Tetrahedron 66 (2010) 2111–2118

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Regiospecific oxidation of polycyclic aromatic phenols to quinones by hypervalent iodine reagents

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ARTICLE INFO

Article history:
Received 30 July 2009
Received in revised form 3 December 2009
Accepted 4 December 2009
Available online 11 December 2009

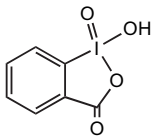
ABSTRACT

The hypervalent iodine reagents *o*-iodoxybenzoic acid (IBX) and bis(trifluoro-acetoxy)iodobenzene (BTI) are shown to be general reagents for regio-controlled oxidation of polycyclic aromatic phenols (PAPs) to specific isomers (*ortho*, *para*, or remote) of polycyclic aromatic quinones (PAQs). The oxidations of a series of PAPs with IBX take place under mild conditions to furnish the corresponding *ortho*-PAQs. In contrast, oxidations of the same series of PAPs with BTI exhibit variable regiospecificity, affording *para*-PAQs where structurally feasible and *ortho*-PAQs or remote PAQ isomers in other cases. The structures of the specific PAQ isomers formed are predictable on the basis of the inherent regioselectivities of the hypervalent iodine reagents in combination with the structural requirements of the phenol precursors. IBX and BTI are recommended as the preferred reagents for regio-controlled oxidation of PAPs to PAQs.

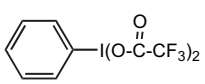
1. Introduction

Although methods for regioselective oxidation of monocyclic phenols to quinones have been extensively investigated, relatively little is known concerning analogous oxidations of polycyclic aromatic phenols (PAPs) to polycyclic aromatic quinones (PAQs). In connection with studies directed toward determination of the role of the quinone metabolites of polycyclic aromatic hydrocarbons (PAHs) in carcinogenesis,[1–10] we required an efficient method for regioselective synthesis of PAQs from PAPs.

The reagent most frequently employed for oxidation of PAPs to PAQs is Fremy's salt $[(KSO_3)_2NO]$.[3,11] However, oxidations with Fremy's salt frequently afford mixtures of *ortho*- and *para*-quinone isomers accompanied by secondary oxidation products, and the results are often erratic and difficult to reproduce. Fremy's salt also has the limitation that aqueous media are required, and PAH compounds are poorly soluble in water.



IBX



BTI

A promising new reagent for regio-controlled oxidation of PAPs is the hypervalent iodine compound *o*-iodoxybenzoic acid (IBX). IBX is a mild oxidant, that is, moderately soluble in organic solvents and is widely employed for oxidation of alcohols.[12] Its use for oxidation of simple phenols to *ortho*-quinones has been described,[13] and we reported several examples of IBX oxidation of PAPs to the corresponding *ortho*-PAQs.[14] Another potentially useful hypervalent iodine reagent is bis(trifluoro-acetoxy)iodobenzene $[(CF_3CO_2)_2IC_6H_5]$ (BTI). Oxidation of several 1-naphthol derivatives by BTI was reported to furnish *para*-naphthoquinones.[15]

2. Results

With the aim of developing more efficient methods for regio-controlled oxidation of PAPs to PAQs, we undertook to investigate the use of the hypervalent iodine reagents IBX and BTI for this purpose. Oxidation of PAPs may result in formation of three types of PAQ isomers—*ortho*, *para*, and/or *remote*. *Remote* quinone isomers are defined as quinones with carbonyl functions in different rings, e.g., pyren-1,6-dione.

Oxidations of a series of PAPs by IBX were conducted at room temperature in DMF. All reactions took place regiospecifically to furnish the corresponding *ortho*-PAQ isomers (Table 1). Thus, IBX oxidation of 1- and 2-naphthol both provided 1,2-naphthoquinone (**1**) as the sole isomeric quinone product. Similarly, IBX oxidations of 1- and 2-phenanthrol both furnished phenanthren-1,2-dione (**3**), and IBX oxidations of 3- and 4-phenanthrol both provided phenanthren-3,4-dione (**5**). It is worthy of note that oxidation of

