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Synthesis of the *o*-Quinones and Other Oxidized Metabolites of Polycyclic Aromatic Hydrocarbons Implicated in Carcinogenesis

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Efficient new syntheses of the *o*-quinone derivatives of benzo[*a*]pyrene (BPQ), 7,12-dimethylbenz-[*a*]anthracene (DMBAQ), and benz[*a*]anthracene (BAQ), implicated as active carcinogenic metabolites of the parent polycyclic aromatic hydrocarbons (PAHs), are reported. These PAH quinones also serve as starting compounds for the synthesis of the other active metabolites of these PAHs thought to be involved in their mechanism(s) of carcinogenesis. The latter include the corresponding *o*-catechols, *trans*-dihydrodiols, and the corresponding *anti*- and *syn*-diol epoxides.

Introduction

Polycyclic aromatic hydrocarbons (PAHs), some of which are potent carcinogens, are widespread environmental pollutants.[1−4] They are formed in the incomplete combustion of fossil fuels and other organic matter, and significant levels are present in tobacco smoke, in many common foods, and in automobile exhaust emissions.

Prior investigations have shown that PAHs, such as benzo[*a*]pyrene (BP), are activated by CYP1A1 enzymes to *trans*-dihydrodiol metabolites (e.g. BP-7,8-diol) that are further transformed to *anti*- and *syn*-diol epoxides (Scheme 1).[2,5] These metabolites react at deoxyguanosine and deoxyadenosine sites at mutational hotspots in DNA to generate stable adducts[6,7] that lead to induction of tumors. Recent evidence supports a second mechanistic pathway that involves oxidation of the dihydrodiols by aldo-keto reductase enzymes (AKRs) to generate catechols, e.g. BP-catechol.[8] These intermediates enter into redox cycles with the related *o*-quinones, e.g. benzo[*a*]-pyrene-7,8-dione (BPQ), generating reactive oxygen species (ROS) that attack DNA.[9,10] The *o*-quinones also react with DNA to form both stable and depurinating adducts.[11,12] A third mechanism has been proposed that entails activation by CYP peroxidase to form PAH radical cations that combine with DNA to yield unstable adducts that are lost by depurination.[13] The relative importance of these pathways is unknown.

In connection with studies designed to clarify this issue, we required methods for efficient synthesis of the various activated PAH metabolites thought to be involved (*trans*-dihydrodiols, *anti*- and *syn*-diol epoxides, catechols, and *o*-quinones), as well as the adducts formed by reactions of the active species (diol epoxides and quinones) at deoxyguanosine (dG) and deoxyadenosine (dA) sites in DNA. The PAHs chosen for study were the following: benz[*a*]anthracene (BA), benzo[*a*]pyrene (BP), and 7,12-dimethylbenz[*a*]anthracene (DMBA). They represent a range of activity from weak or borderline (BA), to moderately active (BP), to highly potent (DMBA).[14] Athough syntheses of oxidized metabolites of these PAHs have been reported,[2,15−19] the methods entail complex multistep

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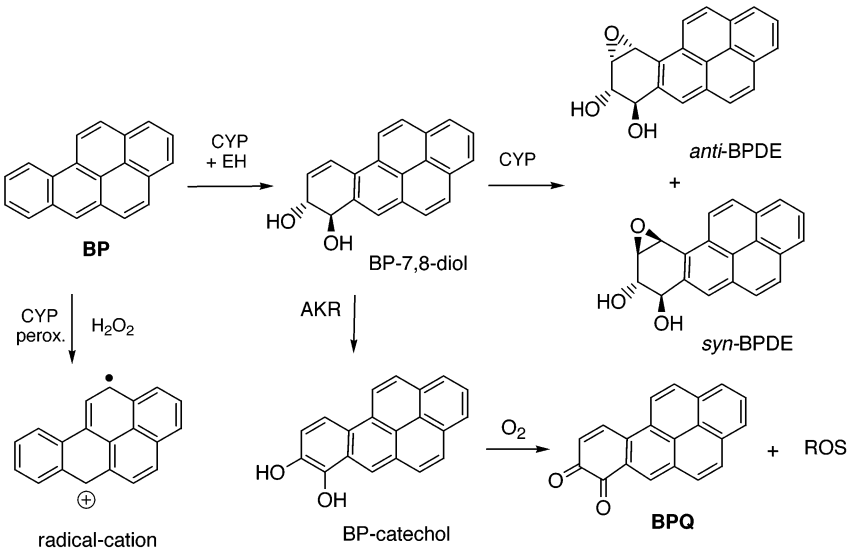

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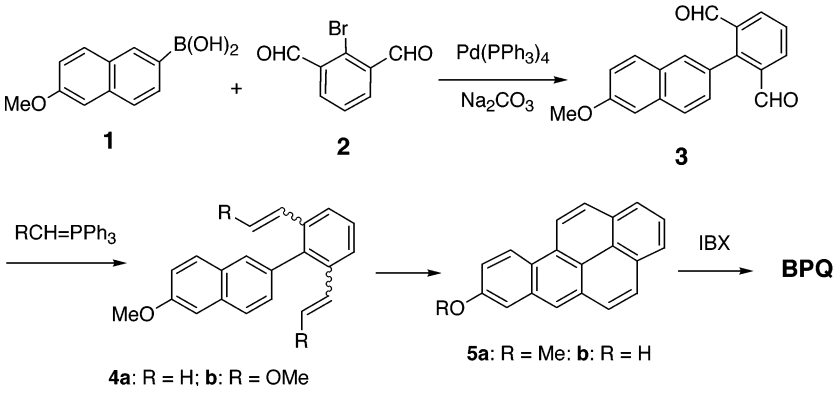
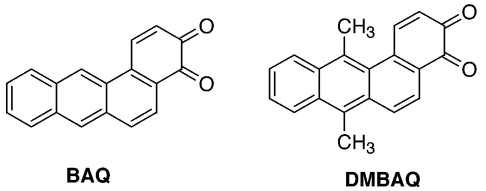


procedures that are mainly suitable for small-scale preparations. Because a longer range objective of these studies was to develop methods for synthesis of the deoxyribonucleoside adducts of the PAH *o*-quinones, we required larger amounts of the quinones than conveniently available by existing methods. Although syntheses of the dG and dA adducts of *anti*- and *syn*-BPDE have been described,[20−27] syntheses of the related adducts of BA and DMBA have not been reported, nor have syntheses of the stable dG and dA adducts of the *o*-quinone metabolites of BP, BA, DMBA, or any other PAH quinone larger than naphthoquinone.[12,28]

We now report efficient new syntheses of the *o*-quinone metabolites of BP, BA, and DMBA. These syntheses are simpler, entail fewer steps, are adaptable to preparative scale synthesis, and afford substantially higher overall yields than older methods.

Results and Discussion

The *o*-quinones of BP, BA, and DMBA (BPQ, BAQ, and DMBAQ) were chosen as the primary synthetic targets. These quinones were needed for biological studies and as potential synthetic precursors of the corresponding *o*-quinone adducts of deoxyguanosine and deoxyadenosine. The PAH *o*-quinones were also expected to serve as starting compounds for the synthesis of other PAH metabolites (*trans*-dihydrodiols, *anti*- and *syn*-diol epoxides, and catechols) known to play a role in carcinogenesis.[2,5−12] The *o*-quinones have the additional practical advantage that they are relatively stable and easily purified.



