

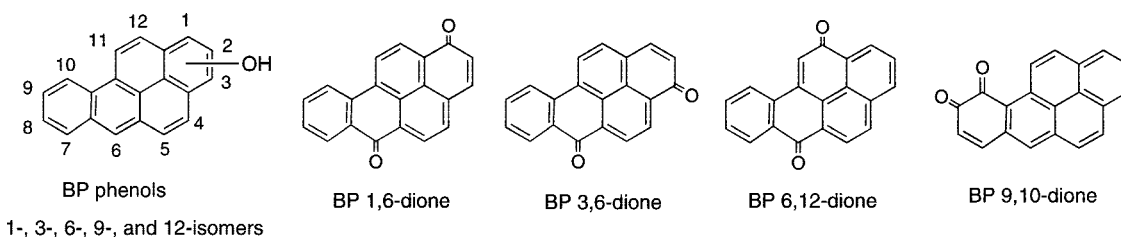
Synthesis of Phenol and Quinone Metabolites of Benzo[*a*]pyrene, a Carcinogenic Component of Tobacco Smoke Implicated in Lung Cancer

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Polycyclic aromatic hydrocarbons (PAHs) are widespread environmental pollutants produced in the combustion of organic matter. PAHs are present in automobile exhaust and tobacco smoke, and they have recently been designated as human carcinogens. Current evidence indicates that PAHs are activated enzymatically to mutagenic metabolites that interact with DNA. There is evidence for three pathways of activation: the *diol epoxide* path, the *radical-cation* path, and the *quinone* path. The relative importance of these paths for human lung cancer has not been established. We now report syntheses of the principal phenol and quinone isomers of the prototype PAH carcinogen benzo[*a*]pyrene (BP) that are known or are suspected to be formed as metabolites of BP in human bronchoalveolar cells. The methods of synthesis were designed to be adaptable to the preparation of the ¹³C-labeled analogues of the BP metabolites. These compounds are needed as standards for sensitive LC–MS/MS methods for analysis of BP metabolites formed in lung cells. Efficient novel syntheses of the 1-, 3-, 6-, 9-, and 12-BP phenols and the BP 1,6-, 3,6-, 6,12-, and 9,10-quinones are now reported. The syntheses of the BP phenols (except 6-HO-BP) involve the key steps of Pd-catalyzed Suzuki–Miyaura cross-coupling of a naphthalene boronate ester with a substituted aryl bromide or triflate ester. The BP quinones were synthesized from the corresponding BP phenols by direct oxidation with the hypervalent iodine reagents IBX or TBI. These reagents exhibited different regioselectivities. IBX oxidation of the 7- and 9-BP phenols provided the *ortho*-quinone isomers (BP 7,8- and 9,10-diones, respectively), whereas TBI oxidation of the 1-, 3-, and 12-BP phenols furnished BP quinone isomers with carbonyl functions in separate rings (BP 1,6-, 3,6-, and 6,12-diones, respectively).

Introduction

Polycyclic aromatic hydrocarbons (PAHs) are widespread environmental pollutants that are produced in the combustion of organic matter.^{1–3} PAHs are components of automobile and diesel engine exhaust⁴ and tobacco smoke,^{5–7} and they are

implicated as causative agents for lung cancer,^{2,5–10} the principal category of adult cancer death in the U.S. population.¹¹

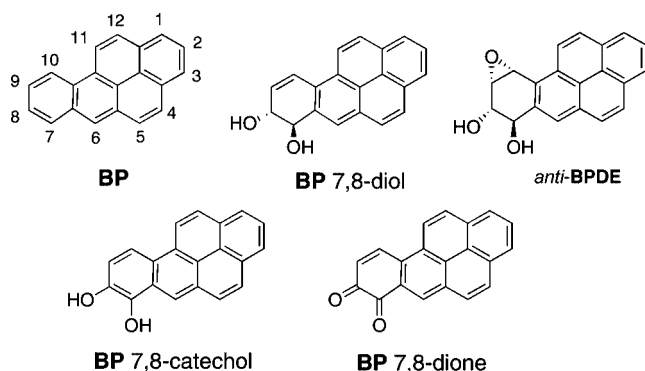
For PAHs to exert their carcinogenic effects, metabolic activation is required.³ Benzo[*a*]pyrene (BP) is the prototype PAH carcinogen that has been most intensively investigated. Three activation pathways have been proposed. The most studied path involves cytochrome P-450 (CYP)-mediated formation of BP *trans*-7,8-dihydrodiol (BP 7,8-diol) and its oxidation to the highly mutagenic BP *trans*-7,8-diol-*anti*-9,10-epoxide (*anti*-BPDE).^{3,12} A second path entails aldo–keto reductase (AKR)-

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mediated oxidation of BP 7,8-diol to BP 7,8-catechol, which enters into a redox cycle with O₂ to form a quinone (BP 7,8-dione) along with reactive oxygen species (ROS) that attack DNA.^{13–16} The third path entails peroxidase-mediated oxidation of BP to form a radical cation that reacts with DNA, leading to the formation of depurinated adducts.^{17,18} The relative importance of these activation routes for human cancer has not been established.



Numerous studies of the metabolism of BP by rodent liver microsomes and other model cell systems have been conducted.^{3,19,20} However, most of these investigations were carried out without an appreciation of all the participating pathways or sufficiently sensitive analytical methods or standards to adequately characterize all the metabolites formed. More recently, human bronchoalveolar H358 cells were introduced as a model to study the metabolic profile of BP in normal human lung epithelial cells.^{21,22} Development of a stable isotope dilution, liquid

chromatography tandem mass spectrometric analytical method to quantify the adducts formed with DNA by the metabolites of BP was also reported.²³

Enhancement of the scope and sensitivity of the LC–MS analytical methodology requires ¹³C-labeled analogues of BP and its metabolites as authentic standards. In this connection, we recently reported syntheses of ¹³C₂-BP, ¹³C₂-BP 7,8-diol, ¹³C₂-BP 7,8-dione, and ¹³C₂-8-HO-BP.²⁴ We now report improved new syntheses of the principal phenol and quinone isomers of BP formed in its metabolism in human bronchoalveolar H358 cells.²¹ The synthetic approaches were designed to be adaptable to syntheses of the corresponding ¹³C-labeled analogues of these BP metabolites with two or more ¹³C atoms in the PAH ring system.

Results

The phenol and quinone isomers of BP chosen as synthetic targets for this investigation include the 1-, 3-, 6-, 9-, and 12-phenol isomers (1-HO-BP, 3-HO-BP, 6-HO-BP, 9-HO-BP, and 12-HO-BP) and the 1,6-, 3,6-, 6,12-, and 9,10-quinone isomers (BP 1,6-dione, BP 3,6-dione, BP 6,12-dione, and BP 9,10-dione). Although not all of these isomers have been identified as metabolites of BP in H358 cells,²¹ the evidence suggests that some phenol isomers may not have survived sufficiently long enough to be detected due to the facility of their oxidation to quinones or higher-oxidized products. For example, 6-HO-BP was not found as a metabolite, yet BP 1,6-dione and BP 3,6-dione were identified as the principal BP quinone metabolites.²¹ The fact that 6-HO-BP is a metabolic precursor of the BP 1,6-, 3,6-, and 6,12-diones²⁰ suggests that 6-HO-BP is formed but fails to persist due to its further oxidation to the BP 1,6-, 3,6-, and 6,12-diones. Other unidentified BP phenol or quinone isomers, for which standards were not available, may also have been formed but escaped detection because they happen to coelute on chromatography with an isomer for which a standard was available. Satisfactory resolution of these questions requires that the isomeric BP phenol and quinone metabolites that were not available for the initial metabolism studies should be synthesized to serve as additional analytical standards.

