A New and Concise Synthesis of 3-Hydroxybenzo[*c*]phenanthrene and 12-Hydroxybenzo[*g*]chrysene, Useful Intermediates for the Synthesis of Fjord-Region Diol Epoxides of Benzo[*c*]phenanthrene and Benzo[*g*]chrysene

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A new strategy which involves a palladium-catalyzed cross-coupling reaction has been developed for the rapid synthesis of 3-hydroxybenzo[*c*]phenanthrene (**5**) and 12-hydroxybenzo[*g*]chrysene (**6**). These phenolic compounds are the key intermediates for the synthesis of highly carcinogenic fjord-region diol epoxide metabolites **3** and **4** of benzo[*c*]phenanthrene (**1**) and benzo[*g*]chrysene (**2**). The cross-coupling reaction of 2-bromo-5-methoxybenzaldehyde (**9**) with naphthalene-1-boronic acid (**7**) and phenanthrene-9-boronic acid (**8**) produced 2-(1-naphthyl)-5-methoxybenzaldehyde (**10**) and 2-(9-phenanthryl)-5-methoxybenzaldehyde (**11**), respectively, in quantitative yields. After reaction of these aldehydes with trimethylsulfonium iodide under phase-transfer conditions or with the Wittig reagent obtained from (methoxymethyl)triphenylphosphonium bromide and phenyllithium to generate an oxiranyl or methoxyethene side chain, the acid-catalyzed cyclization with methanesulfonic acid (or boron trifluoride) produced 3-methoxybenzo[*c*]phenanthrene (**16**) and 12-methoxybenzo[*g*]chrysene (**17**) in 61−64% yields. Finally, demethylation of these methoxy derivatives **16** and **17** with boron tribromide resulted in the formation of the hydroxy analogues **5** and **6**, respectively. The availability of this short and high-yielding regiospecific method for the synthesis of phenols **5** and **6** should allow the preparative-scale synthesis of the fjord-region diol epoxides **3** and **4**. These diol epoxides are required as starting compounds for the synthesis of site-specifically modified oligonucleotides which are critically needed to elucidate the mechanism of carcinogenesis at the molecular level.

Polycyclic aromatic hydrocarbons (PAHs) are widespread environmental contaminants which are introduced into our environment by the combustion of organic matters.[1] Some PAHs are potent carcinogens, and their metabolism by cytochrome P-450 and epoxide hydrolase to bay-region diol epoxides is considered to be involved in the carcinogenic action of these chemicals.[2−4] The covalent binding of bay-region diol epoxide intermediates to cellular DNA is believed to be involved in tumor-induction. The additional steric constraint in the bay region has been found to significantly enhance the carcinogenic activity of the bay-region diol epoxide derivatives.[5,6] The fjord-region diol epoxides **3** and **4** of benzo[*c*]phenanthrene (**1**) and benzo[*g*]chrysene (**2**), which have additional crowding in the bay region, exhibit significantly higher levels of carcinogenic activity.[7−10] Furthermore, in contrast to bay-region diol epoxides which react predominantly at the deoxyguanosine residue of cellular DNA, fjord-region diol epoxides react extensively with the deoxyadenosine residue of cellular DNA.[11−13] Since fjord-region diol epoxides **3** and **4** display high carcinogenic activity and a high level of covalent binding to DNA with the deoxyadenosine residues, these metabolites are of particular interest for the further elucidation of the mechanism of PAH-induced carcinogenesis, especially, at the molecular level.