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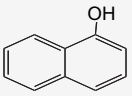
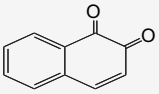
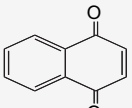
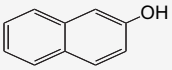
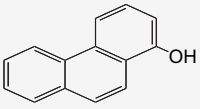
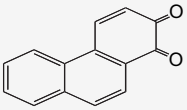
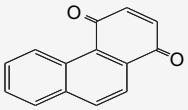
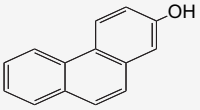
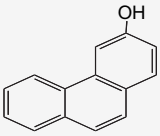
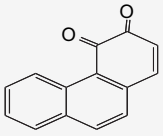
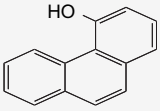
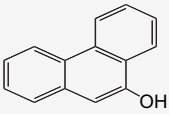
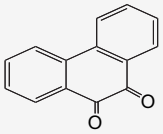
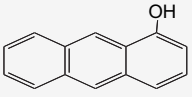
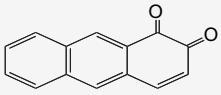
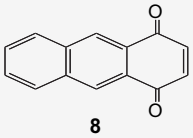
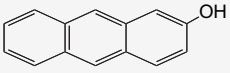
0040-4020/$ – see front matter © 2009 Published by Elsevier Ltd.
doi:10.1016/j.tet.2009.12.022

Table 1
Oxidation of Polycyclic Aromatic Phenols to Quinones by IBX and BTI[a]

Phenol	IBX	Yield (%)	BTI	Yield (%)
	 **1**	53	 **2**	68
	**1**	51	**1**	61
	 **3**	70	 **4**	75
	**3**	51	**3**	68
	 **5**	59	**5**	38
	**5**	62	**4**	50
	 **6**	61	**6**	95
	 **7**	63	 **8**	67
	**7**	65	**7**	69

[a] IBX oxidations were conducted in DMF at room temperature. BTI reactions were carried out in aqueous DMF at 0 °C.

4-phenanthrol by IBX proceeded readily despite the severe steric crowding of the hydroxyl group in the bay molecular region. Finally, IBX oxidation of 9-phenanthrol provided phenanthren-9,10-dione (**6**), and IBX oxidations of 1- and 2-anthracenol both took place *ortho*-regiospecifically to furnish anthracen-1,2-dione (**7**). Oxidation of 9-anthracenol by IBX could not investigated because this phenol exists exclusively as the anthrone tautomer under the conditions employed.

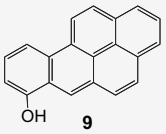
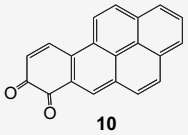
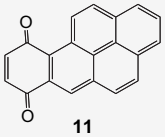
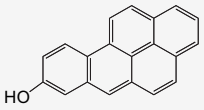
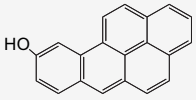
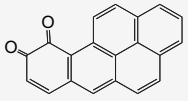
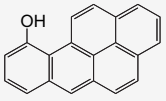
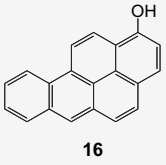
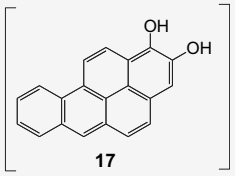
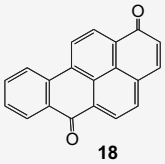
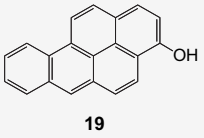
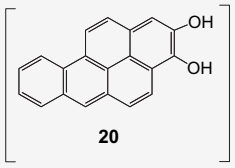
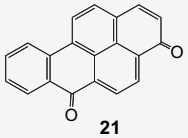
The analogous oxidations with BTI were carried out in aqueous DMF at 0 °C. They exhibited variable regioselectivities, affording *para*-PAQs in some cases and *ortho*-PAQs in others (Table 1). Oxidation of 1-naphthol by BTI gave 1,4-naphthoquinone (**2**), but oxidation of 2-naphthol by BTI furnished 1,2-naphthoquinone (**1**). Oxidations of 1- and 4-phenanthrol by BTI both provided phenanthren-1,4-dione (**4**).

