), 7.46–7.55 (m, 2 $H_{9,10}$), 7.64 (d, 1 H_5), 8.02 (d, 1 H_{11}), 8.24 (d, 1 $H_{6,8}$, J = 9.2), 8.28 (d, 1 $H_{6,8}$, J = 9.0), 8.44 (s, 3 H_{12}), $J_{4,OH}$ = 4.8, $J_{5,6}$ = 9.2, $J_{10,11}$ = 8.0.

***trans*-3-Bromo-4-hydroxy-12-methyl-1,2,3,4-tetrahydrobenz[*a*]anthracene (32).** Alkene **16** (49 mg) was dissolved in freshly distilled THF (5 mL), and H_2O (1.25 mL) was added. The mixture was cooled to 0 °C and protected from light. Acidic water (0.7 mL of a solution of 1 drop of HCl in 4 mL of H_2O) was added, and the solution was stirred at 0 °C for 5 min. The mixture was poured into H_2O and extracted with ether. The ether phase was washed with cold H_2O, dried ($MgSO_4$), filtered, and evaporated at 0 °C. The residue (62 mg) was purified by dry column chromatography at 0 °C, with 10% EtOAc in petroleum ether as eluting solvent. This gave 35 mg of **32**. Recrystallization from ether/petroleum ether at −20 °C gave 29 mg (48%, based on NBA) of **32**, mp 116–117 °C: ^{1}H NMR δ 2.17–2.30 (m, 1 H), 2.36 (d, 1 H_{OH}), 2.43–2.55 (m, 1 H), 3.21 (s, 3 $H_{12\text{-Me}}$), 3.54–3.62 (m, 2 H), 4.54 (m, H_3), 5.11 (m, H_4), 7.44–7.55 (m, 3 H), 7.83 (d, 1 H, J = 8.8), 7.95 (d, 1 H, J = 8.1), 8.22 (s, 1 H_7), $J_{3\text{-OH}}$ = $J_{3,4}$ = 5.3; mass spectrum (12 eV), m/z (relative intensity) 324 (87), 322 (100), 342 (4.7), 340 (4.3).

***trans*-3-Bromo-4-hydroxy-7,12-dimethyl-1,2,3,4-tetrahydrobenz[*a*]anthracene (33).** A two-necked 100-mL round-bottomed flask containing a magnetic stir bar was evacuated employing vacuum pump and filled with N_2. The process was repeated five times. Into this reaction flask was placed alkene **24** (0.135 g, 0.52 mmol), AcOH (3 mL), THF (12 mL), and distilled water (6 mL). The mixture was stirred at 12 °C for 10 min under N_2. Then, NBA (0.072 g, 0.52 mmol) was added, and the mixture

was further stirred at 12 °C for 15 min. The reaction mixture was poured into ice-cold water containing $NaHCO_3$ and extracted with EtOAc (2 × 75 mL). The combined organic extracts were washed with saturated $NaHCO_3$ solution and brine to neutrality. The solvent was dried and removed under oil pump vacuum at −15 °C. The residue was chromatographed on silica gel at 0 °C with *n*-hexane (75 mL), CH_2Cl_2–*n*-hexane (1:9, 175 mL), and CH_2Cl_2 (250 mL), which gave a bromohydrin **33** (75 mg, 41%), mp 133–135 °C: ^1H NMR δ 2.1–2.2 (m, 1 H_2), 2.35–2.47 (m, 1 H_2), 2.65 (d, 1 H_{OH}), 3.03 (s, 3 $H_{7\text{-}Me}$), 3.12 (s, 3 $H_{12\text{-}Me}$), 3.4–3.6 (m, 2 H_1), 4.53 (m, 1 H_3), 5.10 (t, J_{app} = 5.4, 1 H_4), 7.51–7.54 (m, 3 $H_{5,9,10}$), 8.17 (d, 1 H_6), 8.25–8.30 (m, 2 $H_{8,11}$), $J_{4,OH}$ = 5.1, $J_{5,6}$ = 9.2; mass spectrum, *m/z* (relative intensity) 356 (14), 354 (13), 338 (26), 336 (26), 323 (10), 321 (10), 275 (8), 274 (22), 260 (13), 258 (15), 256 (69); exact mass calcd for $C_{20}H_{19}OBr$ 356.0594 and 354.0614, obsd 356.0587 and 354.0611. Chromatography also gave bromoacetate **34** (4.2 mg, 2%), mp 81–84 °C: ^1H NMR δ 2.1–2.35 (m, 2 H_2), 2.17 (s, 3 $H_{4\text{-}Ac}$), 3.03 (s, 3 $H_{7\text{-}Me}$), 3.17 (s, 3 $H_{12\text{-}Me}$), 3.45 (m, 1 H_1), 3.56–3.74 (m, 1 H_1), 4.52–4.60 (m, 1 H_3), 6.40 (d, 1 H_4), 7.17 (d, 1 H_5), 7.46–7.56 (m, 2 $H_{9,10}$), 8.14 (d, 1 H_6), 8.22–8.33 (m, 2 $H_{8,11}$), $J_{3,4}$ = 4.7, $J_{5,6}$ = 9.2; mass spectrum, *m/z* (relative intensity) 398 (13), 396 (17), 316 (23), 275 (17), 274 (58), 260 (11), 259 (33), 258 (69), 257 (100), 256 (25), 242 (91); exact mass calcd for $C_{22}H_{21}O_2Br$ 398.0699 and 396.0719, obsd 398.0704 and 396.0725.