Recent advances[14] have shown that the biochemical event(s) that leads a diol epoxide−DNA adduct to induce tumorigenic effects may be correlated with the preferred conformation of the adduct in DNA template. Consequently, site-specifically modified oligonucleotides have emerged as useful probes for identifying the conformation-related mutational events that lead to tumorigenesis.[15,16] Since the synthesis of site-specifically modified oligonucleotides involves multistep synthesis and re-

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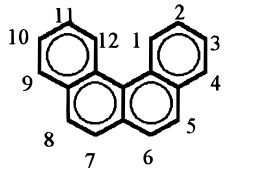

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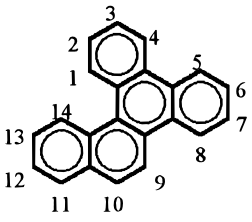

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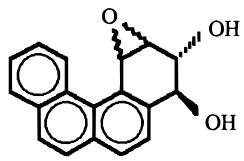

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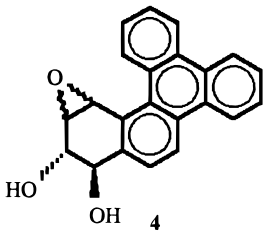

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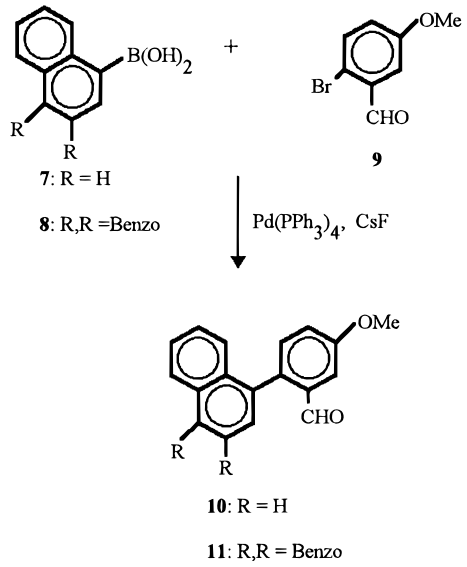
quires fjord-region diol epoxides as key starting materials, a practical and short synthesis of the fjord-region diol epoxides of **1** and **2** is needed. A number of approaches have been developed[17−22] for the synthesis of **3** and **4** during recent years. The most convenient approach[17−20] for the synthesis of **3** involves 3-hydroxy- (**5**) or 4-hydroxybenzo[*c*]phenanthrene (**5a**), and for **4** it involves either 12-hydroxy- (**6**), 11-hydroxy- (**6a**), or 11,12-dihydroxybenzo[*g*]chrysene (**6b**). Although the yield of **6b** or its diacetate has not been reported,[20] the other phenolic compounds **5**, **5a**, **6**, and **6a** are best obtained in 4−6 steps with 16−31% yields from commercially or easily accessible starting materials by two general methods.[17−20] One of the general methods which can be adaptable to the large scale synthesis of **5** is not only nonregiospecific but also requires a relatively large number of steps, thereby making the overall synthesis of **5** less efficient.[17] The other general method, while requiring a smaller number of steps for the synthesis of **5a**,[18] **6a**,[19] or **6b**,[20] involves oxidative photocyclization, which works only under high dilution conditions (10^{-3}−10^{-4} molar in benzene); consequently, this method is not suitable for the synthesis of these phenolic compounds on a preparative scale. Furthermore, the formation of **5a** and **6a** occurred in low yield (<50%), presumably due to a side reaction involving the elimination of *o*-methoxy group during photocyclization.[23] In view of these synthetic difficulties associated with the existing methods, a more convenient and rapid approach is needed for the synthesis of these phenols in desired amounts in a short amount of time from readily accessible starting materials. I now report such an efficient approach for the synthesis of 3-hydroxybenzo[*c*]phenanthrene (**5**) and 12-hydroxybenzo[*g*]chrysene (**6**). This synthetic approach, which involves a palladium-catalyzed cross-coupling reaction (Suzuki reaction[24]) of easily accessible reactants is, in principle, adaptable to large scale synthesis of **5** and **6** in four convenient steps.