In contrast, oxidations of 2- and 3-phenanthrol with BTI provided the *ortho*-quinone isomers, **3** and **5**, respectively. Oxidation of 9-phenanthrol by BTI also took place regiospecifically to furnish the corresponding *ortho*-quinone, phenanthren-9,10-dione (**6**). And finally, BTI oxidation of 1-anthracenol gave the *para*-quinone isomer, anthracen-1,4-dione (**8**), whereas analogous oxidation of 2-anthracenol gave the *ortho*-quinone isomer, anthracen-1,2-dione (**7**).

In order to further probe the scope of IBX/BTI oxidation of PAPs for the synthesis of PAQs, several additional examples were investigated (Table 2). The phenol and quinone isomers of benzo[*a*]pyrene (BaP) were of particular interest because several phenol and quinone isomers are among the principal metabolites of this widespread environmental carcinogen,[10b] and recent research has implicated BaP-7,8-dione (**10**) as an active metabolite of BaP that contributes to induction of lung cancer.[1,10] Oxidations of the 7- and 8-phenols of BaP (**9** and **12**) with IBX both took place *ortho*-regiospecifically to furnish **10**.[16] Analogous oxidations of the BaP 9- and 10-phenols (**13** and **15**) with IBX also took place *ortho*-regiospecifically to furnish BaP-9,10-dione (**14**).

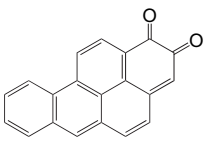
The oxidations of the same BaP phenol isomers with BTI took a different course. Oxidations of the 7- and 10-phenols of BaP

Table 2
Oxidation of phenol isomers of benzo[*a*]pyrene by IBX and BTI

Phenol	IBX	Yield (%)	BTI	Yield (%)
 **9**	 **10**	68	 **11**	60
 **12**	**10**	80	**10**	46
 **13**	 **14**	82	**14**	82
 **15**	**14**	95	**11**	47
 **16**	 **17**		 **18**	78 reported
 **19**	 **20**		 **21**	82 (reported)

(**9** and **15**) with BTI both furnished the *para*-quinone isomer, BaP-7,10-dione (**11**), as the sole product. In contrast, analogous oxidations of the 8- and 9-phenols of BaP (**12** and **13**) with BTI provided the *ortho*-quinone isomers, BaP-7,8-dione (**10**) and BaP-9,10-dione (**14**), respectively. These findings parallel the findings from the analogous oxidations of the phenol isomers of phenanthrene and anthracene.

The 1- and 3-phenol isomers of BaP (**16**, **19**) differ structurally from the phenol isomers of BaP considered thus far (**9**, **12**, **13**, **15**) by the location of the phenolic OH group in a pyrenyl ring rather than a benzo ring. Attempted oxidation of **16** and **19** by IBX failed to furnish the expected *ortho*-quinone isomers, BaP-1,2-dione (**22**) and BaP-2,3-dione (**23**) (neither of these isomers are known). TLC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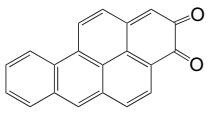
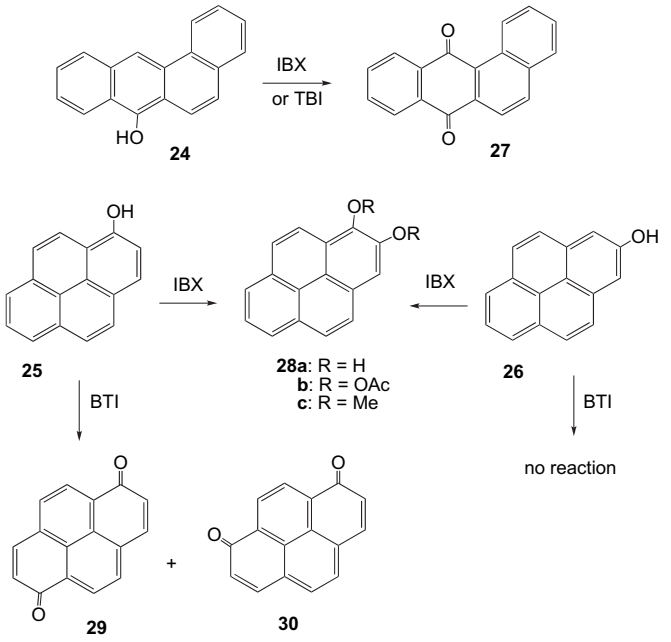