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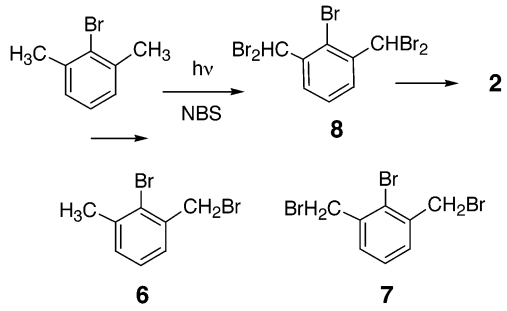
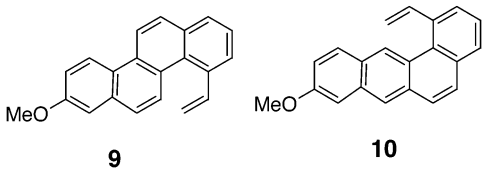


Synthesis of PAH *o*-Quinones. The synthetic route to BPQ (Scheme 2) involves in the key step Suzuki coupling of 6-methoxynaphthaleneboronic acid (**1**) with 2-bromobenzene-1,3-dialdehyde (**2**).[29] The dialdehyde **2** was synthesized from 2-bromoxylene via bromination and hydrolysis (Scheme 3). Initial experiments were conducted in a photochemical apparatus in a reaction vessel equipped with a condenser and a 450-W Hanovia UV lamp in a quartz immersion well with internal cooling. The principal products after 24 h were the mono- and dibromo-substituted derivatives (**6** and **7**). An attempt to increase the reaction rate by heating the solution to reflux had to be aborted, because the reaction became very vigorous and threatened to go out of control. A simpler and less hazardous procedure was to conduct the reaction in an ordinary Pyrex flask irradiated externally by an 85-W UV lamp at reflux temperature. Under this condition, reaction proceeded smoothly to furnish pure 1,3-bis(dibromomethyl)2-bromobenzene (**8**) (91%).[30]

Hydrolysis of **8** by the reported procedure[31] with $NaOAc/CaCO_3$ as the base and tetrabutylammonium bromide as a phase transfer agent afforded **2** in low yield. Addition of toluene to aid solution of **1** failed to improve the yield of **2**. Efficient hydrolysis of **8** was accomplished by the use of aqueous formic acid or $AgNO_3$ in aqueous CH_3CN.[31] Both methods were superior to the literature procedure,[30] requiring shorter reaction times and affording higher yields.

Coupling of **2** with **3** took place smoothly in the presence of $(Ph_3P)_4Pd$ and Na_2CO_3 (Scheme 2) to furnish 2-(2-methoxynaphthalene-6-yl)benzene-1,3-dialdehyde (**3**). Double Wittig reaction of **3** with methylenetriphenylphosphine gave the divinyl compound **4a** (R = H). Oxidative photocyclization of **4a** (R = H) in the presence of iodine and 1,2-epoxybutane[29] with a low wattage (85 W) UV lamp was slow, affording 8-methoxybenzo[*a*]pyrene (**5a**) in low yield, even at reflux temperature. However, the relative slowness of the reaction made it feasible to monitor the reaction by TLC and trap the primary product. This was identified by its ^1H NMR spectrum as the chrysene derivative (**9**) formed by cyclization to the 1-position of the naphthalene ring. The benz[*a*]anthracene structure (**10**) expected to be formed by the alternative mode of cyclization was ruled out by the absence of the characteristic singlet peaks expected for the 7,12-protons of this structure.



9 **10**

Photocyclization of **4a** was considerably faster with a 450-W UV lamp, and reaction was complete in ~1 h. The principal product was shown by TLC and NMR to be **5a** (60%) accompanied by a polymeric byproduct. An inherent limitation of the photochemical method is the need for dilute solutions to minimize polymerization and other secondary reactions.[33] As a consequence, photocyclization is relatively impractical for preparative scale synthesis.

A more practical synthetic route to **5a** was acid-catalyzed cyclization of the bis-methoxyvinyl analogue **4b**. Compound **4b** was synthesized initially by Wittig reaction of **3** with methoxymethyltriphenylphosphonium chloride and PhLi.[34] Although the yield of **4b** (obtained as a mixture of the *E*- and *Z*-isomers) was acceptable (75%), the relative unavailability of PhLi from commercial sources made it necessary to investigate alternative bases. *t*-BuLi was less satisfactory, affording **4b** in only 50% yield. More satisfactory was potassium *tert*-butoxide,[35] which provided **4b** in 95% yield. Acid-catalyzed cyclization of the mixture of isomers of **4b** took place smoothly to furnish **5a** in excellent yield (95%). Synthesis of **5a** via acid-catalyzed reaction of **4b** has several advantages over the photochemical method that include relative safety of operation, no special equipment required, adaptability to preparative scale synthesis, as well as higher yields. Demethylation of **5a** with BBr_3 furnished the free phenol, benzo[*a*]pyren-8-ol (**5b**), in good overall yield. The physical and spectral properties of **5a** and **5b** matched those of authentic samples.

Conversion of PAH *β*-phenols, such as **5b**, to *o*-quinones is usually accomplished by oxidation with Fremy's salt $[(KSO_3)_2NO]$.[2,36,37] However, this reagent requires aqueous conditions that are poorly compatible with the relative insolubilities of PAH compounds in water. Oxidations of PAH *β*-phenols with Fremy's salt are notoriously erratic and difficult to reproduce. For this reason, we investigated the use of *o*-iodoxybenzoic acid (IBX) as a potential alternative reagent. IBX is a mild oxidant that is soluble in organic solvents and is widely employed for oxidation of alcohols.[38] Oxidations with IBX, like those with Fremy's reagent, are thought to proceed principally via a one-electron-transfer mechanism. Oxidation of **5b** with IBX took place smoothly in DMF to furnish BPQ as the major product. Magdziak et al.[39] recently reported oxidation of several monocyclic phenols by IBX and concluded that at least one electron-donating group was

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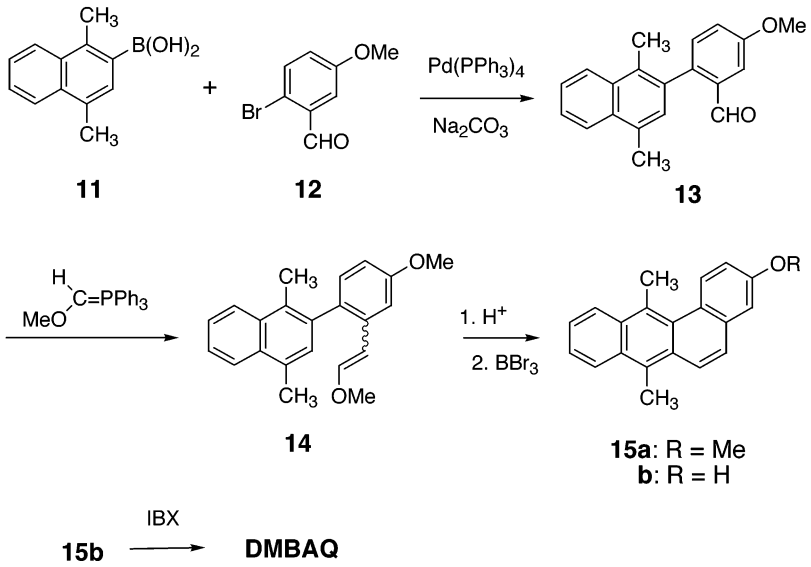
SCHEME 4



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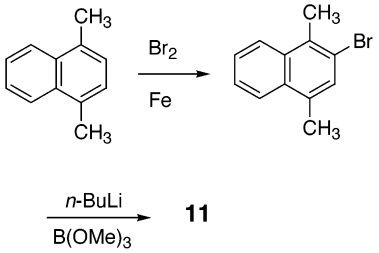

required for oxidation to occur. However, oxidation of **5b** and other polycyclic phenols studied, all of which lack electron-donating groups, with IBX took place readily. Apparently, a polycyclic aromatic ring system is sufficient to facilitate oxidation by this reagent.