Scheme 1



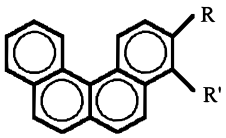
7: R = H

8: R,R =Benzo

9

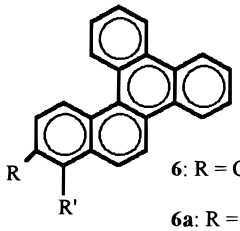
10: R = H

11: R,R = Benzo



5: R = OH, R' = H

5a: R = H, R' = OH



6: R = OH, R' = H

6a: R = H, R' = OH

6b: R = R' = OH

Results and Discussion

The pioneering discovery of Suzuki reaction[24] has set a foundation for the synthetic development of PAHs and their highly functionalized derivatives.[25,26] However, the application of this reaction to developing an efficient route to the synthesis of carcinogenic PAH metabolites has been explored only recently.[27] In an earlier study, Wright et al.[28] demonstrated that the palladium-catalyzed cross-coupling reaction of phenylboronic acid with *p*-bromobenzaldehyde occurred in high yield in the presence of cesium fluoride under anhydrous conditions. On the basis of this study, we envisaged analogous reaction between arylboronic acids and 2-bromo-5-methoxybenzaldehyde as the key step in planning our strategy for the synthesis of 3-hydroxybenzo[*c*]phenanthrene (**5**) and 12-hydroxybenzo[*g*]chrysene (**6**) (see Scheme 1). The required boronic acids, naphthalene-1-boronic acid (**7**)[29] and phenanthrene-9-boronic acid (**8**),[30] and 2-bromo-5-methoxybenzaldehyde (**9**)[31] were readily accessible according to the literature procedures. Thus, the coupling reaction of **7** or **8** with **9** in the presence of anhydrous CsF and a

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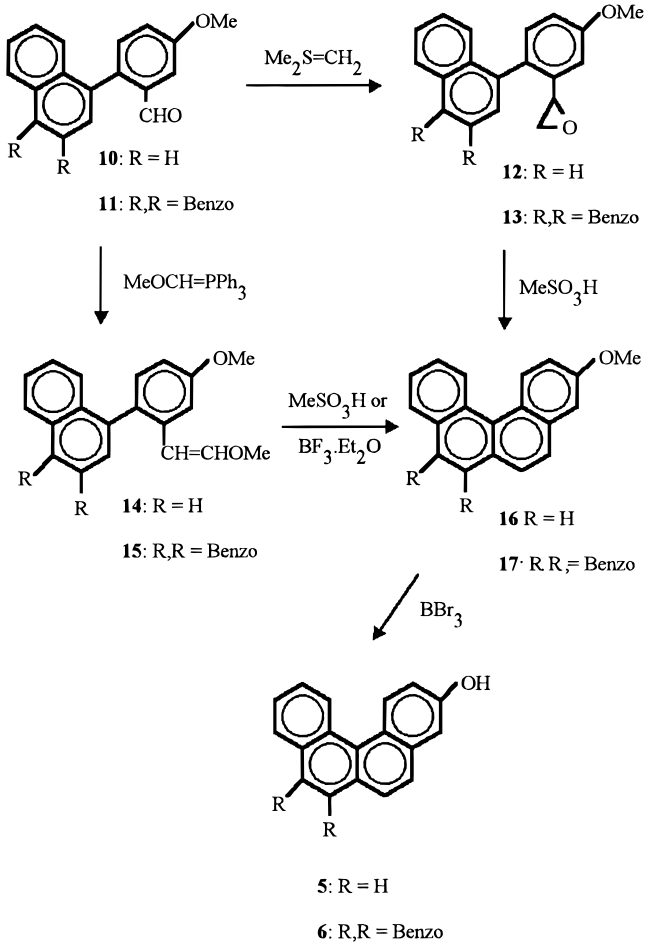
Scheme 2



catalytic amount of $Pd(PPh_3)_4$ produced **10** or **11** in nearly quantitative yield (96−100%). The cross-coupling reaction of relatively unhindered boronic acid with *ortho*-substituted aryl halides has been reported to proceed in moderate to high yields only if strong bases such as aqueous NaOH or $Ba(OH)_2$ are used.[32−34] However, these bases are not entirely compatible with the aldehyde group present in **9**. The present examples demonstrated that the yield of the coupling product was very high even when using relatively hindered boronic acid **7** or **8** in the coupling reaction with *ortho*-substituted aryl halide in the presence of CsF. Presumably, the high affinity of the fluoride ion for boron, the considerable stability of the product fluoborate ion, the relative weak basicity and poor nucleophilicity of the fluoride ion, the weakness of the palladium−fluoride bond, and the anhydrous conditions all contribute to the high yield of the coupling products.