Syntheses of all 12 BP phenol isomers by classical synthetic methods have been described in the literature.^{25,26} However, these syntheses involve relatively large numbers of steps, and

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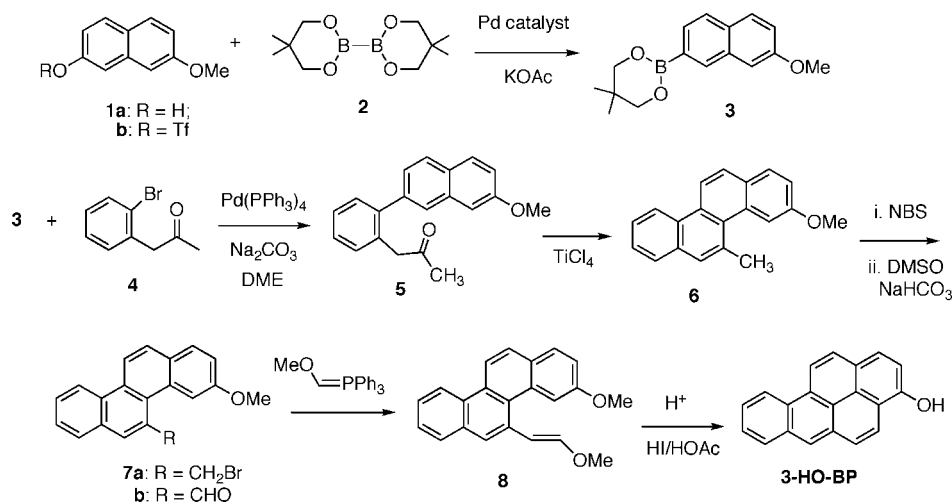
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SCHEME 1

TABLE 1. Optimization of Conditions for the Synthesis of **3**^a

entry	catalyst	solvent	time (h)	yield (%)
1	Pd(dppf)Cl ₂	DMSO	2	40
2	Pd(pph ₃) ₄	DMSO	3	35
3	Pd(dppf) Cl ₂	CH ₃ CN	5	40
4	Pd(dppf)Cl ₂	THF	3	70
5	Pd(dppf)Cl ₂	dioxane	1.5	82

^a Experimental: To a two-neck flask flushed with N₂ were added Pd catalyst (0.03 mmol), **2** (1.2 mmol), and a solution of **1b** (1.0 mmol) in a solvent (8 mL). The mixture was stirred at 80 °C for the time indicated, the solvent was removed under vacuum, and the residue was chromatographed on silica gel.

they were not designed to serve as the basis of methods for efficient syntheses of the ¹³C-labeled analogues of the BP phenol isomers.

Benzo[*a*]pyren-3-ol (3-HO-BP). 3-HO-BP was the principal phenol isomer detected as a metabolite of BP in H358 cells.²¹ Synthesis of 3-HO-BP was accomplished via the reaction sequence in Scheme 1. The key step entailed Pd-catalyzed Suzuki–Miyaura cross-coupling of the 2-boronate ester of 7-methoxynaphthalene (**3**) with 2-bromophenylacetone (**4**). The boronate ester **3** was prepared from 7-methoxy-2-naphthol **1a** via initial conversion to its triflate ester **1b** by the procedure reported.²⁷ Reaction of **1b** (1 mmol) with bis(neopentylglycolato)diboron **2** (1.2 mmol) in the presence of Pd(dppf)Cl₂ (0.03 mmol) as catalyst and KOAc as base took place in DMSO at 80 °C to afford the boronate ester **3** in moderate yield (40%). A brief study of this reaction was undertaken with the aim of improving the yield of **3** (Table 1). It was not significantly enhanced by the use of Pd(PPh₃)₄ as catalyst, increasing reaction time, or the use of CH₃CN as solvent. On the other hand, the yield of **3** was significantly improved and reaction time was decreased with the use of THF or dioxane as solvent. The optimum yield (82%) was obtained with dioxane as solvent.

Cross-coupling of **3** with **4** took place in the presence of Pd(PPh₃)₄ and Na₂CO₃ in DME to furnish 2-(7-methoxynaphthyl)phenylacetone **5** as principal product (62%). It was recently shown²⁸ that acid-catalyzed cyclization of an analogue of **5**,

lacking a methoxy group, was accompanied by secondary rearrangement of the bay region methyl group of the product to the adjacent ring position due to steric crowding. Rearrangement was diminished by the use of TiCl₄ as catalyst. TiCl₄-catalyzed cyclization of **5** furnished 3-methoxy-5-methylchrysene **6** as major product (74%). Conversion of the methyl group of **6** to an aldehyde function was accomplished via bromination with NBS to give 5-bromomethyl-3-methoxychrysene **7a**, and reaction of **7a** with DMSO and NaHCO₃ yielded 5-formyl-3-methoxychrysene **7b**. Although **7a** was unstable, satisfactory yields of **7b** could be obtained by the direct use of **7a** without isolation. Wittig reaction of **7b** with methoxymethylenetriphenylphosphine furnished 3-methoxy-5-(2-methoxyvinyl)chrysene **8** as a mixture of *E*- and *Z*-isomers. Acid-catalyzed cyclization of **8** gave 3-methoxybenzo[*a*]pyrene (76% from **7b**), and demethylation by treatment with BBr₃ provided 3-HO-BP.

Benzo[*a*]pyren-1-ol (1-HO-BP). Synthesis of 1-HO-BP was carried out by a procedure analogous to that for the preparation of 3-HO-BP (Scheme 2).²⁹ The 2-boronate ester of 5-methoxynaphthalene (**10**) was prepared from 5-methoxy-2-naphthol **9a** via conversion to the triflate ester **9b**, followed by reaction of **9b** with **2** in the presence of Pd(dppf)Cl₂ by the procedure for the preparation of **3**. Cross-coupling of **10** with **4** with Pd(PPh₃)₄ and Na₂CO₃ in DME gave 2-(5-methoxynaphthyl)phenylacetone **11** (77%). TiCl₄-catalyzed cyclodehydration of **11** afforded 1-methoxy-5-methylchrysene **12** (68%), and reaction of **12** with NBS gave **13a**, which was converted to 5-formyl-1-methoxychrysene **13b** (74%) by reaction with DMSO and NaHCO₃.^{28,30}

Wittig reaction of **13b** with methoxymethylenetriphenylphosphine yielded 1-methoxy-5-(2-methoxyvinyl)chrysene **14** (90%) as a mixture of *E*- and *Z*-isomers. Acid-catalyzed cyclization of **14** afforded 1-methoxybenzo[*a*]pyrene. Attempted demethylation by treatment with BBr₃ was unsuccessful, but conversion of 1-MeO-BP to 1-HO-BP was accomplished by treatment with HI/HOAc. The usefulness of HI/HOAc for demethylation of aryl ethers was noted in an earlier study,³² but the scope of the