Analogous synthesis of DMBAQ (Scheme 4) required 1,4-dimethyl-2-naphthalene boronic acid (**11**) and 2-bromo-5-methoxybenzaldehyde (**12**) as starting compounds. The boronic acid **11** was synthesized (Scheme 5) by Fe-catalyzed bromination of 1,4-dimethylnaphthalene to furnish 2-bromo-1,4-dimethylnaphthalene,[40] followed by consecutive reaction with *n*-BuLi and trimethylborate, and hydrolysis of the resulting dimethylborate ester.[41] The bromoaldehyde **12** was prepared from 3-methoxybenzaldehyde by the published method.[42−44]

Coupling of **11** with **12** took place smoothly in the presence of $(Ph_3P)_4Pd$ to furnish 5-methoxy-2-(1,4-dimethylnaphthalen-2-yl)benzaldehyde (**13**) (Scheme 4). This adduct was converted to the corresponding enol ether **14** by Wittig reaction with methoxymethylenetriphenylphosphine. Enol ether **14** was shown by NMR analysis to be a mixture of *E*- and *Z*-isomers. Acid-catalyzed cyclization of the mixture by treatment with methanesulfonic acid furnished 3-methoxy-7,12-dimethylbenz[*a*]anthracene (**15a**: R = Me). Demethylation with BBr_3 provided the free phenol 7,12-dimethylbenz[*a*]anthracen-3-ol (**15b**: R = H) in good overall yield. The proton and carbon NMR spectra and physical properties of **15b** were in good agreement with the values reported.[19,36]

Conversion of **15b** to DMBAQ was accomplished by oxidation with IBX in DMF by the procedure employed for synthesis of BPQ. Reaction took place smoothly to furnish DMBAQ as a deep purple crystalline solid. It is notable that oxidation of the methyl groups of **15b** did not occur to significant extent under the conditions employed, despite the fact that IBX has been employed as a reagent for oxidation of benzylic methyl groups.[38] The proton NMR spectrum and physical properties of DMBAQ were in good agreement with its structural assignment and with the values reported.[19,36,40,45]

Synthesis of BAQ was not feasible by direct application of the method used for DMBAQ. Specifically, cyclization of the methoxyvinyl intermediate analogous to **14** lacking methyl groups in the naphthalene ring was expected to take place preferentially in the unsubstituted 1-position of the naphthalene ring, resulting in formation of a chrysene derivative, rather than a benz[*a*]anthracene derivative. To favor the desired mode of cyclization, methoxy groups were employed to block the alternative mode of cyclization. Although only a single blocking group was required, it was convenient to employ the 1,4-dimethoxynaphthalene derivative, i.e. 2-bromo-1,4-dimethoxynaphthalene (**16**), as the starting compound.

Synthesis of BAQ was accomplished by Pd-catalyzed coupling of **16** with 2-formyl-4-methoxyboronic acid (**17**) (Scheme 6). Compound **16** was prepared by reductive methylation of 2-bromonaphthalene-1,4-dione with $NaBH_4$ and dimethyl sulfate. 2-Formyl-4-methoxyphenylboronic acid (**17**) was synthesized from 2-bromo-4-methoxybenzaldehyde by the published method.[42] Suzuki coupling of **16** with **17** afforded 5-methoxy-2-(1,4-dimethoxynaphthalen-2-yl)benzaldehyde (**18**). Reaction of **18** with methoxymethylenetriphenylphosphine provided the enol ether **19** (as a mixture of *E*- and *Z*-isomers). Acid-catalyzed cyclization of the mixture with methanesulfonic acid furnished 3,7,12-trimethoxybenz[*a*]anthracene (**20**).

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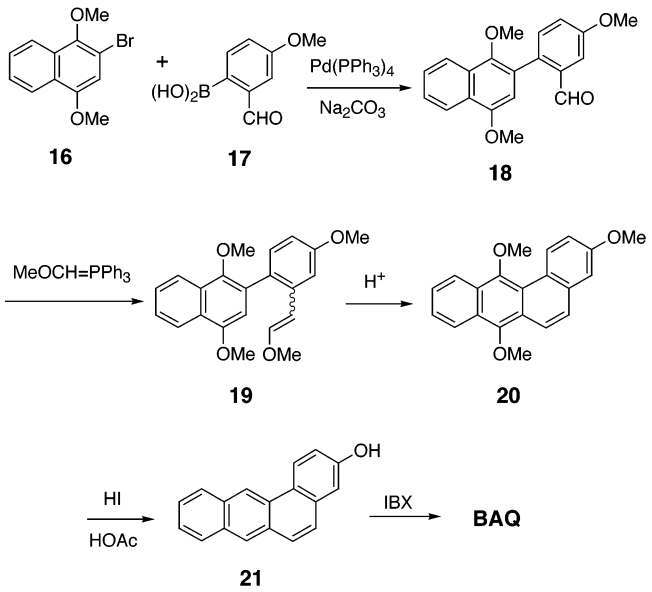
SCHEME 6



Regioselective removal of the 7,12-methoxy groups of **20** without concurrent loss of the 3-methoxy group presented a challenge. It was accomplished by reduction of **20** with HI in acetic acid.[46] The remarkable regioselectivity of this reduction is likely due to the greater reactivity of the meso region sites of benz[*a*]anthracene in most reactions.[46] Although reductive cleavage of the 3-methoxy group did not occur, demethylation of **20** took place to yield the phenol 3-hydroxybenz[*a*]anthracene (**21**) as the principal product. Oxidation of **21** with IBX in DMF gave BAQ in good overall yield. The spectral and physical properties of **21** and BAQ were in good agreement with the values reported.[2]

Synthesis of the *o*-Catechols and Other Oxidized PAH Metabolites. The *o*-catechol derivatives of BP, BA, and DMBA were synthesized by reduction of the corresponding *o*-quinones with $NaBH_4$ in DMA by the reported procedure.[47] Reduction of BPQ provided 7,8-dihydroxybenzo[*a*]pyrene (BP-catechol) isolated as its dibenzoate or diacetate ester (**22**) (Scheme 7). BP-catechol, like most other PAH catechols, undergoes facile autoxidation on exposure to air to regenerate the quinone along with other minor oxidized products. Formation of BPQ was readily detectable by its intense purple color. In contrast to the catechols, the diester derivatives of the catechols are relatively stable solids that may be readily purified and characterized. They may be reconverted to the corresponding catechols, as needed for experimental studies. The facility of autoxidation of BP-catechol is consistent with its observed rapid conversion to BPQ in vivo.[8−12] Reduction of DMBAQ and BAQ with $NaBH_4$ in DMF (Scheme 7) gave the corresponding *o*-catechols, 3,4-dihydroxy-7,12-dimethylbenz[*a*]anthracene (**23a**) and 3,4-dihydroxybenz[*a*]anthracene (**24a**), respectively, isolated as their more stable diacetate derivatives, **23b** and **24b**.

Reduction of PAH *o*-quinones with $NaBH_4$ in the presence of O_2 was previously shown[36] to provide the corresponding *trans*-dihydrodiols. Reduction of BPQ with

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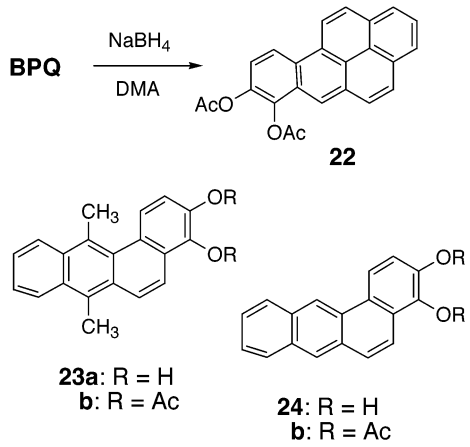

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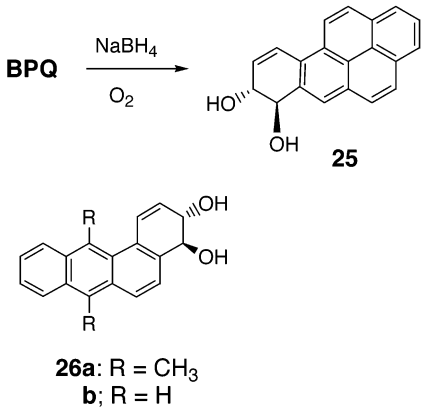

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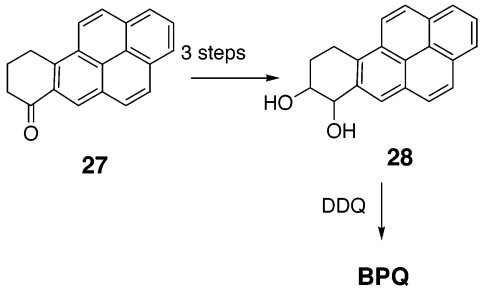

$NaBH_4/O_2$ afforded smoothly *trans*-7,8-dihydro-7,8-dihydroxybenzo[*a*]pyrene (**25**) (Scheme 8). Analogous reduction of DMBAQ and BAQ furnished *trans*-3,4-dihydroxy-3,4-dihydro-7,12-dimethylbenz[*a*]anthracene (**26a**) and *trans*-3,4-dihydroxy-3,4-dihydrobenz[*a*]anthracene (**26b**), respectively.