Two approaches were investigated for converting **10** and **11** to the corresponding 3-methoxybenzo[*c*]phenanthrene (**16**) and 12-methoxybenzo[*g*]chrysene (**17**) (Scheme 2). In one approach, the aldehydes **10** and **11** were reacted under phase transfer reaction conditions with trimethylsulfonium iodide to produce the corresponding ethylene oxide derivatives **12** and **13**, respectively, as a mixture of diastereomers (^{1}H NMR). The restricted rotation between aryl−aryl bond and the presence of a chiral center at the benzylic carbon of the ethylene oxide functionality were responsible for producing **12** and **13** as a mixture of diastereomers. The acid-catalyzed cyclodehydration of **12** and **13** took place smoothly with methanesulfonic acid in CH_2Cl_2 to provide 3-methoxybenzo[*c*]phenanthrene (**16**) and 12-methoxybenzo[*g*]chrysene (**17**) in 62% and 42% yields, respectively. When the cyclodehydration reaction of **13** was effected with $BF_3{\cdot}Et_2O$ in Et_2O, **17** was obtained in slightly higher yield (50%). In the second approach, the aldehydes **10** and **11** were treated with the Wittig reagent[19] obtained from (methoxymethyl)triphenylphosphonium bromide and phenyllithium to produce the methoxyethene derivatives **14** and **15** in 54% and 83% yields, respectively, as a ∼1:1 mixture of *cis* and *trans* isomers. The acid-catalyzed cyclization of the *cis*/*trans* mixture of **14** and **15** with methanesulfonic acid in methylene chloride at 0 °C afforded the corresponding **16** and **17** in 60% and 79% yields, respectively. In none of the cases, the acid-catalyzed cyclization occurred at the *peri*-position (C-8) of the epoxides **12** and **13** or methoxyethenes **14** and **15** to produce undesirable seven-membered products. Comparison of the two approaches used for the two step synthesis of **16** and **17** from the corresponding aldehydes **10** and **11** indicated that the first approach produced **16** in better yield. On the other hand, **17** was produced in better yield following the second approach. Finally, the methoxy PAHs **16** and **17** were demethylated (BBr_3/CH_2Cl_2) to 3-hydroxybenzo[*c*]phenanthrene (**5**) and 12-hydroxybenzo[*g*]chrysene (**6**) in 86−98% yields. The reaction sequence, phenol → *o*-quinone → dihydrodiol → diol epoxide, is well established in the literature[17,20] for the conversion of the phenols **5** and **6** to the corresponding fjord-region diol epoxides **3** and **4**, respectively.

In summary, the present study describes a highly efficient application of the palladium-catalyzed cross-coupling reaction of readily accessible reactants to the concise synthesis of 3-hydroxybenzo[*c*]phenanthrene (**5**) and 12-hydroxybenzo[*g*]chrysene (**6**). The overall yields of these phenols **5** and **6** from bromo aldehyde **9** were 61 and 64%, respectively, which represent a significant improvement over the previous methodologies. In addition to providing a practical and concise synthesis of **5** and **6**, the method holds promise as a general synthetic route to substituted benzo[*c*]phenanthrene and benzo[*g*]chrysene, and their metabolites.

Experimental Section

Naphthalene-1-boronic acid (**7**)[29] and phenanthrene-9-boronic acid (**8**)[30] were prepared as described in the literature. 2-Bromo-5-methoxybenzaldehyde (**9**)[31] was synthesized by a published procedure. All reagents and solvents (anhydrous or otherwise) were used as received without additional purification. Dry column grade silica gel was purchased from E. Merck. ^{1}H NMR spectra were recorded on a 400 MHz NMR spectrometer (Brucker) in d_6-acetone with tetramethylsilane (TMS) as internal standard at the NMR facility of Roswell Park Cancer Institute, Buffalo, NY. Chemical shifts were reported in ppm downfield from the internal standard. All melting points were uncorrected.