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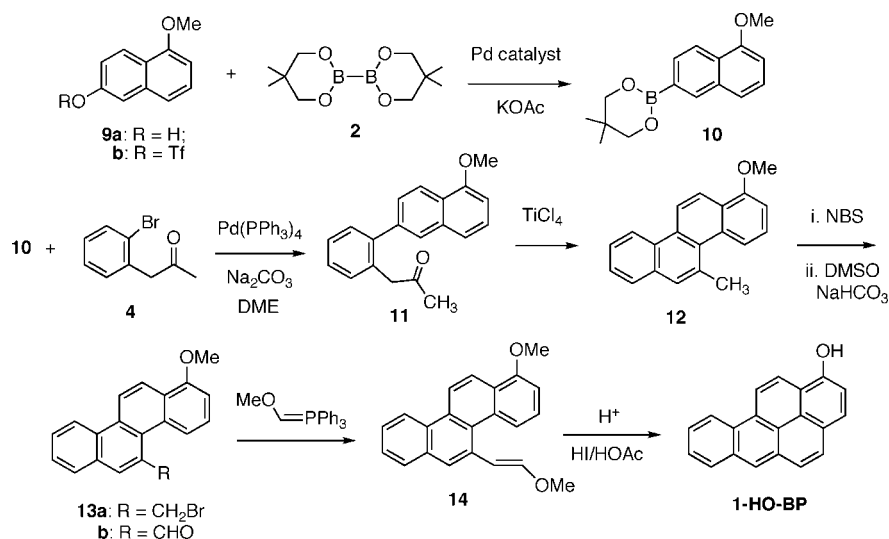
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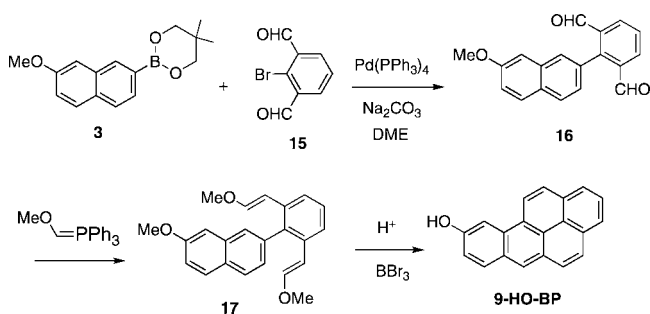
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SCHEME 2



SCHEME 3



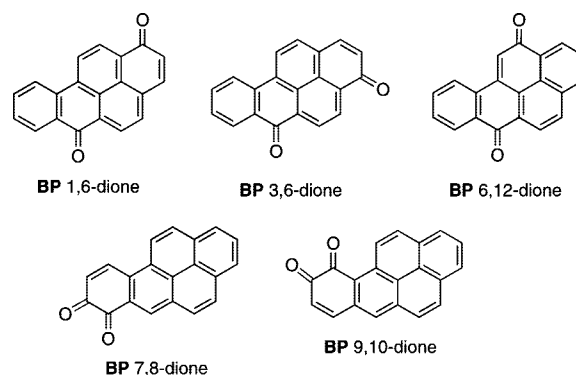
method was not explored. It appears that HI/HOAc may be superior to BBr_3 as a reagent for demethylation of PAH methyl ethers.

Benzo[*a*]pyren-9-ol (9-HO-BP). Synthesis of 9-HO-BP was carried out by a procedure analogous to that reported for the preparation of 7-benzo[*a*]pyren-7-ol (Scheme 3).^{31,32} 2-Bromobenzene-1,3-dialdehyde **15** was synthesized by the reported method,³¹ and Suzuki–Miyaura coupling of **15** with the boronate ester **3**, catalyzed by $\text{Pd}(\text{PPh}_3)_4$, furnished the dialdehyde adduct **16**. Double Wittig reaction of **16** with (methoxymethylene)triphenylphosphine ($\text{CH}_3\text{OCH}=\text{PPh}_3$)²⁴ provided the di(methoxyvinyl) derivative (**17**) as a mixture of *E*- and *Z*-isomers. Acid-catalyzed cyclization of **17** furnished 9-methoxybenzo[*a*]pyrene, and demethylation with BBr_3 gave 9-HO-BP.

Benzo[*a*]pyren-12-ol (12-HO-BP). Synthesis of 12-HO-BP is outlined in Scheme 4. The 2-boronate ester of 1-methylnaphthalene (**19**) was prepared from 1-methyl-2-naphthol **18a** via conversion to the triflate ester **18b**, followed by reaction of **18b** with **2** in the presence of $\text{Pd}(\text{dppf})\text{Cl}_2$. Reaction of **19** with 2-bromobenzaldehyde in the presence of $\text{Pd}(\text{PPh}_3)_4$ and Na_2CO_3 in DME gave 2-(1-methylnaphthalen-2-yl)benzaldehyde **20** (74%), and reaction of **20** with methoxymethylenetriphenylphosphine furnished **21** as a mixture of *E*- and *Z*-isomers. Acid-catalyzed cyclization of **21** afforded 12-methylbenz[*a*]anthracene **22a**. This was converted to 12-HO-BP via bromination with NBS to yield **22b**, reaction of **22b** with KCN to provide **22c**, hydrolysis of **22c** with KOH in ethylene glycol to yield **22d**, and acid-catalyzed cyclization of **22d** to furnish 12-HO-BP.^{26g}

Benzo[*a*]pyren-6-ol (6-HO-BP). The most convenient synthetic precursors of 6-HO-BP and $^{13}\text{C}_2$ -6-HO-BP are BP and $^{13}\text{C}_2$ -BP themselves. An efficient synthesis of $^{13}\text{C}_2$ -BP was recently reported.²⁴ Direct synthesis of 6-HO-BP from BP was accomplished via initial Vilsmeier–Haack reaction of BP with POCl_3 and DMF to furnish 8-formylbenzo[*a*]pyrene **23** (Scheme 5).³³ Baeyer–Villiger oxidation of **23** with *m*-chloroperbenzoic acid provides 8-formyloxybenzo[*a*]pyrene **24**. The formate ester derivative was relatively stable, in contrast to 6-HO-BP that exhibited a strong tendency to undergo oxidative decomposition on exposure to air. The ease of autoxidation of 6-HO-BP accords with the earlier findings of Lorentzen et al.,^{20c} who showed the principal products of autoxidation of 6-HO-BP to be the BP 1,6-, 3,6-, and 6,12-diones.

Synthesis of BP Quinones. Direct oxidation of BP with chromium reagents, ceric ammonium nitrate, and other oxidants has been shown by various investigators to furnish mixtures of BP quinones that are difficult to separate.³⁴ This problem was reinvestigated by Cho and Harvey,³⁵ who used careful chromatographic techniques to isolate and identify the pure BP 1,6-, 3,6-, and 6,12-dione isomers. They were obtained in yields of 40, 20, and 7%, respectively. However, this approach is impractical for the synthesis of the individual pure ^{13}C -labeled BP 1,6-, 3,6-, and 6,12-diones.

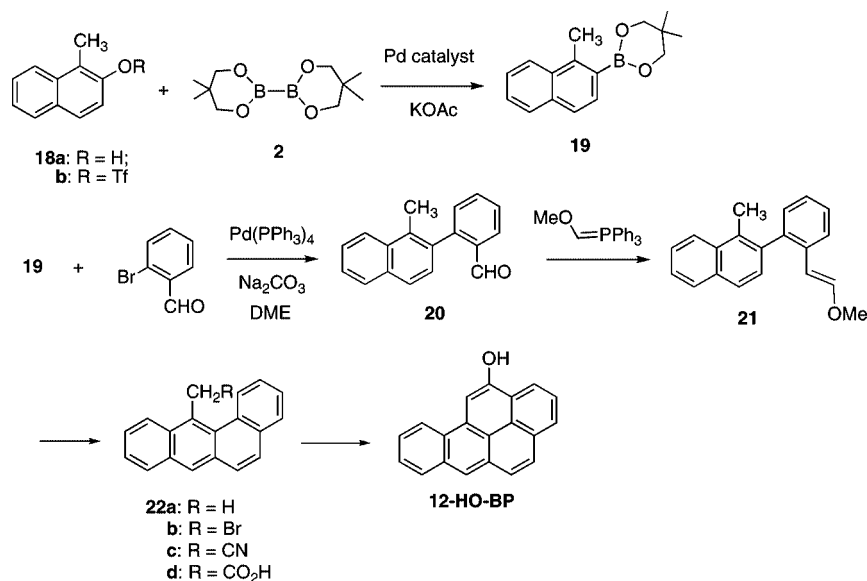


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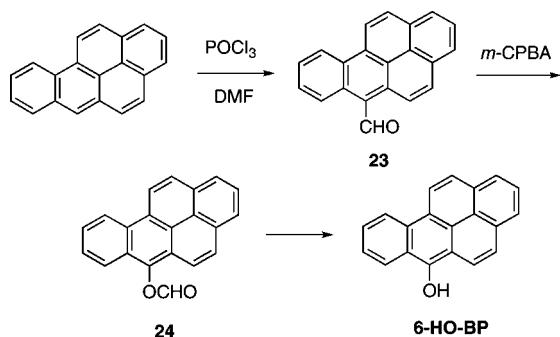
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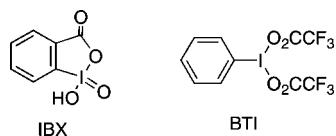
SCHEME 4



SCHEME 5



A more promising synthetic route to the BP quinones of interest is via oxidation of the individual BP phenol isomers. In a prior study, we showed that oxidation of 8-HO-BP with the hypervalent iodine reagent *o*-iodoxybenzoic acid (IBX) provided convenient synthetic access to BP 7,8-dione.^{24,32} We now report that oxidation of 9-HO-BP with IBX by a similar procedure furnished BP 9,10-dione in good yield (82%).