Comparison of Methods of Synthesis of PAH Quinones. The classic synthesis of BPQ[4,48] entails a seven-step sequence from pyrene based on the Haworth method for fusing additional rings onto polycyclic aromatic ring systems (Scheme 9).[2,4] Specifically, it involves Friedel−Crafts reaction of pyrene with succinic anhydride and $AlCl_3$, reduction of the keto group of the keto-acid product (obtained as a mixture of isomers), acid-catalyzed cyclization to form 7-keto-7,8,9,10-tetrahydrobenzo[*a*]pyrene (**27**),[49] reduction to the alcohol with

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$NaBH_4$, acid-catalyzed dehydration to 9,10-dihydrobenzo-[*a*]pyrene, reaction with OsO_4 to form the *cis*-7,8-tetrahydrodiol (**28**), and finally oxidation with DDQ.[50,51]

The new synthetic approach to BPQ (Scheme 2) involves fewer steps, requires no tedious separations of isomers or product mixtures, and affords a higher overall yield than the older method. It involves in the key initial step Suzuki coupling of 6-methoxynaphthaleneboronic acid (**1**) with 2-bromobenzene-1,3-dialdehyde (**2**). The 1,3-dialdehyde product (**3**) was readily transformed to the 1,3-dimethoxyvinyl derivative (**4a**: R = OMe) by the Wittig method. Although **4a** was obtained as a mixture of *E*- and *Z*-isomers, their separation was unnecessary because of their facile interconversion in the subsequent acid-catalyzed cyclization step to yield **5a**.

A noteworthy feature of this synthesis is the use of the hypervalent iodine(V) reagent IBX for oxidation of the PAH β-phenols to PAH *o*-quinones. Oxidation of **5b** by IBX took place readily in DMF to provide BPQ in good overall yield. The principal advantage of IBX over Fremy's salt is that it allows oxidation of the relatively water insoluble PAH compounds to be conducted in organic solvents. On the basis of the relatively few examples studied to date, it also appears that IBX is a milder, more reliable oxidant than Fremy's salt, and its use does not result in excessive oxidation of the PAH substrates.

Extension of this synthetic approach to BAQ and DMBAQ provided improved synthetic access to these quinones, making them more accessible for biological studies and as starting compounds for the synthesis of their related oxidized metabolites and their adducts with deoxyadenosine and deoxyguanosine. This synthetic method is applicable, in principle, to the synthesis of numerous other PAH quinones and their related oxidized metabolites. The potential scope of the method is further illustrated by its recent utilization as the basis of an improved synthesis of benzo[*a*]pyrene.[52]

Experimental Section

Materials and Methods. *o*-Iodoxybenzoic acid (IBX) was prepared by the improved procedure of Frigerio et al.[53] with oxone in place of bromate for the oxidation of 2-iodobenzoic acid. 6-Methoxynaphthaleneboronic acid (**1**) obtained from a commercial source was shown by TLC to contain an impurity that could be removed by trituration with CH_2Cl_2. Removal of the contaminant after reaction of **1** was considerably more difficult. 2-Bromo-5-methoxybenzaldehyde (**12**) was prepared from 3-methoxybenzaldehyde by the published method.[42−44] 2-Formyl-4-methoxyphenylboronic acid (**17**) was prepared from 2-bromo-4-methoxybenzaldehyde by the literature procedure.[42] Methoxymethyltriphenylphosphonium chloride was dried under vacuum for 24 h prior to use. THF was freshly distilled from sodium benzophenone ketal.

NMR spectra were recorded on a 400- or 500-MHz spectrometer in $CDCl_3$ with tetramethylsilane as internal standard unless stated otherwise. Integration was consistent with all structural assignments. All melting points are uncorrected. **Caution**: The *o*-quinone, *o*-catechol, dihydrodiol, and diol epoxide derivatives of benzo[*a*]pyrene, benz[*a*]anthracene, and 7,12-dimethyl benz[*a*]anthracene are potentially hazardous and should be handled with care in accordance with "NIH Guidelines for the Laboratory Use of Chemical Carcinogens".

1,3-Bis(dibromomethyl)-2-bromobenzene (8). A solution of 2-bromo-*m*-xylene (13.3 mL, 100 mmol), NBS (142.4 g, 800 mmol), and AIBN (100 mg) in benzene (1 L) under argon in a 250-mL round-bottom flask was heated at reflux and irradiated with an external 85-W UV lamp. After 24 h, TLC showed a mixture of the symmetrical di- and tetrabromo-substituted derivatives, **7** (40%) and **8** (60%). After 48 h, TLC showed the product composition to be **7** (20%) and **8** (80%). Additional portions of NBS (71.2 g, 400 mmol) and AIBN (50 mg) were added, and reaction was continued for another 24 h. At that time, TLC showed the reaction to be essentially complete. The reaction mixture was allowed to stand overnight and the precipitate of succinimide and unreacted NBS was removed by filtration and washed with benzene (3 × 100 mL) and 10% aqueous sodium hydrogensulfite (500 mL). The organic layer was separated, dried over $NaSO_4$, and evaporated to dryness. The residue was chromatographed on a silica gel column eluted with 5% EtOAc to give crude **8**, which was triturated with hexane (2 × 50 mL) to remove trace amounts of **7**. Pure **8** (45.6 g, 91%) was obtained as white platelets: mp 150−151 °C (lit.[28] mp 148−149 °C); ^{1}H NMR δ 8.03 (d, 2, J = 7.9 Hz), 7.52 (t, 1, J = 8.0 Hz), 7.12 (s, 2), in good agreement with reported values.[30]

2-Bromobenzene-1,3-dialdehyde (2). Method 1: Hydrolysis with $AgNO_3$. To a solution of **8** (1.00 g, 2 mmol) in acetonitrile (25 mL) was added a solution of $AgNO_3$ (1.70 g, 10 mmol) and 10 mL of water, and the mixture was heated at reflux under argon for 2 h. The solution was allowed to cool, AgBr was filtered off and washed with CH_2Cl_2 (3 × 20 mL), and the combined filtrate was washed with water (25 mL) and dried over $NaSO_4$. The solvent was evaporated and the residue was purified by passage through a short column of silica gel to yield **2** (396 mg, 93%) as a white solid: mp 135−136 °C (lit.[32] mp 132−134 °C); ^{1}H NMR δ 10.45 (s, 2), 8.13 (d, 2, J = 7.5 Hz), 7.58 (t, 1, J = 7.5 Hz) in agreement with reported values.[32]

Method 2: Hydrolysis in Formic Acid. A mixture of **8** (1.01 g, 2 mmol) and 88% formic acid (20 mL) was refluxed under argon for 12 h. After cooling, the solution was concentrated under reduced pressure, poured into water (40 mL), and extracted with CH_2Cl_2 (3 × 20 mL). The combined extracts were dried and evaporated to dryness, and the residue was purified by chromatography on a column of silica gel to yield **2** (405 mg, 94%): mp 135−136 °C; ^{1}H NMR spectrum was identical with an authentic sample.

2-(2-Methoxynaphthalene-6-yl)benzene-1,3-dialdehyde (3). To a solution of **2** (18.5 g, 87 mmol) in DME (270 mL) under argon was added $Pd(PPh_3)_4$ (2.8 g. 2.4 mmol). The resulting yellow solution was stirred for 20 min, then a solution of **1** (18.9 g, 94 mmol) in ethanol (330 mL) was added. The clear solution became cloudy. After 20 min, $NaCO_3$ (210 mL of a 2 M solution) was added, and the mixture was heated at reflux overnight. Then the solution was cooled and concentrated under reduced pressure. CH_2Cl_2 (500 mL) was added, and the organic phase was washed with water and brine, then dried over $NaSO_4$. The solvent was removed under reduced pressure, and the residue was purified by chromatography on a silica gel column. Elution with 10−20% EtOAc in hexane provided **3** (23.1 g, 91%) as a white solid: mp 142−144 °C; ^{1}H NMR δ 9.82 (s, 2), 8.23 (dd, 2, J = 8.0, 0.5 Hz), 7.85 (d, 1, J = 8.5 Hz), 7.75 (d, 1, J = 9.0 Hz), 7.74 (s, 1), 7.63 (dd, 1, J = 7.5, 2.5 Hz), 7.41 (dd, 1, J = 8.5, 1.0 Hz), 7.23 (m, 2), 3.94 (s, 3); ^{13}C NMR δ 191.0, 158.6, 148.2, 134.9, 134.3, 132.6, 132.5, 130.3, 129.5, 129.4, 128.5, 128.2, 128.1, 128.0, 127.2, 127.0, 126.3, 120.3, 105.6, 55.3. Anal. Calcd for $C_{19}H_{14}O_3$: C, 78.61; H, 4.86. Found: C, 78.45; H, 4.89.