2-(1-Naphthyl)-5-methoxybenzaldehyde (10). A mixture of naphthalene-1-boronic acid (**7**) (4.04 g, 0.023 mol), 2-bromo-5-methoxybenzaldehyde (**9**) (4.57 g, 0.02 mol), anhydrous CsF (7.23 g, 0.047 mol), and $Pd(PPh_3)_4$ (0.82 g, 0.0007 mol) in anhydrous DME (100 mL) was heated under reflux for 18 h under argon. The reaction was monitored by TLC

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(15% EtOAc−hexane) until no more bromide was detected. The reaction mixture was then cooled and extracted with a mixture of EtOAc (200 mL) and water (200 mL). The EtOAc layer was separated, dried (Na_2SO_4), and concentrated to yield a solid. The crude product was recrystallized from CH_2Cl_2−hexane to give 5.57 g (100% yield) of **10** as a light yellow crystalline solid, mp 115−116 °C. ^{1}H NMR (d_6-acetone): δ 4.0 (s, 3 H), 7.37−7.65 (m, 9 H), 8.05 (d, 1 H, J = 9.7 Hz), 9.56 (s, 1 H). ^{13}C NMR ($CDCl_3$): δ 191.4 (CHO), 159.4, 137.1, 135.6, 135.1, 133.4, 133.0, 132.9, 128.5, 128.4, 128.3, 126.6, 126.1, 125.8, 125.0, 121.4, 109.4, 55.6 (OMe). Anal. Calcd for $C_{18}H_{14}O_2$: C, 82.4; H, 5.3. Found: C, 82.3; H, 5.4.

3-Methoxybenzo[*c*]phenanthrene (16). Method A. The two-phase system containing aldehyde **10** (2.0 g, 7.6 mmol) in 50 mL of CH_2Cl_2 and 25 mL of 50% aqueous NaOH was treated with trimethylsulfonium iodide (3.16 g, 15.5 mmol) and tetrabutylammonium iodide (30 mg). The mixture was stirred vigorously under reflux, and the progress of the reaction was monitored by ^{1}H NMR spectroscopy which showed that the completion of the reaction required 96 h. After completion of the reaction, the mixture was poured into ice-cold water, and the product was isolated by extraction with CH_2Cl_2. The organic phase was washed with water, dried over Na_2SO_4, and filtered, and the solvent was removed by rotary evaporation to afford 2.3 g (100%) of sufficiently pure 1-(2-(epoxyethyl)-4-methoxyphenyl)naphthalene (**12**) as a light yellow syrupy oil. ^{1}H NMR (d_6-acetone): δ 2.64−2.72 (m, 2 H), 3.29−3.33 (m, 1 H), 3.90 (s, 3 H), 6.85−8.02 (m, 10 H).