Attempts to oxidize 1-HO-BP or 3-HO-BP by IBX were not successful, failing to provide either the unknown *ortho*-quinone isomers (BP 1,2- or 2,3-dione) or the BP 1,6- or 3,6-quinone isomers. Transformation of 1-HO-BP and 3-HO-BP to the desired BP quinone isomers (BP 1,6-dione and BP 3,6-dione) was accomplished by direct oxidation with another hypervalent iodine reagent, [bis(trifluoroacetoxy)iodo]benzene (BTI). BP 1,6-dione and BP 3,6-dione were obtained in yields of 82 and 85%, respectively. Similarly, oxidation of 12-HO-BP by BTI provided BP 6,12-dione. BTI was shown previously to oxidize substituted 1-naphthols to 1,4-naphthoquinones,³⁶ but no examples of its

use for oxidation of PAH phenols with larger ring systems have been reported. BTI holds promise as a reagent for regioselective oxidation of PAH phenols to quinones with carbonyl functions in separate rings, such as the BP 1,6- and 3,6-diones.

Discussion

Oxidative metabolism of BP and other PAHs in mammalian cells is part of the normal process of enzymatic detoxification of xenobiotic substances.^{3a,16,19} Metabolism of BP by P-450 microsomal enzymes affords initially arene oxides that may either rearrange to phenols or undergo epoxide hydrolase-catalyzed hydration to furnish *trans*-dihydrodiols, such as the BP *trans*-7,8- or *trans*-9,10-dihydrodiols. These primary metabolites are converted to glucuronides or other water-soluble conjugates that are eventually excreted. However, some of the primary metabolites are able to survive and undergo further oxidative metabolism to quinones, diol epoxides, and other potentially carcinogenic species.

This paper reports efficient syntheses of the principal phenol and quinone isomers of BP that have been identified or are suspected to be formed as metabolites of BP in normal human bronchoalveolar cells.²¹ The BP phenols include the 1-, 3-, 6-, 9-, and 12-phenol isomers (1-HO-BP, 3-HO-BP, 6-HO-BP, 9-HO-BP, and 12-HO-BP). The BP quinone isomers are the BP 1,6-, 3,6-, 6,12-, and 9,10-diones.

The syntheses of the BP phenols involve the key steps of Pd-catalyzed Suzuki cross-coupling of a naphthalene boronate ester derivative with an aryl bromide or a triflate ester. The BP quinones were synthesized from the BP phenols by oxidation with the hypervalent iodine reagents IBX and BTI. These reagents exhibited different regiospecificities of oxidation. Reaction of IBX with 7-HO- and 9-HO-BP yielded the *ortho*-quinone isomers (BP 7,8- and 9,10-diones, respectively), whereas reaction of BTI with 1-HO-, 3-HO-, and 12-HO-BP furnished exclusively quinone isomers with carbonyl functions in separate rings (BP 1,6-, 3,6-, and 6,12-diones, respectively). The remarkable regioselectivities of these oxidations are consistent with the mechanisms. Oxidations with IBX are thought to proceed via initial reaction of the reagent with the

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phenol to form an intermediate complex.^{37,38} This is followed by intramolecular transfer of an oxygen atom from the IBX component of the complex to the carbon atom adjacent to the hydroxyl group of the phenolic component, leading to the formation of an *ortho*-quinone product. Oxidations with BTI also entail initial reaction of the reagent with the phenol to form an intermediate complex.³⁷ This reacts with water, generally at a less sterically restricted para position, thereby generating a *para*-catechol intermediate that undergoes further oxidation to yield a quinone product. The BP 1-, 3-, and 12-phenols lack a para position, so that the reactions of their intermediate complexes with water take place at the most reactive alternative site, the 6-position, to generate the BP 1,6-, 3,6-, and 6,12-diones, respectively.³⁹ These are the first examples of oxidation of PAH phenols with TBI to afford PAH quinones with carbonyl functions in separate rings.

The synthetic approaches to the BP phenol and quinone metabolites outlined above were designed to be adaptable to the preparation of ¹³C-labeled analogues of these compounds. The isotopically labeled compounds are needed as substrates and/or standards for metabolism and other studies in normal human lung cells. Syntheses of the ¹³C-labeled analogues are in progress. This work is virtually complete, and the findings will be reported shortly.

The methods reported herein for synthesis of BP phenol derivatives via Suzuki cross-coupling are potentially broad in scope. They are expected to provide convenient synthetic access to many other PAHs and their substituted derivatives.

Experimental Section

Caution. Benzo[*a*]pyrene (BP) has been designated a human carcinogen by the World Health Organization.² BP should be handled with appropriate caution following the procedures recommended in the publication: *NIH Guidelines for the Laboratory Use of Chemical Carcinogens*. The phenol and quinone isomers of BP have not been designated as carcinogenic hazards, but prudence suggests that they also be handled with caution.

2-(7-Methoxynaphthyl)phenylacetone (5). To a solution of 2-bromophenylacetone **4** (0.852 g, 4.0 mmol) in DME (10 mL) under argon was added Pd(PPh₃)₄ (46 mg, 0.40 mmol), and the resulting solution was stirred for 20 min. Then the boronic ester **3** (1.30 g, 4.8 mmol) and EtOH (15 mL) were added. Stirring was continued for 20 min, then Na₂CO₃ (4 mL of a 2 M solution) was added, and the solution was heated at reflux for 4 h, then cooled to room temperature. The precipitate was filtered off, washed with EtOAc (50 mL), and the filtrate was evaporated to dryness. The residue was dissolved in EtOAc (80 mL), washed with water (3 × 15 mL), dried over Na₂SO₄, and evaporated to dryness. Chromatography of the residue on a column of silica gel eluted with hexane/EtOAc (20:1) afforded **5** (0.72 g, 62%): ¹H NMR (500 MHz, CDCl₃) δ 7.85–7.78 (m, 2 H), 7.42 (s, 1 H), 7.45–7.30 (m, 3 H), 7.30–7.20 (m, 3 H), 7.17 (s, 1 H), 3.96 (s, 3 H), 3.77 (s, 2 H), 2.02 (s, 3 H); ¹³C NMR (125.8 MHz, CDCl₃) δ 206.3, 157.8, 142.2, 139.1, 134.2, 132.1, 130.4, 130.0, 129.0, 127.6, 127.38, 127.35, 126.8, 126.5, 124.8, 118.8, 105.6, 55.0, 48.1, 29.4; HRMS (M⁺) calcd for C₂₀H₁₈O₂ (M⁺) 290.1307, found 290.1309.