2-Methoxy-6-(2,6-divinylphenyl)naphthalene (4a). To a solution of methyltriphenylphosphonium bromide (34.0 g,

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(51) Compound **5** may also be prepared by oxidation of benzo[*a*]-pyrene-8-ol with Fremy's salt or phenylselenenic anhydride, ref 36.
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95 mmol) in 300 mL of dry THF was added dropwise 38.0 mL of a 2.5 M solution of *n*-butyllithium in hexane at 0 °C under argon. The solution became yellow then orange. It was stirred for 30 min, then a solution of **3** (9,2 g, 32 mmol) in dry CH_2Cl_2 (80 mL) was added dropwise, and stirring was continued overnight at room temperature. Water (2 mL) was added to quench the reaction, and after 30 min the solution was filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column eluted with 3−5% EtOAc in hexane to yield **4a** (8.2 g, 90%) as a white solid: mp 88−89 °C; ^{1}H NMR δ 7.70 (d, 1, J = 8.5 Hz), 7.65 (d, 1, J = 8.5 Hz), 7.52 (d, 2, J = 8.0 Hz), 7.47 (d, 1, J = 1.0 Hz), 7.28 (t, 1, J = 8.0 Hz), 7.18 (dd, 1, J = 8.5, 1.5 Hz), 7.11 (m, 2), 6.34 (dd, 2, J = 17.5, 11.0 Hz), 5.55 (dd, 2, J = 17.5, 1.5 Hz), 4.97 (dd, 2, J = 11.0, 1.0 Hz), 3.87 (s, 3); ^{13}C NMR 157.89, 139.55, 136.94, 135.88, 134.02, 133.55, 129.55, 129.21, 129.14, 128.59, 127.58, 126.49, 125.79, 124.72, 124.51, 124.26, 124.51, 119.18, 114.97, 114.54, 105.65, 55.36. Anal. Calcd for $C_{21}H_{18}O$: C, 88.08; H, 6.34. Found: C, 87.78; H, 6.35.

8-Methoxybenzo[*a*]pyrene (5a). Method 1: Photocyclization with an 85-W UV Lamp. Argon was bubbled through a solution of **4a** (300 mg, 1.06 mmol) and I_2 (620 mg, 2.5 mmol) in 500 mL of benzene for 15 min. Epoxybutane (20 mL) was added, and the solution was irradiated by an external 85-W UV lamp. TLC indicated that no reaction took place over a 3-h period. The irradiated solution was then heated at reflux. After 1 day the product mixture was shown by TLC to consist of equal amounts of unreacted **4a**, a partially cyclized intermediate, and **5a**. After 2 additional days under these conditions, TLC showed the principal products to be **5a** plus polymeric byproducts. The usual workup afforded the crude product, which was purified by chromatography on a short column of silica gel. Elution with 7−10% EtOAc in hexane gave **5a** (149 mg, 50%) as a yellow solid whose ^{1}H NMR spectrum was identical with that of authentic **5a**.

Method 2: Photocyclization with a 450-W UV Lamp. The reaction was conducted in a quartz photoreactor with a 450-W Hanovia UV lamp in an inner well and external water cooling. Argon was bubbled through a solution of **4a** (260 mg, 0.91 mmol) and I_2 (462 mg, 1.8 mmol) in 500 mL of benzene for 15 min. 1,2-Epoxybutane (20 mL) was added, and the mixture was irradiated. After 30 min, TLC showed that **4a** was largely consumed, and the products were the partially cyclized intermediate **9** and **5a**. After another 30 min, the products were mainly **5a** and polymeric byproducts. The usual workup followed by chromatography on a short column of silica gel eluted with 7−10% ethyl acetate in hexane gave **5a** (149 mg, 60%) as a yellow solid whose ^{1}H NMR spectrum matched that of authentic **5a**.

The partially cyclized intermediate was identified as the chrysene derivative **9**: mp 136−137 °C; ^{1}H NMR δ 8.94 (d, 1, J = 9.0 Hz), 8.67 (d, 1, J = 9.0 Hz), 8.62 (d, 1, J = 9.0 Hz), 7.95 (d, 1, J = 9.0 Hz), 7.90 (d, 1, J = 7.5 Hz), 7.82 (d, 1, J = 9.0 Hz), 7.69 (d, 1, J = 7.0 Hz), 7.56−7.61 (m, 2), 7.34 (dd, 1, J = 9.0, 3.0 Hz), 7.31 (d, 1, J = 2.5 Hz), 5.87 (dd, 1, J = 17.5, 1.5 Hz), 5.50 (dd, 1, J = 11.0, 1.5 Hz), 3.99 (s, 3); ^{13}C NMR δ 158.1, 141.7, 137.3, 133.0, 132.5, 129.7, 129.2, 128.6, 128.3, 127.8, 127.4, 127.1, 125.6, 124.9, 124.8, 124.7, 121.3, 117.8, 114.1, 107.1, 53.4. Anal. Calcd for $C_{21}H_{16}O$: C, 88.70; H, 5.67. Found: C, 88.94; H, 5.62.

2-(2,6-Bis{2-methoxyvinyl}phenyl)-6-methoxynaphthalene (4b). Method 1: Phenyllithium. To a solution of dry methoxymethyltriphenylphosphonium chloride (10.0 g, 31 mmol) in anhydrous ether (300 mL) under argon at −78 °C was added dropwise a 1.8 M solution of phenyllithium (16.7 mL, 31 mmol) in ether. The mixture was stirred at −78 °C for 0.5 h, allowed to warm to −15 °C for 0.5 h, and then cooled back to −78 °C. The dialdehyde **3** (1.4 g, 4.8 mmol) was added and stirring was continued for an additional hour. The solution was allowed to warm to ambient temperature, and stirring was continued overnight. Then the solvent was removed under vacuum, and the crude product was purified by chromatography on a silica gel column. Elution with 8−10% ethyl acetate in hexane afforded **4b** as a mixture of *E*- and *Z*-isomers as an oil (75%): ^{1}H NMR δ 7.91 (m, 1), 7.70 (m, 2), 7.50 (m, 1), 7.09−7.21 (m, 5), 6.78 (dd, 1, J = 8.0, 7.5 Hz), 5.83 (dd, 1, J = 7.5, 7.5 Hz), 5.37 (t, 1, J = 12.5 Hz), 4.76 (dd, 1, J = 7.5, 8.0 Hz), 3.87 (s, 3), 3.62 (d, 3), 3.27 (d, 3). Anal. Calcd for $C_{23}H_{22}O_3$: C, 79.74; H, 6.40. Found: C, 79.65; H, 6.55.

Method 2: *tert*-Butyllithium. Similar reaction with *t*-BuLi gave **4b** (50%).

Method 3: *t*-BuOK. To a solution of predried methoxymethyltriphenylphosphonium chloride (23.12 g, 69.1 mmol) in 200 mL of dry ether under argon was added dropwise a 1.0 M solution of *t*-BuOK (69.1 mL, 69.1 mmol) in dry THF at room temperature. The resulting red solution was stirred at room temperature for 1 h, then a solution of **3** (8.0 g, 27.6 mmol) in 100 mL of THF was added dropwise. After being stirred overnight, the solution was evaporated to dryness under vacuum, and the crude product was purified by chromatography on a silica gel column. Elution with 5−15% EtOAc in hexane to gave a mixture of *E*- and *Z*-isomers of **4b** (9.1 g, 95%) as an oil.