To a stirred solution of the epoxide **12** (2.54 g) in anhydrous CH_2Cl_2 (125 mL) under argon was added dropwise methanesulfonic acid (5 mL) in 2−3 min. The mixture was stirred at rt for 4 h. The mixture was poured on to ice-cold 10% aqueous NaOH and extracted with CH_2Cl_2. The organic phase was washed with cold water, dried (Na_2SO_4), and concentrated under vacuum to yield a dark oil. The oil was chromatographed on dry column grade silica gel using 5% EtOAc−hexane as eluant to provide 1.63 g (62% based on aldehyde **10**) of pure **16** as a solid. A small sample of this solid was recrystallized from hexane to yield shiny yellow flakes, mp 90−91 °C (lit.[35] mp 89−90 °C). ^{1}H NMR (d_6-acetone): δ 4.01 (s, 3 H, OCH_3), 7.38 (dd, 1 H, H-2, $J_{1,2}$ = 9.2, $J_{2,4}$ = 3.4 Hz), 7.56 (d, 1 H, H-4, $J_{2,4}$ = 3.4), 7.62−7.75 (m, 2 H, H-10, H-11), 7.86−7.97 (m, 4 H, H-5, H-6, H-7, H-8), 8.09 (dd, 1 H, H-9, $J_{9,10}$ = 7.7 Hz, $J_{9,11}$ = 1.4 Hz), 9.07 (d, 1 H, H-1, $J_{1,2}$ = 9.2 Hz), 9.10 (d, 1 H, H_{12}, $J_{11,12}$ = 8.7 Hz). ^{13}C NMR ($CDCl_3$): δ 157.4, 135.0, 133.5, 130.0, 129.6, 129.4, 128.4, 127.8, 127.5, 127.4, 126.8, 126.7, 126.4, 125.9, 125.7, 125.0, 117.0, 107.8, 55.3 (OMe). Anal. Calcd for $C_{19}H_{14}O\cdot{}^1/_8C_6H_{14}$: C, 88.1; H, 5.9. Found: C, 87.7; H, 5.5.

Method B. A 1.8 M solution of phenyllithium (5 mL, 9.0 mmol) in cyclohexane−ether (7:3) was added dropwise to a solution of (methoxymethyl)triphenylphosphonium bromide (2.9 g, 8.45 mmol) in dry Et_2O (100 mL) at − 65 °C under argon. The mixture was stirred at −65 °C for 0.5 h, then warmed to −10 °C for 0.5 h, and then cooled again to −50 °C. Solid aldehyde **10** (0.8 g, 3.05 mmol) was added portionwise during 10 min, and the mixture was stirred at −50 °C for 1 h and then at rt for 15 h. The mixture was treated with ice-cold water, and the Et_2O layer was separated. The aqueous phase was extracted once with Et_2O, and the combined organic phases were washed with ice-cold water and dried (Na_2SO_4). Removal of the solvent gave an oil which was further purified by chromatography on dry column grade silica gel with elution by hexane to remove nonpolar impurities and then by 3% EtOAc−hexane. This gave 0.47 g (54%) of an oil containing a mixture of nearly equal amounts of *cis* and *trans* isomers **14**. Partial ^{1}H NMR (d_6-acetone): for *cis* isomer, two doublets at δ 4.65 and 6.11 (J = 9.9 Hz); for *trans* isomer, two doublets at δ 5.32 and 7.05 (J = 15.4 Hz).

To a stirred solution of the isomeric mixture of **14** (0.37 g) in 25 mL of anhydrous CH_2Cl_2 at 0 °C under argon was added methanesulfonic acid (5 mL) in 5 min. The reaction mixture was then stirred for an additional 1.75−2.5 h at 0 °C, diluted with ice-cold water, and then extracted with Et_2O. The Et_2O layer was washed thrice with cold water and dried over anhydrous Na_2SO_4. Concentration of the solution gave a semisolid which was recrystallized from hexane to give 0.20 g (61%) of **16** as light yellow needles, mp 89−91 °C.

3-Hydroxybenzo[*c*]phenanthrene (5). To a stirred solution of **16** (0.54 g, 2.0 mmol) in dry CH_2Cl_2 (25 mL) was added a 1 M solution of BBr_3 (4.2 mL, 4.2 mmol) in CH_2Cl_2 at 0 °C under argon over a period of 2−3 min. After 12 h at rt, the reaction mixture was hydrolyzed with ice-cold water, the organic layer was washed with water and dried (Na_2SO_4), and the solvent was removed to afford a solid. Trituration of the solid with hexane gave 0.50 g (98%) of **5** as a crystalline solid, mp 110−112 °C (lit.[35] mp 107−110 °C). ^{1}H NMR (d_6-acetone): δ 7.36 (dd, 1 H, H-2, $J_{1,2}$ = 8.7, $J_{2,4}$ = 3.0 Hz), 7.45 (d, 1 H, H-4, $J_{2,4}$ = 3.0), 7.61−7.74 (m, 2 H, H-10, H-11), 7.81−7.94 (m, 4 H, H-5, H-6, H-7, H-8), 8.08 (dd, 1 H, H-9, $J_{9,10}$ = 7.5 Hz, $J_{9,11}$ = 1.3 Hz), 8.81 (s, 1 H, OH), 9.03 (d, 1 H, H-1, $J_{1,2}$ = 8.7 Hz), 9.10 (d, 1 H, H_{12}, $J_{11,12}$ = 8.7 Hz).