3,4-Epoxy-7-methyl-1,2,3,4-tetrahydrobenz[*a*]anthracene (35). A mixture of bromohydrin **31** (25 mg), Amberlite IRA 400 (−OH) (6.5 g), and dry THF (8 mL) was stirred at room temperature, under Ar, with protection from light, for 45 min. The mixture was filtered, and the resin was washed with dry CH_2Cl_2. The organic phases were combined, and evaporated, leaving 19 mg (99%) of epoxide **35**, mp 134–135 °C: ^1H NMR δ 1.87–1.99 (dt, 1 H), 2.65–2.73 (dd, 1 H), 2.84–2.98 (m, 1 H), 3.56–3.64 (dd, 1 H), 3.89 (br s, H_3), 4.03 (d, H_4), 7.43–7.57 (m, 3 $H_{5,9,10}$), 8.02 (d, H_{11}), 8.22 (d, $H_{6,8}$, *J* = 8.9); 8.28 (d, $H_{6,8}$, *J* = 8.6), 8.54 (s, H_{12}), $J_{3,4}$ = 4.2, $J_{10,11}$ = 7.8; mass spectrum (12 eV), *m/z* (relative intensity) 260 (100), 245 (11); exact mass calcd for $C_{19}H_{16}O$ 260.1201, found 260.1199.

3,4-Epoxy-12-methyl-1,2,3,4-tetrahydrobenz[*a*]anthracene (36). Bromohydrin **32** (70 mg) in dry THF (8 mL) was added to Amberlite IRA 400 (−OH) (15 g), which had been extensively washed with dry THF, and then covered with 2 mL of dry THF. The mixture was stirred, under Ar, protected from light, for 50 min. The mixture was filtered, and the resin was washed with dry CH_2Cl_2. The organic solvents were combined and evaporated at 0 °C to give 53 mg (100%) of epoxide **36**, mp 115–116 °C: ^1H NMR δ 1.47–1.59 (m, 1 H), 2.50–2.58 (m, 1 H), 3.35–3.43 (m, 2 H), 3.81 (br s, 1 H_3), 4.04 (d, 1 H_4), 7.40 (d, 1 H_5), 7.43–7.55 (m, 2 $H_{9,10}$), 7.81 (d, 1 $H_{6,8}$, *J* = 8.5), 7.96 (d, 1 $H_{6,8}$, *J* = 8.4), 8.23 (d, 1 H_{11}), 8.25 (s, 1 H_7), $J_{3,4}$ = 4.2, $J_{5,6}$ = 8.5, $J_{10,11}$ = 8.4; mass spectrum (12 eV), *m/z* (relative intensity) 260 (66), 245 (11); exact mass calcd for $C_{19}H_{16}O$ 260.1201, found 260.1212.

7,12-Dimethyl-3,4-epoxy-1,2,3,4-tetrahydrobenz[*a*]anthracene (37). Into a dry 100-mL round-bottomed flask, containing a magnetic stir bar, was placed Amberlite IRA-400 ($^-$OH) (20 g). The flask was evacuated five times and then filled with N_2 each time. To this was added bromohydrin **33** (75.4 mg, 0.21 mmol) in dry THF (10 mL), just covering the resin. The mixture, protected from light, was stirred under N_2 atmosphere at room temperature for 2 h and then was filtered under suction. The resin was washed with dry CH_2Cl_2 (3 × 15 mL). The filtrate was evaporated at 0 °C under high vacuum to obtain the epoxide **37** (58.1 mg, 99%), mp 137–140 °C: ^1H NMR δ 1.45–1.55 (m, 1 H_2), 2.45–2.58 (m, 1 H_2), 3.06 (s, 3 $H_{7\text{-}Me}$), 3.13 (s, 3 $H_{12\text{-}Me}$), 3.2–3.5 (m, 2 H_1), 3.80 (t, 1 H_3), 4.06 (d, 1 H_4), 7.45 (d, 1 H_5), 7.49–7.53 (m, 2 $H_{9,10}$), 8.15 (d, 1 H_6), 8.24–8.29 (m, 2 $H_{8,11}$), $J_{3,4}$ = 4.2, $J_{5,6}$ = 8.8; mass spectrum, *m/z* (relative intensity) 274 (100), 259 (28), 258 (6), 246 (26), 245 (17), 231 (36); exact mass calcd for $C_{20}H_{18}O$ 274.1353, found 274.1358.

Phase-Transfer-Catalyzed Synthesis of Oligoethylene Glycols and Derivatives

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Received August 10, 1988

An efficient, two-step synthetic method for the addition of ethyleneoxy units to diols is reported. Reaction of HOROH with $Cl(CH_2CH_2O)_nTHP$ and 50% aqueous NaOH in the presence of a phase-transfer catalyst gives $THP(OCH_2CH_2)_nORO(CH_2CH_2O)_nTHP$ from which the protecting groups are readily removed to provide $H(OCH_2CH_2)_nORO(CH_2CH_2O)_nH$ in good-to-excellent yields. The influence of reactant diol structure upon yield has been determined.

Oligoethylene glycols are important building blocks for the synthesis of crown ethers.[1] Although the lower members of the oligoethylene glycol family have been readily accessible as pure compounds for many years, only recently have $HO(CH_2CH_2O)_nH$ with $n > 5$ become commercially available. Functionalized oligoethylene glycols, which are important for the preparation of functionazlied crown ethers and cryptands,[2-5] must be synthesized.

The preparation of individual oligoethylene glycols has been of interest for more than half a century. Most of the reported procedures employ a classical Williamson ether synthesis and provide yields in the 20–45% range.[6-11] In some cases, pure higher oligoethylene glycols were separated from oligoethylene glycol mixtures by fractional

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