8-Methoxybenzo[*a*]pyrene (5a). To a solution of **4b** (9.1 g) in CH_2Cl_2 (500 mL) was added $MeSO_3H$ (0.1 mL) under argon at 0 °C, and the solution was stirred overnight. TLC showed the reaction to be complete. A saturated solution of $NaHCO_3$ (100 mL) was added, and stirring was continued for 15 min. The organic phase was separated, washed with water and brine, dried over $NaSO_4$, and evaporated to dryness. The residue was purified by chromatography on a column of silica gel eluted with 7−10% EtOAc in hexane to provide **5a** (6.2 g, 88%) as a yellow solid: mp 145−147 dec; ^{1}H NMR δ 8.88 (t, 2, J = 10.0 Hz), 8.35 (s, 1), 8.25 (d, 1, J = 9.0 Hz), 8.19 (d, 1, J = 7.5 Hz), 8.06 (d, 1, J = 7.0 Hz), 7.88−7.95 (m, 3), 7.55 (d, 1, J = 2.5 Hz), 7.45 (dd, 1, J = 9.0, 2.5 Hz), 4.03 (s, 3); ^{13}C NMR δ 157.7, 132.6, 131.1, 130.8, 130.2, 127.8, 127.7, 127.5, 125.5, 125.4, 125.3, 124.8, 124.6, 123.6, 123.4, 122.4, 121.9, 118.6, 106.4, 55.4.

Benzo[*a*]pyren-8-ol (5b). To a solution of **5a** (2.1 g, 7.45 mmol) in dry CH_2Cl_2 (500 mL) at −20 °C was added dropwise a solution of BBr_3 (1 M, 40 mL) in CH_2Cl_2. The resulting purple solution was stirred at −20 °C for 30 min and then at room temperature overnight. The reaction mixture was then immersed in a dry ice, ice was added, and the organic solvent was removed at room temperature under reduced pressure. The aqueous suspension was extracted with EtOAc, and the combined extracts were washed with brine, dried over $NaSO_4$, and evaporated to dryness. The residue was chromatographed on a silica gel column eluted with 10−25% EtOAc in hexane to give **5b** (1.7 g, 86.0%) as a yellow solid: mp 224−226 °C dec (lit.[54] mp 228 °C); ^{1}H NMR δ 8.93 (d, 1, J = 9.0 Hz), 8.90 (d, 1, J = 9.0 Hz), 8.29 (s, 1), 8.22 (d, 1, J = 9.0 Hz), 8.16 (d, 1, J = 7.5 Hz), 8.02 (d, 1, J = 7.0 Hz), 7.90 (d, 1, J = 1.5 Hz), 7.89 (s, 1), 7.85 (m, 1), 7.51 (d, 1, J = 2.5 Hz), 7.39 (dd, 1, J = 9.0, 2.5 Hz); the observed chemical shifts were in good agreement with reported values;[53] ^{13}C NMR δ 155.4, 133.2, 131.1, 130.7, 130.0, 127.5, 127.3, 127.2, 125.1, 125.0, 124.3, 122.9, 122.7, 121.8, 121.5, 118.0, 109.3.

Benzo[*a*]pyren-7,8-dione (BPQ). To a solution of **5b** (1.7 g, 6.3 mmol) in dry DMF (50 mL) at room temperature was added IBX[53] (1.8 g, 6.4 mmol) under argon. The resulting purple solution was stirred for 1 h, 500 mL of EtOAc was added, and the organic layer was washed with water (3 × 100 mL) and with brine. A purple precipitate in the organic phase was removed by filtration and subsequently shown to be pure BPQ. The filtrate was evaporated to dryness under reduced pressure and the residue was purified by chromatography on a silica gel column. Elution with EtOAc:hexane (1:2) gave BPQ (combined wt = 1.65 g, 92.2%) as a purple solid: mp 271−273 °C (lit.[36] mp >260 °C); ^{1}H NMR δ 8.86 (s, 1), 8.50 (d, 1, J =

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10.5 Hz), 8.38 (d, 1, J = 10.5 Hz, 9.5 Hz), 8.10−8.27 (m, 6), 6.60 (d, 1, J = 10.5 Hz); the observed chemical shifts were in agreement with reported values except that a peak at δ 7.62 was not observed.[36]

2-Bromo-1,4-dimethylnaphalene. To a solution of 1,4-dimethylnaphthalene (4.68 g, 30.0 mmol) in CH_2Cl_2 (50 mL) in an ice−water bath in subdued light was added iron powder (200 mg, 3.6 mmol). To this suspension was added a solution of bromine (4.77 g, 30.0 mmol) in CH_2Cl_2 (25 mL) dropwise over 30 min. The resulting mixture was stirred for 2 h at 0 °C, then poured into a saturated $NaCO_3$ solution, extracted with CH_2Cl_2, and dried over $NaSO_4$. Evaporation of the solvent under reduced pressure afforded **7** (6.80 g, 96.5%) as a slightly yellow semisolid that solidified on standing: mp 40−41 °C (lit.[40] mp 40−42 °C); ^{1}H NMR δ 7.97−8.08 (m, 2), 7.55−7.57 (m, 2), 7.50 (s, 1), 2.79 (s, 3), 2.66 (s, 3).

1,4-Dimethyl-2-naphthalene Boronic Acid (11). Procedure A: To a solution of 2-bromo-1,4-dimethylnaphthalene (2.35 g, 10 mmol) in anhydrous THF (20 mL) under argon at −78 °C was added *n*-BuLi (1.6 M in hexane, 6.40 mL, 10.2 mmol) dropwise over 10 min. The resulting solution was stirred at −78 °C for 1 h, then a solution of trimethyl borate (2.10 g, 20 mmol) in THF (20 mL) was added over 10 min. The solution was stirred at −78 °C for 3 h, then warmed to room temperature, and a solution of 10 M HCl was added. The solution was extracted with ether, dried over $NaSO_4$, and evaporated to dryness to give crude **11**, which was washed with CH_2Cl_2 to give **11** (0.94 g, 47.2%) as a white powder.

Procedure B: To a solution of *n*-BuLi (1.6 M in hexane, 12.8 mL, 20.5 mmol) in anhydrous THF (20 mL) under argon at −78 °C was added dropwise a solution of 2-bromo-1,4-dimethylnaphthalene (2.35 g, 10 mmol) in THF (40 mL) over 2 h. The mixture was stirred at −78 °C for 30 min, then a solution of trimethyl borate (2.10 g, 20.0 mmol) in THF (20 mL) was added over 10 min. The resulting solution was stirred at −78 °C for 3 h and warmed to room temperature, and a solution of 10 M HCl solution was added. The solution was extracted with ether, dried over $NaSO_4$, and evaporated to dryness to give **11** (1.80 g, 90.0%) as a white powder: mp 198−199 °C (lit.[55] mp 310−312 °C); ^{1}H NMR δ 8.08 (dd, 1, J = 3.2, 4.75 Hz), 8.00 (dd, 1, J = 3.1, 4.75 Hz), 7.56 (dd, 2, J = 3.1, 8.0 Hz), 7.35 (s, 1), 2.74 (s, 3), 2.62 (s, 3).

5-Methoxy-2-(1,4-dimethylnaphthalen-2-yl)benzaldehyde (13). To a solution of **11** (1.99 g, 10 mmol) and **12** (2.16 g, 10 mmol) in DME (20 mL) under argon was added $Pd(PPh_3)_4$ (300 mg, 0.2 mmol). The resulting mixture was stirred for 5 min, then ethanol (10 mL) and a 2.0 M sodium carbonate solution (10 mL) were added, and the mixture was heated at reflux overnight. Most of the solvent was removed by evaporation under reduced pressure, and the solution was extracted with EtOAc, dried over $NaSO_4$, evaporated to dryness, and purified by silica gel chromatography. Elution with EtOAc−hexanes (1:30) gave **13** (2.63 g, 91%): mp 103−104 °C (lit.[55] mp 104−105 °C); ^{1}H NMR δ 9.73 (s, 1), 8.06−8.11 (m, 2), 7.58−7.62 (m, 2), 7.54 (d, 2, J = 2.66 Hz), 7.22−7.30 (m, 2), 7.18 (s, 1), 3.94 (s, 3), 2.69 (s, 3), 2.43 (s, 3); ^{13} H NMR δ 192.3, 159.1, 139.5, 134.9, 133.8, 132.7, 132.4, 132.3, 131.9, 130.7, 129.3, 126.3, 125.8, 124.9, 124.7, 121.4, 109.2, 55.6, 19.2, 16.2.