23

monitoring of these reactions showed disappearance of the phenols with concurrent formation of more polar products that decomposed on standing. These unstable products are believed to be the catechol intermediates, BaP-1,2-diol (**17**) and BaP-2,3-diol (**20**). Polycyclic aromatic catechols are known to be unstable and susceptible to oxidative decomposition in air. The catechol structures are supported by evidence from similar oxidations of the structurally related pyrene phenols (see below). In contrast, reactions of **16** and **19** with BTI took place readily to furnish the *remote* quinone isomers, BaP-1,6-dione (**18**) and BaP-3,6-dione (**21**). TLC showed that significant amounts of other quinone isomers were not formed. Reaction at the 6-position is consistent with the well-established propensity of BaP to undergo all types of reactions at the 6-position.[3]

Oxidations of three additional PAH phenols (**24**–**26**) with IBX and BTI were also investigated (Scheme 1). Oxidations of benz[*a*]anthracen-7-ol (**24**) with IBX and BTI both gave the *para*-quinone isomer, benz[*a*]anthracen-7,12-dione (**27**) as the sole product. This is the only example of IBX oxidation furnishing a *para*-quinone isomer.

Oxidation of 1-pyrenol (**25**) with IBX (Scheme 1) followed a course similar to the oxidations of the 1- and 3-phenols of BaP (**16**, **19**). Disappearance of **25** was shown by TLC to be accompanied by formation of an unstable more polar product believed to be the catechol, pyrene-1,2-diol (**28a**). The amount of **28a** formed increased with higher temperature, excess IBX, and longer reaction time. When reaction appeared complete acetylation of **28a** with Ac_2O/pyridine furnished the stable catechol diacetate (**28b**). Its NMR spectrum was consistent with this structural assignment. Oxidation of 1-pyrenol (**25**) with BTI provided a mixture of the pyrene-1,6- and 1,8-dione isomers (**29**,**30**) in 3:2 ratio. Oxidation of 2-pyrenol (**26**) with IBX proceeded similarly to oxidation of 1-pyrenol (**25**), furnishing an air-sensitive catechol that was



Scheme 1.

acetylated to yield the catechol diacetate (**28b**). However, BTI failed to react with **26**.

3. Discussion

These studies demonstrate that the hypervalent iodine compounds IBX and BTI are general reagents for regio-controlled oxidation of PAPs to specific PAQ isomers (*ortho*, *para*, or remote) under mild conditions. The IBX oxidations are regiospecific, providing exclusively the *ortho*-PAQs. The only exception is benz[*a*]anthracen-7-ol (**24**), which is incapable of forming an *ortho*-isomer. In contrast, the BTI oxidations exhibit variable regiospecificities, affording *para*-PAQ isomers where structurally possible and *ortho*-PAQs or remote PAQs in other cases.

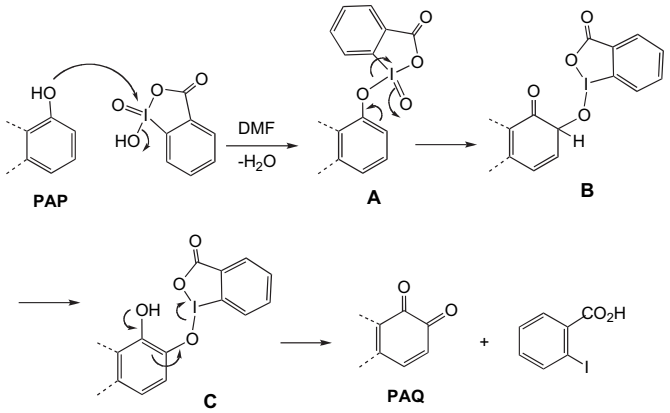


Figure 1. Plausible mechanism for IBX oxidation of PAPs to PAQs.