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(39) Electrophilic reactions of BP are well known to take place preferentially at the 6-position, in accordance with molecular orbital theoretical prediction (ref 3a). The presence of electron-donating groups, such as methoxy, in the 1-, 3-, or 12-positions would likely increase the likelihood of substitution in the 6-position. A reviewer has pointed out that there are 36 possible BP quinone structures and that the BP quinones formed as metabolites are among those with the largest number of Kekulé structures (six). Dias, J. *J. Chem. Inf. Comput. Sci.* **1999**, *30*, 53–61.

3-Methoxy-5-methylchrysene (6). To a dry flask was added a solution of **5** (460 mg, 1.6 mmol) in CH₂Cl₂ (15 mL) under argon. Then a solution of TiCl₄ (1.6 mL, 1 M in CH₂Cl₂) was added dropwise at –78 °C. The resulting mixture was stirred for 3.5 h at 0 °C, and the reaction was monitored by TLC. The reaction was quenched by pouring on crushed ice (15 g), extracted with EtOAc (3 × 50 mL), and the combined organic layer was washed with water and dried over Na₂SO₄. After evaporation of the solvent under reduced pressure, the residue was purified by chromatography on a silica gel column. Elution with hexane/EtOAc (10:1) afforded **6** and a small amount of an unidentified isomer. Crystallization from EtOH gave pure **6** (321 mg, 74%): ¹H NMR (500 MHz, CDCl₃) δ 8.73 (d, *J* = 8.5 Hz, 1 H), 8.64 (d, *J* = 9.0 Hz, 1 H), 8.41 (d, *J* = 2.0 Hz, 1 H), 7.94–7.90 (m, 3 H), 7.83 (s, 1 H), 7.70–7.55 (m, 2 H), 7.32 (dd, *J* = 8.5 and 2.0 Hz, 1 H), 4.04 (s, 3 H), 3.28 (s, 3 H); ¹³C NMR (125.8 MHz, CDCl₃) δ 157.2, 133.0, 132.9, 131.7, 130.4, 130.2, 129.8, 129.7, 128.8, 128.4, 127.4, 127.2, 126.5, 126.0, 123.3, 119.5, 116.1, 109.4, 55.5, 27.7; MS (APCI) *m/z* = 273 (100%).

3-Methoxy-5-formylchrysene (7b). To a dry flask containing a solution of **6** (272 mg, 1 mmol) in CCl₄ (10 mL) under argon were added NBS (196 mg, 1.1 mmol) and benzoyl peroxide (6 mg), and the mixture was heated at reflux for 3 h, and the reaction monitored by TLC. Then the mixture was cooled to room temperature, and the precipitate of **7a** was filtered off and washed with CCl₄ (2 mL). To the resulting solution were added DMSO (2.8 mL) and NaHCO₃ (168 mg, 2 mmol), and the mixture was heated at 80–90 °C for 3.0 h (the reaction was monitored by TLC). The mixture was diluted with EtOAc (100 mL), washed with water (3 × 30 mL), and dried over Na₂SO₄. After evaporation of the solvent under reduced pressure, the residue was purified by chromatography on a silica gel column. Elution with hexane/EtOAc (40:1) furnished **7b** (170 mg, 60%): ¹H NMR (500 MHz, CDCl₃) δ 10.69 (s, 1 H), 8.73 (d, *J* = 9.5 Hz, 1 H), 8.56 (d, *J* = 9.0 Hz, 1 H), 8.40 (s, 1 H), 8.11 (d, *J* = 7.5 Hz, 1 H), 8.01 (d, *J* = 8.5 Hz, 1 H), 7.96 (d, *J* = 8.5 Hz, 1 H), 7.82 (t, *J* = 8.5 Hz, 1 H), 7.72 (t, *J* = 7.5 Hz, 1 H), 7.46 (d, *J* = 2.0 Hz, 1 H), 7.35 (dd, *J* = 9.0 and 2.0 Hz, 1 H), 4.00 (s, 3 H); ¹³C NMR (125.8 MHz, CDCl₃) δ 193.2, 158.4, 133.8, 132.3, 130.6, 130.5, 130.4, 130.3, 130.2, 129.9, 129.2, 128.1, 128.0, 127.3, 126.0, 123.3, 118.8, 117.9, 109.2, 55.6; HRMS (M⁺) calcd for C₂₀H₁₄O₂ 286.0994, found 286.0984.

3-Methoxybenzo[*α*]pyrene. To a suspension of methoxymethyltriphenylphosphonium chloride (222 mg, 0.65 mmol) in anhydrous THF (1.0 mL) under argon at room temperature was added *t*-BuOK (0.65 mL, 1 M in THF) dropwise. The resulting mixture was stirred at room temperature for 1.5 h, and a solution of **7b** (160 mg, 0.54 mmol) in THF (2 mL) was added. Stirring was continued for 1.5 h, and the reaction was monitored by TLC. Diethyl ether (50 mL) was added, and the precipitate was filtered off and washed with Et₂O (30 mL). Following removal of the solvent under pressure, the residue was purified by quick chromatography on a silica gel column. Elution with hexane/EtOAc (10:1) provided **8** (156 mg, 92%) as an oil, shown by ¹H NMR analysis to consist of a 1:1 mixture of *E*- and *Z*-isomers, that was used directly in the next step.

To this solution of **8** (156 mg, 0.50 mmol) in CH₂Cl₂ (5 mL) was added CH₃SO₃H (50 μL) at 0 °C, and the mixture was stirred at room temperature for 3 h as the reaction was monitored by TLC. EtOAc (50 mL) was added, and the solution was washed with a saturated NaHCO₃ solution and dried over Na₂SO₄. After evaporation of the solvent under reduced pressure, the residue was purified by chromatography on a silica gel column. Elution with hexane/Et₂O (20:1) gave 3-methoxybenzo[*α*]pyrene (115 mg, 83%): ¹H NMR (500 MHz, CDCl₃) δ 9.02 (d, *J* = 8.5 Hz, 1 H), 8.90 (d, *J* = 8.0 Hz, 1 H), 8.47 (s, 1 H), 8.34 (d, *J* = 9.5 Hz, 1 H), 8.30–8.15 (m, 3 H), 8.00 (d, *J* = 9.5 Hz, 1 H), 7.86–7.75 (m, 2 H), 7.65 (d, *J* = 8.0 Hz, 1 H), 4.21 (s, 3 H); ¹³C NMR (125.8 MHz, CDCl₃) δ 153.5, 131.6, 130.3, 128.8, 128.0, 127.9, 127.4, 127.0, 126.5, 126.3, 126.0, 125.9, 125.5, 123.9, 123.6, 123.1, 121.4, 119.9, 119.6, 109.9, 56.3; MS (APCI) *m/z* = 283 (100%).

Benzo[α]pyren-3-ol (3-HO-BP). To a suspension of 3-methoxybenzo[α]pyrene (56 mg, 0.2 mmol) in HOAc (7 mL) was added HI (7 mL of a 57% solution) under argon. The mixture was stirred for 1.5 h at 140 °C, and the reaction was monitored by TLC. The mixture was cooled to ambient temperature and poured onto crushed ice (50 g). The solid precipitate was filtered off, washed with water, and then dissolved in EtOAc. The solution was washed with brine and dried over Na₂SO₄. Evaporation of the solvent under vacuum gave a residue that was purified by chromatography on a silica gel column. Elution with hexane/EtOAc (4:1) gave 3-HO-BP (40 mg, 75%): ¹H NMR (500 MHz, acetone-*d*₆) δ 9.53 (br s, 1H), 9.08 (d, *J* = 8.0 Hz, 1H), 8.94 (d, *J* = 9.0 Hz, 1H), 8.49 (s, 1H), 8.35–8.20 (m, 3H), 8.19 (d, *J* = 8.5 Hz, 1H), 7.99 (d, *J* = 9.5 Hz, 1H), 7.85–7.70 (m, 2H), 7.69 (d, *J* = 8.0 Hz, 1H); ¹³C NMR (125.8 MHz, acetone-*d*₆) δ 151.8, 131.7, 130.5, 128.6, 128.1, 127.8, 127.7, 126.73, 126.70, 126.3, 126.1, 125.6, 125.5, 123.9, 123.1, 123.0, 121.7, 119.3, 117.6, 115.0; MS (APCI) *m/z* = 269 (70%), 283 (100%).