2-(9-Phenanthryl)-5-methoxybenzaldehyde (11). A mixture of phenanthrene-9-boronic acid (**8**) (3.67 g, 0.0165 mmol), **9** (3.22 g, 0.015 mmol), anhydrous CsF (5.5 g, 0.036 mol), and $Pd(PPh_3)_4$ (0.60 g, 0.0005 mol) in anhydrous DME (75 mL) was heated under reflux for 18 h under argon. The reaction mixture was worked up as described for **10** to produce a semisolid. Trituration of the semisolid with Et_2O−hexane gave 4.67 g (100% yield) of sufficiently pure **11** as a crystalline solid. A small sample of the crystalline solid was recrystallized from CH_2Cl_2/hexane to produce **11** as light yellow granules, mp 118.5−119 °C. ^{1}H NMR (d_6-acetone): δ 4.00 (s, 3 H), 7.39−7.82 (m, 9 H), 8.02 (dd, 1 H, J = 7.8 Hz, J = 1.3 Hz), 8.89 (d, 1 H, J = 7.8 Hz), 8.94 (d, 1 H, J = 7.8), 9.7 (s, 1 H). ^{13}C NMR ($CDCl_3$): δ 191.8 (CHO), 159.4, 137.0, 135.8, 133.7, 132.9, 132.2, 130.9, 130.2, 130.1, 129.4, 128.6, 127.1 (2 C), 127.0, 126.9, 126.8, 122.9, 122.5, 121.4, 109.5, 55.6 (OMe). Anal. Calcd for $C_{22}H_{16}O_2$: C, 84.6; H, 5.1. Found: C, 84.9; H, 5.2.

12-Methoxybenzo[*g*]chrysene (17). Method A. A biphasic reaction mixture consisted of aldehyde **11** (1.5 g, 4.8 mmol) in 70 mL of CH_2Cl_2 and 20 mL of 50% NaOH was added with trimethylsulfonium iodide (2.0 g, 9.8 mmol) and tetrabutylammonium iodide (50 mg). The mixture was stirred vigorously under reflux, and the reaction was monitored by ^{1}H NMR spectroscopy for the presence of an aldehyde peak at ∼9.7 ppm. After 96 h of reflux, no aldehyde peak was present. The product was isolated by extraction as described in the case of **12** to afford 1.6 g (100%) of sufficiently pure 9-(2-(epoxyethyl)-4-methoxyphenyl)phenanthrene (**13**) as a light-yellow syrupy oil. ^{1}H NMR (d_6-acetone): δ 2.62−2.87 (m, 2 H), 3.38−3.44 (m, 1 H), 3.90 (s, 3 H), 6.87−8.95 (m, 12 H).