3.1. Mechanisms of oxidation of PAPs to PAQs

The observed regioselectivities are consistent with current understanding of the mechanisms of these types of oxidations. The strict *ortho*-selectivity of the IBX-mediated oxidations of PAPs is most satisfactorily explained by the ionic mechanism proposed by Quideau and associates for IBX-mediated oxidation of 1-naphthol.[17,18] This pathway (Fig. 1) entails initial reaction of the phenol with the iodine atom of IBX to form an intermediate complex (**A**) with loss of H_2O. Complex **A** may then undergo sigmatropic transfer of oxygen from the λ^5-iodanyl moiety to the carbon atom adjacent to the oxygen function of the PAP with concomitant reduction to the λ^3-iodanyl state to form **B**. Then, only a tautomeric shift (**C**) is needed to generate the *ortho*-PAQ along with a two-electron displacement to form reduced 2-iodobenzoic acid. It is not necessary to postulate formation of a catechol intermediate, and the observed stoichiometry is consistent with this mechanism.

The variable regiospecificities observed in the BTI-mediated oxidations of PAPs are explicable in terms of a mechanism that involves initial reaction of the phenols with BTI with displacement of trifluoroacetate to form intermediate **A** (Fig. 2).[15] The second oxygen atom derives from reaction of **A** with water. For simple

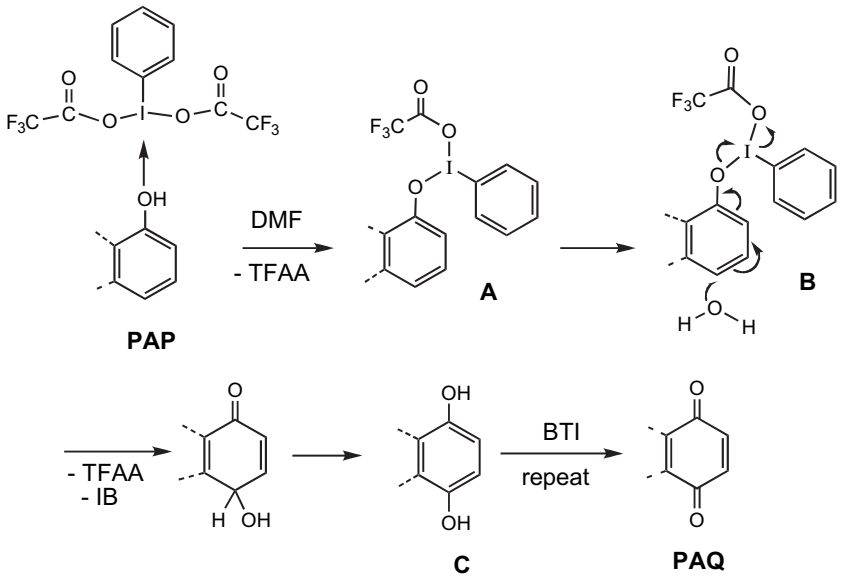
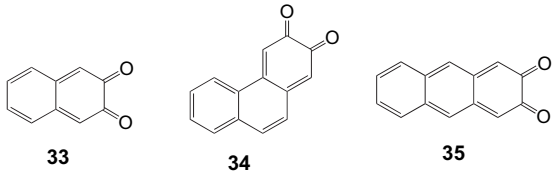


Figure 2. Plausible mechanism for BTI oxidation of PAPs to PAQs.

phenols that possess an unsubstituted *para*-position, such as 1-naphthol, reaction takes place preferentially at this position (**B**), generating a *para*-ketol that rearranges to a *para*-catechol (**C**). Intermediate **C** then undergoes a second oxidation via a similar pathway to yield a *para*-**PAQ** plus iodobenzene and trifluoroacetic acid. In contrast to the IBX-mediated oxidations that require only one equivalent of IBX, two equivalents of BTI are required for complete conversion to the **PAQ** via this pathway, and this agrees with the observed stoichiometry.