2-(5-Methoxynaphthalen-2-yl)phenylacetone (11). To a solution of 2-bromophenylacetone **4** (1.214 g, 5.7 mmol) in DME (16 mL) under argon was added Pd(PPh₃)₄ (66 mg, 0.057 mmol). The resulting solution was stirred for 20 min, then boronic ester **10** (1.85 g, 6.84 mmol) and EtOH (23 mL) were added. After 20 min, a solution of Na₂CO₃ (2 M, 5.7 mL) was added, the mixture was heated at reflux for 4 h, and the reaction was monitored by TLC. The solution was cooled to room temperature, and the precipitate was filtered off and washed with EtOAc (50 mL). The filtrate was evaporated to dryness, and the residue was dissolved in EtOAc (100 mL), washed with water (3 \times 20 mL), and dried over Na₂SO₄. After evaporation of the solvent under reduced pressure, the residue was purified by chromatography on a silica gel column eluted with hexane/EtOAc (20:1) to afford **11** (1.27 g, 77%): ¹H NMR (500 MHz, CDCl₃) δ 8.33 (d, *J* = 8.5 Hz, 1H), 7.70 (d, *J* = 1.5 Hz, 1H), 7.50–7.35 (m, 6H), 7.32–7.28 (m, 1H), 6.91–6.87 (m, 1H), 4.06 (s, 3H), 3.75 (s, 2H), 2.01 (s, 3H); ¹³C NMR (125.8 MHz, CDCl₃) δ 206.6, 155.5, 142.4, 139.4, 134.3, 132.3, 130.7, 130.4, 127.8, 127.4, 127.2, 126.7, 126.6, 124.5, 122.1, 120.3, 104.0, 55.6, 48.4, 29.7; HRMS calcd for C₂₀H₁₈O₂ (M⁺) 290.1307, found 290.1309.

1-Methoxy-5-methylchrysene (12). To a dry flask was added a solution of **11** (670 mg, 2.3 mmol) in CH₂Cl₂ (21 mL) under argon. Then a solution of TiCl₄ (2.3 mL, 1 M in CH₂Cl₂) was added dropwise at –78 °C, and the resulting mixture was stirred for 3.5 h at 0 °C. The reaction was monitored by TLC and then quenched by pouring onto crushed ice (20 g). The mixture was extracted with EtOAc (3 \times 50 mL), and the combined extracts were washed with water and dried over Na₂SO₄. After evaporation of the solvent under reduced pressure, the residue was purified by chromatography on a silica gel column. Elution with hexane/EtOAc (10:1) afforded **12** along with a minor unidentified compound. Recrystallization from EtOH gave pure **12** (425 mg, 68%): ¹H NMR (500 MHz, CDCl₃) δ 8.80–8.72 (m, 2H), 8.56 (d, *J* = 8.5 Hz, 1H), 8.53 (d, *J* = 9.5 Hz, 1H), 7.90 (dd, *J* = 9.0 and 1.5 Hz, 1H), 7.85 (s, 1H), 7.70–7.55 (m, 3H), 7.05 (d, *J* = 7.5 Hz, 1H), 4.11 (s, 3H), 3.23 (s, 3H); ¹³C NMR (125.8 MHz, CDCl₃) δ 155.4, 133.2, 132.6, 131.6, 130.3, 130.0, 129.4, 129.1, 127.2, 126.3, 125.7, 125.1, 124.7, 123.1, 120.9, 120.7, 120.0, 104.6, 55.5, 27.8; MS (APCI) *m/z* = 273 (100%).

1-Methoxy-5-formylchrysene (13b). Bromination of **12** (272 mg, 1 mmol) with NBS (196 mg, 1.1 mmol) was carried out by the procedure employed for the preparation of **7a**. The product **13a** was reacted with DMSO (2.83 mL) and NaHCO₃ (168 mg, 2 mmol) according to the procedure employed for the synthesis of **7b**. Purification of the product by chromatography on silica gel gave **13b** (213 mg, 74%): ¹H NMR (500 MHz, CDCl₃) δ 10.60 (s, 1H), 8.72 (d, *J* = 8.5 Hz, 1H), 8.64 (d, *J* = 9.0 Hz, 1H), 8.52 (d, *J* = 9.5 Hz, 1H), 8.41 (s, 1H), 8.09 (d, *J* = 8.0 Hz, 1H), 7.78 (t, *J* = 7.5 Hz, 1H), 7.75–7.50 (m, 3H), 7.05 (d, *J* = 7.5 Hz, 1H), 4.09 (s, 3H); ¹³C NMR (125.8 MHz, CDCl₃) δ 193.2, 155.8, 133.7,

132.0, 130.6, 130.41, 130.40, 130.0, 129.9, 129.1, 127.2, 126.7, 126.3, 124.6, 123.3, 122.1, 120.9, 120.2, 105.6, 55.8; HRMS calcd for C₂₀H₁₄O₂ (M⁺) 286.0994, found 286.0999.

1-Methoxybenzo[α]pyrene (1-MeO-BP). The conversion of **13b** (162 mg, 0.566 mmol) to 1-MeO-BP was carried out by a procedure analogous to that employed for the synthesis of 3-MeO-BP from **7b**. 1-MeO-BP was obtained (117 mg, 73%): ¹H NMR (500 MHz, CDCl₃) δ 9.05–8.95 (m, 2H), 8.67 (d, *J* = 9.5 Hz, 1H), 8.38 (s, 1H), 8.24 (dd, *J* = 9.5 and 2.0 Hz, 1H), 7.96 (d, *J* = 8.5 Hz, 1H), 7.83–7.75 (m, 3H), 7.42–7.37 (m, 2H), 4.17 (s, 3H); ¹³C NMR (125.8 MHz, CDCl₃) δ 154.1, 131.6, 130.3, 128.7, 128.0, 127.8, 127.7, 126.4, 126.1, 125.6, 125.5, 125.23, 125.19, 124.0, 123.8, 123.1, 121.6, 121.4, 121.3, 106.5, 56.0; MS (APCI) *m/z* = 283 (100%).

Benzo[α]pyrene-1-ol (1-HO-BP). To a suspension of 1-MeO-BP (74 mg, 0.262 mmol) in HOAc (9 mL) was added a HI solution (57%, 9 mL) under argon. The mixture was stirred for 1.5 h at 140 °C, and the reaction was monitored by TLC. Then the mixture was cooled to room temperature and poured onto crushed ice (50 g). The resulting precipitate was filtered off and washed with water. Then it was dissolved in EtOAc, washed with brine, and dried over Na₂SO₄. After evaporation of the solvent under vacuum, the residue was purified by chromatography on a silica gel column. Elution with hexane/EtOAc (4:1) provided 1-HO-BP (56 mg, 80%): ¹H NMR (500 MHz, DMSO-*d*₆) δ 10.80 (br s, 1H), 9.20–9.10 (m, 2H), 8.60 (d, *J* = 9.0 Hz, 1H), 8.54 (s, 1H), 8.32 (d, *J* = 8.0 Hz, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.92–7.75 (m, 4H), 7.52 (d, *J* = 8.0 Hz, 1H); ¹³C NMR (125.8 MHz, DMSO-*d*₆) δ 153.1, 131.6, 130.4, 129.0, 128.4, 128.1, 127.5, 126.8, 126.6, 126.5, 126.2, 124.9, 124.0, 123.9, 123.8, 123.6, 122.4, 121.4, 120.5, 112.1; MS (APCI) *m/z* = 269 (70%), 283 (100%).