2-(4-Methoxy-2-[2-methoxyvinyl]phenyl)-1,4-dimethylnaphthalene (14). Reaction of methoxymethyltriphenylphosphonium chloride (1.88 g, 5.50 mmol) and phenyllithium (3.1 mL of a 1.8 M solution in hexanes, 5.50 mmol) with **13** (800 mg, 2.75 mmol) was carried out by the procedure employed for the synthesis of **4b**. The crude product was purified by chromatography on a silica gel column. Elution with EtOAc−hexanes (1:50) gave **14** (0.78 g, 88.9%) as an oil that solidified on standing: mp 102−104 °C; ^{1}H NMR (E/Z = 1) δ 8.09 (dd, 2, J = 1.0, 7.5 Hz), 8.03 (dd, 2, J = 1.0, 7.5 Hz), 7.81 (d, 1, J = 3.0 Hz), 7.53−7.57 (m, 4), 7.13 (s, 2), 7.09 (d, 1, J = 3.5 Hz), 7.07 (d, 1, J = 3.5 Hz), 6.98 (d, 1, J = 3.0 Hz), 6.94 (d, 1, J = 13.0 Hz), 6.80 (dd, 1, J = 1.5, 2.0 Hz), 6.78 (dd, 1, J = 1.5, 1.5 Hz), 5.94 (d, 1, J = 7.5 Hz), 5.46 (d, 1, J = 13.0 Hz), 4.85 (d, 1, J = 7.5 Hz), 3.88 (s, 3), 3.87 (s, 3), 3.74 (s, 3), 3.39 (s, 3), 2.67 (s, 3), 2.38 (s, 3); the ^{1}H NMR spectral data agreed with the data previously reported.[55]

7,12-Dimethyl-3-methoxybenz[*a*]anthracene (15a). To a solution of **14** (0.64 g, 2.0 mmol) in CH_2Cl_2 (50 mL) was added $MeSO_3H$ (0.48 g, 5.0 mmol) dropwise over 5 min. TLC showed that reaction was complete within 10 min. The reaction mixture was poured into a saturated solution of $NaHCO_3$ (50 mL), extracted with CH_2Cl_2, dried over $NaSO_4$, and purified by passage through a Florisil column. Elution with hexanes−CH_2Cl_2 (8:1) gave **15a** (0.52 g, 91%): mp 131−132 °C (lit.[19] mp 131−132 °C): ^{1}H NMR δ 8.43 (d, 1, J = 9.0 Hz), 8.34−8.37 (m, 2), 8.06 (d, 1, J = 10.0 Hz), 7.59−7.66 (m, 2), 7.54 (d, 1, J = 10.0 Hz), 7.27 (d, 1, J = 3.5 Hz), 7.19 (dd, 1, J = 3.0, 9.0 Hz), 4.00 (s, 3), 3.34 (s, 3), 3.10 (s, 3).

7,12-Dimethylbenz[*a*]anthracene-3,4-dione (DMBAQ). To a solution of **15a** (140 mg, 0.5 mmol) in CH_2Cl_2 (20 mL) under argon was added by syringe a solution of BBr_3 (1.0 M in CH_2Cl_2, 5 mL, 5 mmol). The resulting mixture was stirred overnight at room temperature, quenched with water, extracted with CH_2Cl_2, washed with a $NaCO_3$ solution and water, dried over $NaSO_4$, and evaporated to dryness to yield 7,12-dimethylbenz[*a*]anthracen-3-ol (**15b**) as an oily solid used directly in the next step.

To a solution of **15b** in DMF (2 mL) was added IBX (130 mg, 0.5 mmol), and the resulting solution turned dark within 10 min. TLC indicated that reaction was complete. The mixture was poured onto ice water (50 mL) and filtered. The solid product was purified by chromatography on a Florisil column. Elution with EtOAc−hexanes (1:8) gave DMBAQ as a deep green solid (0.10 g, 71%): mp 156−157 °C (lit.[19] mp 157−158 °C); ^{1}H NMR (DMSO) δ 8.49 (d, 1, J = 9.0 Hz), 8.36−8.42 (m, 2), 8.29 (d, 1, J = 10.5 Hz), 7.90 (d, 1, J = 9.0 Hz), 7.70 (dd, 2, J = 6.0, 7.0 Hz), 6.41 (d, 1, J = 10.5 Hz), 3.19 (s, 3), 3.07 (s, 3).

1,4-Dimethoxynaphthalene. To a solution of 1,4-naphthoquinone (15.8 g, 100 mmol) in ethanol (100 mL) and water (100 mL) was added $NaBH_4$ (6.8 g, 200 mmol) in portions over 30 min. The resulting mixture was stirred for another 30 min, then a solution of KOH (10 M, 40 mL) was added and the resulting mixture was stirred for 30 min, then heated to reflux, and dimethyl sulfate (50.4 g, 400 mmol) was added over 1 h. The resulting mixture was stirred at reflux overnight, then it was cooled to room temperature, extracted with EtOAc, and purified by chromatography on a silica gel column to give 1,4-dimethoxynaphthalene (17.8 g, 95%): mp 85−86 °C (lit.[56] mp 86−87 °C); ^{1}H NMR δ 8.20 (dd, 2, J = 3.3, 6.5 Hz), 7.50 (dd, 2, J = 3.3, 6.5 Hz), 6.69 (s, 2), 3.96 (s, 6).

2-Bromo-1,4-dimethoxynaphthalene (16). To a solution of 1,4-dimethoxynaphthalene (17.8 g, 95 mmol) dissolved in CCl_4 (100 mL) in an ice bath at 0 °C was added a catalytic amount of iron powder, followed by bromine (15.0 g, 95 mmol), over 30 min. The resulting mixture was stirred for 3 h, then the mixture was poured into a saturated $NaCO_3$ solution, extracted with CH_2Cl_2, and chromatographed on a silica gel column. Elution with hexanes−EtOAc (20:1) gave **16** (22.4 g, 88%): mp 58−59 °C (lit.[56] mp 56−58 °C); ^{1}H NMR δ 8.20 (d, 1, J = 0.5, 8.5 Hz), 8.05 (dd, 1, J = 0.5, 8.5 Hz), 7.47−7.57 (m, 2), 6.87 (s, 1), 3.98 (s, 3), 3.95 (s, 3).

5-Methoxy-2-(1,4-dimethoxynaphthalen-2-yl)benzaldehyde (18). To a solution of **16** (13.5 g, 50 mmol) in DME (100 mL) were added 2-formyl-4-methoxyphenyl boronic acid **17** (9.0 g, 50 mmol) and $Pd(PPh_3)_4$ (1.0 g), and the resulting mixture was stirred for 10 min. EtOH (100 mL) and 50 mL of a 2.0 M KOH solution were added, and the resulting mixture was stirred at reflux overnight. The solution was cooled to room temperature, solvents were removed under reduced pressure,

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and the residue was extracted with EtOAc, and purified by chromatography on a silica gel column. Elution with hexanes−CH_2Cl_2 (4:1) gave **18** (11.2 g, 70%): mp 160−161 °C; ^{1}H NMR δ 9.86 (s, 1), 8.29 (dd, 1, J = 1.5, 8.5 Hz), 8.14 (dd, 1, J = 1.5, 8.5 Hz), 7.54−7.62 (m, 2), 7.47 (d, 1, J = 8.5 Hz), 7.28 (dd, 1, J = 3.0, 8.5 Hz), 6.73 (s, 1), 4.01 (s, 3), 3.95 (s, 3), 3.40 (s, 3); ^{13}C NMR ($CDCl_3$) δ 192.3, 159.3, 151.9, 146.9, 134.6, 132.2, 128.4, 127.1, 126.5, 126.1, 125.1, 122.3, 122.2, 121.2, 109.6, 106.1, 60.7, 55.7, 55.6. Anal. Calcd for $C_{20}H_{18}O_4$: C, 74.52; H, 5.63. Found: C, 74.29; H, 5.55.