The structural dependency of the regioselectivities of BTI-mediated oxidation is also readily explicable on the basis of the same mechanism. The principal determinant is the availability of an unsubstituted *para*-position. Oxidation of PAPs that possess such a position (1-naphthol, 1-phenanthrol, 4-phenanthrol, 1-anthracenol, 9, 15, and 24) yield the *para*-PAQs. On the other hand, oxidations of PAPs that lack an unsubstituted *para*-position (all others), furnish the *ortho*-PAQ isomers. In the former instances, the initially-formed intermediate **A** (Fig. 2) reacts with water at the less sterically restricted *para*-position, yielding the *para*-**PAQ** isomer. In cases where the PAP lacks an unsubstituted *para*-position, e.g., 2-naphthol, reaction can only occur at a relatively crowded *ortho*-position, resulting in formation of an *ortho*-**PAQ**.

Where more than a one *ortho*-position is available, reaction with water takes place preferentially at a position adjacent to a fused aromatic ring. Thus, BTI oxidations of 2-naphthol, 2-phenanthrol, 3-phenanthrol, and 2-anthracenol occur at the *ortho* site adjacent to the aromatic ring to furnish **1**, **3**, **5**, and **7**, respectively. The alternative *ortho*-quinone isomers [naphthalen-2,3-one (**31**), phenanthren-2,3-dione (**32**), and anthracen-2,3-one (**33**)] were not detected, nor were any *remote* quinone isomers. Preferential oxidation at an *ortho* site adjacent to a fused aromatic ring is likely due to the stabilizing effect of the aromatic system on the reaction intermediate.

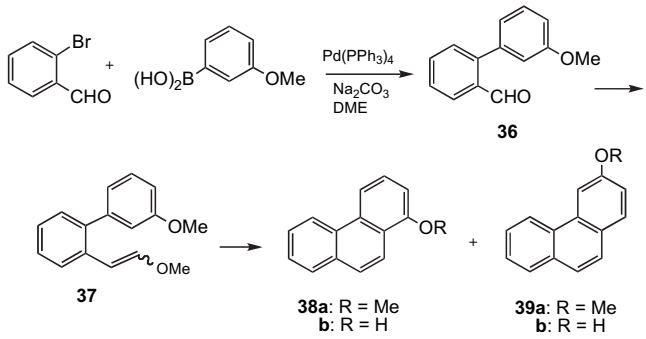


3.2. Comparison of IBX- and BTI-mediated oxidation of PAPs with other methods

The observed regiospecificities of the oxidations of PAPs with IBX and BTI contrast with the lower regioselectivities reported for oxidations of PAPs with other reagents. Fremy's salt, the reagent most frequently employed proceeds via a radical mechanism and exhibits variable regioselectivity, often providing mixtures of *ortho*- and *para*-quinone isomers as well as secondary products. For example, oxidation of 1-phenanthrol by Fremy's salt affords the 1,2- and 1,4-quinones (**3** and **4**) in approximately equal ratio.[19] In contrast, oxidation of the same phenol by IBX gave only the *ortho*-quinone (**3**), and its oxidation by BTI provided only the *para*-quinone (**4**). Both reactions were regiospecific within experimental limits. An alternative reagent that has also been employed for oxidation of PAPs is phenylseleninic anhydride [$(PhSeO)_2O$],[20] also known as Barton's reagent. It tends to furnish predominantly the *ortho*-PAQ isomers, but the results are variable.[20] On the basis of the demonstrated regioselectivity and predictability of IBX and BTI in combination with the relative convenience and simplicity of the procedures for their use, we recommend them as the reagents of choice for oxidation of PAPs to PAQs.