2-(7-Methoxynaphthalene-6-yl)benzene-1,3-dialdehyde (16). 2-Bromobenzene-1,3-dialdehyde **15** was synthesized by the reported method.³¹ To a solution of **15** (104 mg, 0.49 mmol) in DME (1 mL) under argon was added Pd(PPh₃)₄ (6 mg, 0.005 mmol). The resulting solution was stirred for 20 min, then boronic ester **3** (175 mg, 0.65 mmol) and EtOH (1.6 mL) were added. After 20 min, a solution of Na₂CO₃ (2 M, 0.5 mL) was added, the mixture was heated at reflux for 4 h, and the reaction was monitored by TLC. Then it was cooled to room temperature, and the precipitate was filtered off and washed with EtOAc (20 mL). The filtrate was evaporated to dryness. The residue was dissolved in EtOAc (30 mL), washed with water (3 \times 10 mL), and dried over Na₂SO₄. After evaporation of the solvent under reduced pressure, the residue was purified by chromatography on a silica gel column. Elution with hexane/EtOAc (10:1) afforded **16** (124 mg, 88%): ¹H NMR (500 MHz, CDCl₃) δ 9.85 (s, 2H), 8.27 (d, *J* = 8.0 Hz, 2H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.74 (s, 1H), 7.68 (t, *J* = 8.0 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 1H), 7.17 (s, 1H), 3.94 (s, 3H); ¹³C NMR (125.8 MHz, CDCl₃) δ 190.9, 158.7, 148.2, 134.8, 133.8, 132.6, 130.2, 129.34, 129.31, 128.4, 128.3, 127.9, 125.8, 120.2, 105.7, 55.3; HRMS calcd for C₁₉H₁₄O₃ (M⁺) 290.0943, found 290.0948.

9-Methoxybenzo[α]pyrene. To a suspension of methoxymethyltriphenylphosphonium chloride (324 mg, 0.95 mmol) in anhydrous THF (1.5 mL) under argon at room temperature was added *t*-BuOK (0.95 mL, 1 M in THF) dropwise. The resulting mixture was stirred at room temperature for 1.5 h, and a solution of **15** (120 mg, 0.395 mmol) in THF (2 mL) was added. The resulting mixture was stirred for 1.5 h, monitored by TLC, and quenched by dilution with Et₂O (50 mL). The precipitate was filtered off, washed with Et₂O (30 mL), and the solvent was removed under pressure. The residue was chromatographed on a silica gel column eluted with hexane/EtOAc (10:1) to provide **17** as an oil (123 mg, 90%) that was used directly in the next step.

To a solution of **17** (123 mg, 0.36 mmol) in CH₂Cl₂ (4.5 mL) was added CH₃SO₃H (50 μ L) at 0 °C. The mixture was stirred for 2.5 h at room temperature, and the reaction was monitored by TLC. Reaction was quenched by dilution with EtOAc (50 mL), and the

solution was washed with a saturated NaHCO₃ solution and dried over Na₂SO₄. After evaporation of the solvent under reduced pressure, the residue was purified by chromatography on a silica gel column. Elution with hexane/Et₂O (20:1) afforded 9-methoxybenzo[*a*]pyrene (71 mg, 70%): ¹H NMR (500 MHz, CDCl₃) δ 8.81 (d, *J* = 9.0 Hz, 1 H), 8.35 (s, 1 H), 8.23–8.15 (m, 3 H), 8.12 (d, *J* = 9.0 Hz, 1 H), 8.05 (d, *J* = 7.5 Hz, 1 H), 7.97 (t, *J* = 7.5 Hz, 1 H), 7.91 (d, *J* = 9.0 Hz, 1 H), 7.84 (d, *J* = 9.0 Hz, 1 H), 7.43 (dd, *J* = 9.0 and 2.0 Hz, 1 H), 4.10 (s, 3 H); ¹³C NMR (125.8 MHz, CDCl₃) δ 158.0, 131.8, 131.5, 130.5, 129.4, 128.2, 127.9, 126.9, 126.73, 126.70, 126.1, 126.0, 125.5, 125.0, 124.6, 124.4, 124.1, 122.1, 118.5, 101.9, 55.5; MS (APCI) *m/z* = 283 (100%).

Benzo[*a*]pyren-9-ol (9-HO-BP). To a solution of 9-MeO-BP (64 mg, 0.226 mmol) in dry CH₂Cl₂ (15 mL) at –20 °C was added dropwise a solution of BBr₃ (1 M in CH₂Cl₂, 1.2 mL). 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 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 Na₂SO₄, and evaporated to dryness. The residue was chromatographed on a silica gel column eluted with 10–25% EtOAc in hexane to give 9-HO-BP (44 mg, 72%): ¹H NMR (500 MHz, acetone-*d*₆) δ 9.11 (br s, 1 H), 8.90 (d, *J* = 9.0 Hz, 1 H), 8.50 (s, 1 H), 8.45 (d, *J* = 2.0 Hz, 1 H), 8.29 (d, *J* = 9.0 Hz, 1 H), 8.22 (t, *J* = 7.5 Hz, 2 H), 8.08 (d, *J* = 7.5 Hz, 1 H), 8.00–7.90 (m, 2 H), 7.87 (d, *J* = 9.0 Hz, 1 H), 7.49 (dd, *J* = 9.0 and 2.0 Hz, 1 H); ¹³C NMR (125.8 MHz, acetone-*d*₆) δ 156.3, 131.9, 131.7, 130.8, 130.1, 128.3, 127.4, 126.9, 126.4, 126.3, 126.2, 125.8, 125.4, 125.0, 124.9, 124.3, 124.0, 122.3, 118.7, 105.1; MS (APCI) *m/z* = 269 (85%), 283 (100%).

1-Methyl-2-naphthyl trifluoromethanesulfonate (18b). To a solution of 1-methylnaphthalen-2-ol (6.32 g, 40 mmol) and pyridine (60 mmol) in CH₂Cl₂ (200 mL) was added Tf₂O (50 mmol) dropwise at 0 °C under argon. The mixture was stirred at room temperature for 3 h, then the reaction was quenched by the addition of water (50 mL). The organic layer was washed with water (3 × 50 mL) and brine (50 mL) and dried over Na₂SO₄. After removal of the solvent under reduced pressure, the residue was purified by chromatography on a silica gel column eluted with hexane/EtOAc (10:1) to afford **18b** (10.67 g, 92%): ¹H NMR (500 MHz, CDCl₃) δ 8.07 (d, *J* = 8.5 Hz, 1 H), 7.90 (d, *J* = 8.0 Hz, 1 H), 7.79 (d, *J* = 8.0 Hz, 1 H), 7.70–7.55 (m, 2 H), 7.39 (d, *J* = 9.0 Hz, 1 H), 2.73 (s, 3 H); ¹³C NMR (125.8 MHz, CDCl₃) δ 145.4, 133.2, 132.4, 128.6, 128.4, 127.3, 126.7, 126.5, 124.6, 119.5, 118.7 (q, *J* = 320.1 Hz), 12.2; ¹⁹F NMR (470.6 MHz, CDCl₃) δ –73.7; HRMS calcd for C₁₂H₉O₃F₃S (M⁺) 290.0225, found 290.0226.