The cyclization of **13** (0.8 g, 2.45 mmol) was performed in a solution of anhydrous Et_2O (60 mL) by dropwise addition of $BF_3\cdot Et_2O$ (3 mL, 24.4 mmol) at 0 °C under argon. The solution was stirred for an additional 8 h at rt. After completion of the reaction (as monitored by TLC), the excess of $BF_3\cdot Et_2O$ was decomposed by addition of ice-cold water. The product was extracted with ether (2 × 50 mL), and the combined organic extracts were successively washed with 10% Na_2CO_3 (2 × 50 mL) and water (1 × 50 mL). After evaporation of the solvent, the residue was chromatographed over dry column grade silica gel using hexane as eluant to produce 0.38 g (50%) of **17** as a crystalline solid. A small sample of the product was recrystallized from hexane to give colorless needles of **17**, mp 129−130 °C. ^{1}H NMR (d_6-acetone): δ 4.03 (s, 3 H, OCH_3), 7.33 (dd, 1 H, H-13, $J_{11,13}$ = 3.0 Hz, $J_{13,14}$ = 9.2 Hz), 7.54 (d, 1 H, H-11, $J_{11,13}$ = 3.0 Hz), 7.67−7.78 (m, 4 H, H-2, H-3, H-6, H-7), 8.46 (d, 1 H, H-10, $J_{9,10}$ = 9.2 Hz), 8.73 (d, 1 H, H-9, $J_{9,10}$ = 9.2 Hz), 8.76−8.90 (m, 5 H, H-1, H-4, H-5, H-8, H-14); ^{13}C NMR ($CDCl_3$) δ 157.3, 134.9, 130.8, 129.9, 129.8, 129.4, 129.3, 129.2, 127.4, 127.1, 126.7, 126.6, 126.5, 126.4, 125.8, 125.0, 123.3, 123.2, 122.9, 121.1, 117.2, 106.9, 55.2 (OMe). Anal. Calcd for $C_{23}H_{16}O$: C, 89.6; H, 5.2. Found: C, 89.6; H, 5.2.

Method B. The reaction of the Wittig reagent generated from (methoxymethyl)triphenylphosphonium bromide (2.9 g, 8.45 mmol) and a 1.8 M solution of phenyllithium (5 mL, 9.0 mmol) in cyclohexane−ether (7:3) with the aldehyde **11** (0.9 g, 2.88 mmol) as described for **14** gave an oil. The purification

(35) Newman, M. S.; Blum, J. *J. Am. Chem. Soc.* **1964**, *86*, 503.

of the oil by chromatography on dry column grade silica gel with hexane followed by 3% EtOAc−hexane gave 0.80 g (82%) of an oil containing a 1:1 mixture of *cis* and *trans* isomers of 1-[1-{2-(1-naphthyl)-5-methoxyphenyl}]-2-methoxyethene (**15**). Partial ^{1}H NMR (d_6-acetone): for *cis* isomer, two doublets at δ 4.73 and 6.00 (J = 8.2 Hz); for *trans* isomer, two doublets at δ 5.40 and 7.10 (J = 13.0 Hz).

Acid-catalyzed cyclization of the isomeric mixture of **15** (0.56 g) in 20 mL of anhydrous CH_2Cl_2 containing methanesulfonic acid (5 mL) was conducted as described for **16** (method B) to produce a semisolid which was triturated and recrystallized from hexane to give 0.48 g (79%) of **17** as colorless needles, mp 129−130 °C.

12-Hydroxybenzo[*g*]chrysene (6). Demethylation of **17** (0.44 g, 1.4 mmol) in dry CH_2Cl_2 (25 mL) with a 1 M solution of BBr_3 (3.0 mL, 3.0 mmol) in methylene chloride was effected under argon as described for **5**. The isolated product was triturated with hexane to give 0.36 g (86%) of **6** as a crystalline solid, mp 218−220 °C (lit.[20] mp 220−221 °C). ^{1}H NMR (d_6-acetone): δ 5.62 (s, 1 H, OH), 7.32 (dd, 1 H, H-13, $J_{11,13}$ = 2.8 Hz, $J_{13,14}$ = 8.5 Hz), 7.44 (d, 1 H, H-11, $J_{11,13}$ = 2.8 Hz), 7.67−7.82 (m, 4 H, H-2, H-3, H-6, H-7), 7.95 (d, 1 H, H-10, $J_{9,10}$ = 8.5 Hz), 8.70 (d, 1 H, H-9, $J_{9,10}$ = 8.5 Hz), 8.75−8.92 (m, 5 H, H-1, H-4, H-5, H-8, H-14).

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Supporting Information Available: ^{13}C NMR spectra of **10**, **16**, **11**, and **17** (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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