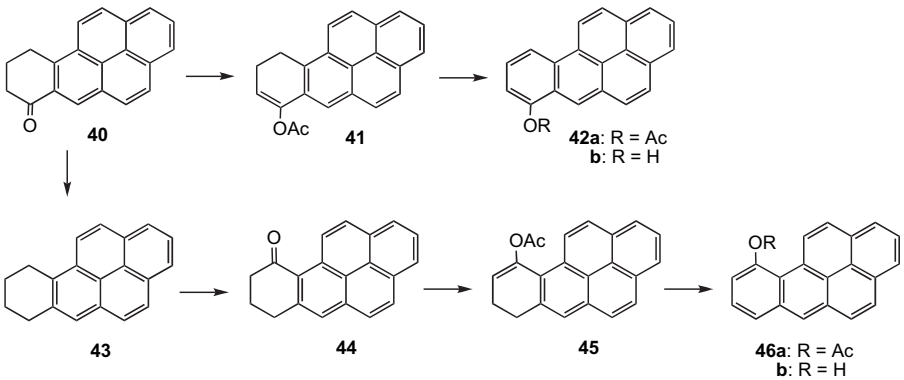
3.2.1. Syntheses of the PAPs. Only three of the PAPs employed in this investigation (1- and 2-naphthol and 9-phenanthrol) were available from commercial sources. Although procedures for the synthesis of the remaining PAPs have been reported, they use classical synthetic methods that entail large numbers of steps and/or have other practical disadvantages. We, therefore, undertook to develop more convenient new synthetic approaches.

Syntheses of the 1-, 3-, and 4-phenols of phenanthrene were accomplished by modification of the Pd-catalyzed Suzuki cross-coupling methodology that we previously reported.[14] Synthesis of 1- and 3-phenanthrenol via this approach is shown in Scheme 2.



Scheme 2.

Reaction of 2-bromoacetaldehyde with 3-methoxyphenylboronic acid in the presence of a $Pd(PPh_3)_4$ catalyst gave 3'-methoxybiphenyl-2-carboxaldehyde (**36**), and Wittig reaction of **36** with methyltriphenylphosphonium chloride and *t*-BuOK in THF gave 3′-methoxy-2-(2-methoxyvinyl)biphenyl (**37**) as a mixture of *E*- and *Z*-isomers. Cyclization of **37** catalyzed by $MeSO_3H$ gave a mixture of 1- and 3-methoxyphenanthrene (**38a** and **39a**). Separation of the



Scheme 3.

isomers by preparative TLC and demethylation by treatment with BBr_3 afforded 1- and 3-phenanthrol (**38b** and **39b**).

4-Phenanthrol was prepared by modification of the same approach, starting with 2-bromobenzaldehyde and 2-methoxyphenylboronic acid. The remaining isomer, 2-phenanthrol, was synthesized by oxidation of 2-acetylphenanthrene to 2-acetoxyphenanthrene with *m*-chloroperbenzoic acid and basic hydrolysis based on a procedure we reported for synthesis of 2-hydroxypyrene derivatives.[21]

The 1-, 3-, 6-, 8-, 9-, and 12-phenol isomers of benzo[*a*]pyrene were synthesized via the modifications of the Pd-catalyzed Suzuki cross-coupling methodology recently reported.[16] 7-Hydroxy-BaP (**42b**) was synthesized from 9,10-dihydrobenzo[*a*]pyrene-7(8*H*)-one (**40**) via conversion to the enol acetate derivative (**41**), dehydrogenation with *o*-chloranil to the phenol acetate (**42a**), and acid-catalyzed hydrolysis (Scheme 3).[22]

Benzo[*a*]pyren-10-ol (**46b**) was synthesized from **40** via indium-catalyzed reduction with Me_3SiHCl[23] to 7,8,9,10-tetrahydrobenzo-[*a*]pyrene (**43**). Oxidation of **43** with DDQ and H_2O[24] gave 7,8-dihydro-BaP-10(9*H*)-one (**44**), and this was transformed to benzo[*a*]pyren-10-ol (**46b**) via acid-catalyzed reaction with Ac_2O to the enol acetate (**45**), followed by dehydrogenation with *o*-chloranil, and acid-catalyzed hydrolysis.

The remaining PAPs, benz[*a*]anthracen-7-ol (**27**) and pyren-1- and -2-ol (**25** and **26**), were prepared by modifications of the published methods.

4. Experimental

4.1. General

Caution. Benzo[*a*]pyrene (BaP) has been designated a human carcinogen by the World Health Organization.[9] Carcinogens should be handled with caution following the procedures recommended in the publication *NIH Guidelines for the Laboratory Use of Chemical Carcinogens*. The phenol and quinone isomers of BaP are not presently considered to pose carcinogenic hazards. However, recent investigations have provided evidence that benzo[*a*]pyren-7,8-dione (**10**) is an active metabolite of BaP that may contribute to initiation of lung cancer.[10a] Prudence dictates that it should be handled with appropriate caution.

o-Iodoxybenzoic acid (IBX) was prepared by the improved procedure reported by Frigero et al.[25] Bis(trifluoroacetoxy)iodobenzene (BTI) was used as supplied by the Aldrich Chemical Co. The ^1H and ^{13}C NMR spectra were determined in $CDCl_3$ unless otherwise stated with TMS as an internal standard.