2-(1-Methyl-2-naphthyl)benzaldehyde (20). Synthesis of **20** was carried out by the procedure for the synthesis of **15**. Reaction of **19** (1.219 g, 4.8 mmol) with 2-bromobenzaldehyde (0.74 g, 4.0 mmol) provided **20** (0.728 g, 74%): ¹H NMR (500 MHz, CDCl₃) δ 9.86 (s, 1 H), 8.15 (d, *J* = 7.5 Hz, 2 H), 7.96 (d, *J* = 8.0 Hz, 1 H), 7.83 (d, *J* = 8.0 Hz, 1 H), 7.75–7.55 (m, 4 H), 7.45–7.37 (m, 2 H), 2.53 (s, 3 H); ¹³C NMR (125.8 MHz, CDCl₃) δ 192.0, 146.2, 134.3, 134.0, 133.5, 133.0, 132.4, 132.1, 131.0, 128.5, 127.9, 127.7, 126.9, 126.6, 126.0, 125.9, 124.3, 16.2; HRMS calcd for C₁₈H₁₄O (M⁺) 246.1045, found 246.1064.

12-Methylbenzo[*a*]anthracene (22a). Synthesis of **22a** was carried out by a procedure based on that employed for the synthesis of 3-MeO-BP. Reaction of **20** (738 mg, 3.0 mmol) by this method gave **22a** (363 mg, 50%): ¹H NMR (500 MHz, CDCl₃) δ 8.65 (d, *J* = 9.0 Hz, 1 H), 8.39 (d, *J* = 9.0 Hz, 1 H), 8.23 (s, 1 H), 8.08 (d, *J* = 8.0 Hz, 1 H), 7.89 (d, *J* = 9.0 Hz, 1 H), 7.80–7.55 (m, 6 H), 3.43 (s, 3 H); ¹³C NMR (125.8 MHz, CDCl₃) δ 133.8, 132.6, 131.52, 131.47, 131.4, 131.2, 129.8, 128.8, 128.4, 128.11, 128.06, 126.9, 126.5, 125.8, 125.4, 125.3, 125.2, 125.1, 20.9; MS (APCI) *m/z* = 243 (100%).

6-Formyloxybenzo[*a*]pyrene (24). 6-Formylbenzo[*a*]pyrene **23** was synthesized from BP by the procedure described previously.³³ To a solution of **23** (219 mg, 0.782 mmol) in CH₂Cl₂ (60 mL) was added *m*-chloroperbenzoic acid (403 mg, 2.35 mmol), and the mixture was stirred at room temperature for 72 h. Sodium thiosulfate (10 mL of a 10% aqueous solution) was added, stirring was continued for 30 min, and the mixture was poured into an aqueous Na₂S₂O₃ solution (10 mL). The aqueous phase was extracted with CH₂Cl₂ (50 mL) and combined with the organic layer, and the combined organic phase was washed with 10% aqueous sodium thiosulfate and brine, dried, and evaporated to dryness. The residue was purified by chromatography on silica gel. Elution with hexane/EtOAc (10:1) afforded pure **24** (93 mg, 40%): ¹H NMR (500 MHz, CDCl₃) δ 9.07 (d, *J* = 8.5 Hz, 1 H), 9.01 (d, *J* = 9.0 Hz, 1 H), 8.78 (s, 1 H), 8.31 (d, *J* = 8.5 Hz, 2 H), 8.26 (d, *J* = 7.5 Hz, 1 H), 8.11 (d, *J* = 7.5 Hz, 1 H), 8.10–7.90 (m, 3 H), 7.90–7.80 (m, 2 H); ¹³C NMR (125.8 MHz, CDCl₃) δ 160.1, 139.4, 131.4, 130.9, 129.5, 128.6, 127.7, 127.0, 126.53, 126.49, 126.47, 126.4, 125.6, 125.0, 124.5, 123.7, 123.4, 121.93, 121.86, 121.2, 120.4; HRMS calcd for C₂₁H₁₂O₂ (M⁺) 296.0837, found 296.0817.

Benzo[*a*]pyren-9,10-dione (BP 9,10-dione). To a solution of 9-HO-BP (27 mg, 0.1 mmol) in DMSO (2 mL) was added IBX (56 mg, 0.2 mmol). The mixture was stirred at room temperature for 2 h. The purple precipitate was filtered off and purified by chromatography on a column of silica gel. Elution with EtOAc/CHCl₃ (1:10) gave BP 9,10-dione (23 mg, 82%) as a purple solid: ¹H NMR (500 MHz, CDCl₃) δ 9.77 (d, *J* = 9.5 Hz, 1 H), 8.40–8.25 (m, 4 H), 8.15–8.10 (m, 2 H), 8.02 (s, 1 H), 7.74 (d, *J* = 10.0 Hz, 1 H), 6.60 (d, *J* = 9.5 Hz, 1 H); ¹³C NMR (125.8 MHz, CDCl₃) δ 181.9, 181.6, 147.6, 136.5, 134.8, 133.7, 133.6, 132.2, 131.4, 130.4, 128.5, 128.2, 128.0, 127.6, 127.5, 127.4, 125.6, 125.5, 123.7, 122.2; MS (APCI) *m/z* = 283 (100%).

Benzo[*a*]pyren-1,6-dione (BP 1,6-dione). To a solution of BTI (63 mg, 0.147 mmol) in CH₃CN/H₂O (v/v = 2/1, 1 mL) was added 1-HO-BP (18 mg, 0.067 mmol) in CH₃CN/acetone/water (v/v/v = 5/2.5/2, 9.5 mL) dropwise under argon, and the mixture was stirred at room temperature for 1.5 h. The orange solid was filtered off and purified by chromatography on a silica gel column. Elution with CHCl₃/EtOAc (10:1) afforded BP-1,6 dione (15 mg, 78%) as an orange solid: ¹H NMR (500 MHz, CDCl₃) δ 8.67 (d, *J* = 7.5 Hz, 1 H), 8.64 (d, *J* = 8.0 Hz, 1 H), 8.56 (d, *J* = 8.0 Hz, 1 H), 8.47 (dd, *J* = 8.0 and 1.5 Hz, 1 H), 8.34 (d, *J* = 8.0 Hz, 1 H), 7.91 (d, *J* = 7.5 Hz, 1 H), 7.80 (dt, *J* = 8.0 and 1.5 Hz, 1 H), 7.74 (d, *J* = 10.0 Hz, 1 H), 7.64 (dt, *J* = 7.5 and 0.5 Hz, 1 H), 6.78 (d, *J* = 10.0 Hz, 1 H); ¹³C NMR (125.8 MHz, CDCl₃) δ 185.3, 183.4, 141.2, 135.1, 134.1, 133.9, 133.6, 131.1, 130.91, 130.86, 130.5, 130.1, 129.9, 129.6, 129.2, 128.7, 127.7, 127.2, 123.99, 123.97; MS (APCI) *m/z* = 283 (100%).

Benzo[*a*]pyren-3,6-dione (BP 3,6-dione). Oxidation of 3-HO-BP (30 mg, 0.112 mmol) with BTI (105 mg, 0.244 mmol) by the procedure employed in the preceding example gave BP 3,6-dione (26 mg, 82%) as a red solid: ¹H NMR (500 MHz, CDCl₃) δ 8.84 (d, *J* = 7.5 Hz, 1 H), 8.74 (d, *J* = 7.5 Hz, 1 H), 8.47 (dd, *J* = 8.0 and 1.0 Hz, 1 H), 8.39 (d, *J* = 7.5 Hz, 1 H), 8.29 (d, *J* = 8.0, 1 H), 7.85–7.70 (m, 3 H), 7.61 (t, *J* = 7.5 Hz, 1 H), 6.73 (d, *J* = 9.5 Hz, 1 H); ¹³C NMR (125.8 MHz, CDCl₃) δ 185.3, 183.6, 141.8, 135.4, 134.1, 132.8, 132.1, 131.4, 131.0, 130.7, 129.7, 129.6, 129.4, 129.1, 129.0, 128.7, 127.98, 127.96, 124.0, 123.5; MS (APCI) *m/z* = 283 (100%).

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Supporting Information Available: ¹H and ¹³C NMR spectra of reported compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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