1,4-Dimethoxy-2-(4-methoxy-2-{2-methoxyvinyl}-phenyl)naphthalene (19). Reaction of **18** with methoxymethylenetriphenylphosphine [generated in situ from methoxymethyltriphenylphosphonium chloride (6.8 g, 20 mmol)] and *t*-BuOK (1.0 M in THF, 20 mL, 20 mmol) by the procedure employed for preparation of **4b** afforded **19** (3.12 g, 89%) as an oil consisting of a mixture of isomers (E/Z = 1): ^{1}H NMR δ 8.28 (d, 2, J = 8.0 Hz), 8.17 (d, 2, J = 8.0 Hz), 7.87 (d, 1, J = 2.5 Hz), 7.26−7.58 (m, 8), 7.04 (d, 1, J = 2.5 Hz), 7.02 (d, 1, J = 12.5 Hz), 6.83−6.86 (m, 2), 6.64 (s, 1), 6.63 (s, 1), 6.06 (d, 1, J = 7.5 Hz), 5.73 (d, 1, J = 12.5 Hz), 5.13 (d, 1, J = 7.5 Hz), 3.96 (s, 6), 3.90 (s, 6), 3.78 (s, 3), 3.53 (s, 6), 3.48 (s, 3). Compound **19** was used directly in the next step.

3,7,12-Trimethoxybenz[*a*]anthracene (20). To a solution of **19** (3.0 g, 8.5 mmol) in CH_2Cl_2 (30 mL) was added a solution of $MeSO_3H$ (1.92 g, 20 mmol) in CH_2Cl_2 (10 mL) dropwise over 10 min. TLC indicated reaction was complete in 10 min. The mixture was poured into saturated $NaCO_3$ solution, extracted with CH_2Cl_2, dried over $NaSO_4$, and evaporated to dryness to give **20** (2.5 g, 92.0%) as a yellow brown solid, mp 164−165 °C, used directly in the next step: ^{1}H NMR δ 9.50 (d, 1, J = 9.0 Hz), 8.34 (dd, 1, J = 1.8, 7.5 Hz), 8.23 (d, 1, 8.0 Hz), 8.04 (d, 1, J = 9.0 Hz), 7.46−7.53 (m, 3), 7.20 (dd, 1, J = 2.5 Hz), 7.16 (s, 1, J = 9.0 Hz), 4.01 (s, 3), 3.88 (s, 3), 3.85 (s, 3); ^{13} H NMR δ 158.3, 150.0, 148.7, 134.4, 129.8, 127.4, 125.9, 125.6, 125.4, 123.7, 122.9, 122.3, 121.7, 120.9, 115.9, 110.0, 63.2, 60.7, 55.4. Anal. Calcd for $C_{21}H_{18}O_3$: C, 79.22; H, 5.70. Found: C, 79.08; H, 5.77.

Benz[*a*]anthracen-3-ol (21). To a solution of **20** (2.8 g, 8.8 mmol) in HOAc (70 mL) was added a 57% solution of HI (30 mL). The resulting solution was heated at reflux for 48 h, cooled to room temperature, and poured into ice−water (500 mL). The solid product was collected to give **21** (1.92 g, 89%): mp 207−208 °C (lit.[57] mp 208−209 °C): ^{1}H NMR δ 9.22 (s, 1), 8.82 (d, 1, J = 9.0 Hz), 8.44 (s, 1), 8.17 (d, 1, J = 8.0 Hz), 8.08 (d, 1, J = 8.0 Hz), 7.83 (d, 1, J = 9.0 Hz), 7.60 (d, 1, J = 9.0 Hz), 7.52−7.58 (m, 2), 7.31 (d, 1, J = 7.5 Hz), 7.27 (dd, 1, J = 4.5, 8.5 Hz).

Benz[*a*]anthracen-3,4-dione (BAQ). To a solution of **21** (1.82 g, 7.5 mmol) in DMSO (5 mL) was added IBX (1.98 g, 7.5 mmol). The resulting mixture was stirred at room temperature for 10 min and poured into ice−water (200 mL), and the solid product was collected and purified by chromatography on a Florsil column. Elution with hexanes−EtOAc (3:1) gave BAQ (1.61 g, 83.0%): mp 212−213 °C (lit.[55] mp 213−214 °C); ^{1}H NMR δ 9.41 (s, 1), 8.81 (d, 1, J = 10.5 Hz), 8.73 (s, 1), 8.29 (d, 1, J = 8.5 Hz), 8.24 (d, 1, J = 8.5 Hz), 8.17 (d, 1, J = 8.5 Hz), 7.99 (d, 1, J = 8.5 Hz), 7.66−7.70 (m, 2H), 6.66 (d, 1, J = 10.5 Hz).

7,8-Diacetoxy benzo[*a*]pyrene (22). To a solution of BPQ (500 mg, 1.77 mmol) in DMF (10 mL) was added portionwise $NaBH_4$ (337 mg, 8.86 mmol). The color changed rapidly from purple to deep red. After 0.5 h, Ac_2O (1.0 mL, excess) and Na_2CO_3 (1.0 g, excess) were added, and the mixture was stirred overnight. The solvent was removed under vacuum, and the residue was dissolved in EtOAc (100 mL), washed with water and brine, and dried over sodium sulfate. After removal of EtOAc under reduced pressure, the residue was chromatographed. Elution with hexane−EtOAc (2:1) gave **22** (531 mg, 80%) as a yellow solid: mp 205−206 °C; ^{1}H NMR δ 8.96 (d, 1 J = 9.5 Hz), 8.94 (d, 1 J = 10.1 Hz), 8.46 (s, 1), 8.32 (d, 1, J = 9.1 Hz), 8.23 (d, 1, J = 7.7 Hz), 8.10 (d, 1, J = 7.2 Hz), 7.99 (t, 1, J = 7.5 Hz), 7.94 (d, 2, J = 9.1 Hz), 7.66 (d, 1, J = 9.2 Hz), 2.60 (s, 3), 2.42 (s, 3); ^{13}C NMR δ 168.5, 168.3, 131.3, 131.2, 130.7, 128.6, 128.3, 128.0, 127.4, 126.9, 126.3, 125.9, 125.8, 125.3, 123.5, 122.0, 121.9, 121.1, 117.1, 20.8, 20.6. Anal. Calcd for $C_{24}H_{16}O_4$: C, 78.25; H, 4.38. Found C, 78.31; H, 4.36.

3,4-Diacetoxy-7,12-dimethylbenz[*a*]anthracene (23b). To a solution of DMBAQ (400 mg, 1.4 mmol) in DMF (5 mL) was added portionwise $NaBH_4$ (270 mg, 7 mmol). The color of the reaction mixture was slightly yellow, and TLC indicated that the reaction was complete. To the resulting mixture was added pyridine (3.0 mL) followed by acetic anhydride (1.0 mL, excess). The solution was stirred overnight, then poured onto ice water (100 mL) and filtered, and the solid was collected and purified by chromatography on a silica gel column to afford **23b** (0.32 g, 61.5%): mp 188−190 °C (lit.[36] mp 165 °C); ^{1}H NMR δ 8.36−8.40 (m, 3), 8.13 (d, 1, J = 9.5 Hz), 7.64−7.70 (m, 2), 7.60 (d, 1, J = 9.5 Hz), 7.41(d, 1, J = 9.0 Hz), 3.35 (s, 3), 3.08 (s, 3), 2.52 (s, 3), 2.41 (s, 3); although the mp of **23b** was higher than the reported value, its ^{1}H NMR spectrum was in good agreement with that of the authentic compound.[36]

3,4-Diacetoxybenz[*a*]anthracene (24b). Reduction of BAQ (200 mg, 0.8 mmol) with $NaBH_4$ (0.27 g, 7 mmol) by the procedure employed for the preparation of **23b** afforded **24b** (150 mg, 57%): mp 212−214 °C; ^{1}H NMR δ 9.02 (s, 1), 8.65 (d, 1, J = 9.0 Hz), 8.28 (s, 1), 8.02 (d, 1, J = 8.5 Hz), 7.96 (d, 1, J = 8.5 Hz), 7.76 (d, 1, J = 9.0 Hz), 7.55 (d, 1, J = 9.0 Hz), 7.47 (dd, 2, J = 3.5, 8.5 Hz), 7.44 (d, 1, J = 8.5 Hz), 2.39 (s, 3), 2.28 (s, 3). Anal. Calcd for $C_{22}H_{16}O_4$: C, 76.73; H, 4.68. Found C, 76.61; H, 4.26.

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