4.2. Synthesis of polycyclic aromatic phenols

4.2.1. Phenanthrol isomers. 1-, 3-, and 4-phenanthrol were synthesized by the Pd-catalyzed Suzuki cross-coupling methodology previously reported.[14] Syntheses of 1- and 3-phenanthrol (**38b** and **39b**) are depicted in Scheme 2.

*4.2.2. 3′-Methoxybiphenyl-2-carboxaldehyde (**36**).* To a solution of 2-bromobenzaldehyde (3.68 g, 20 mmol) in dimethoxyethane (50 mL) under argon was added $Pd(PPh_3)_4$ (462 mg, 0.4 mmol). The resulting solution was stirred at room temperature for 20 min, then a solution of 3-methoxyphenylboronic acid (3.65 g, 24 mmol) in EtOH (38 mL) was added. After 20 min, a solution of Na_2CO_3 (6.36 g) in water (30 mL) was added, and the mixture was heated at reflux overnight. The solution was cooled and concentrated under reduced pressure. The residue was treated with CH_2Cl_2 (50 mL ×3) and water, and the organic phase was washed with brine and dried over anhydrous Na_2SO_4. The solvent was removed by vacuum, and the residue was purified by chromatography on a silica gel column eluted with EtOAc/hexanes (1:10) to yield **36** as a yellow oil (381 mg, 90%). The NMR data were in agreement with the values reported.[26]

*4.2.3. 3′-Methoxy-2-(2-methoxyvinyl)biphenyl (**37**).* To a solution of methyltriphenyl-phosphonium chloride (3.24 g, 9.5 mmol) in dry ether (30 mL) under argon was added dropwise a 1.0 M solution of *t*-BuOK (9.5 mL, 9.5 mmol) in dry THF at room temperature for 1 h, then a solution of **36** (800 mg, 3.8 mmol) in THF (30 mL) was added dropwise. The solution was stirred overnight and then evaporated to dryness under vacuum, and the crude product was purified by chromatography on a column of silica gel eluted with EtOAc/hexanes (1:40) to give a mixture of the *E*- and *Z*-isomers of **37** as a yellow oil (848 mg, 93%) that was used directly in the next step.

*4.2.4. 1-Methoxy- and 3-methoxyphenanthrene (**38a** and **39a**).* To a solution of **37** (180 mg, 0.75 mmol) in CH_2Cl_2 (10 mL) was added $MeSO_3H$ (0.05 mL) under argon at 0 °C, and the solution was stirred overnight. TLC showed the reaction to be complete. A saturated solution of $NaHCO_3$ (2 mL) was added, and stirring was continued for 15 min. Then the organic layers were evaporated to dryness. The residue was purified by preparative TLC with EtOAc/hexanes (1:50). The first fraction was **39a** (84 mg, 54%), and the second fraction was **38a** (39 mg, 25%). The NMR data for **38a** and **39a** were in agreement with the values reported.[25]

*4.2.5. 1-Phenanthrol (**38b**).* To a solution of **38a** (60 mg, 0.31 mmol) in dry CH_2Cl_2 (15 mL) at -78 °C was added dropwise a solution of BBr_3 (1 M, 0.5 mL) in CH_2Cl_2, and the resulting solution was stirred overnight, allowing the solution to warm to room temperature. The solution was then cooled to 0 °C, reaction was quenched with water (1 mL), and solvent was removed under reduced pressure. The aqueous suspension was extracted with EtOAc (15 mL ×3), the collected organic layers were washed with brine, dried over anhydrous Na_2SO_4 and evaporated to dryness. Chromatography of the residue on a silica gel column eluted with EtOAc/hexanes (1:2) gave **38b** as a yellow solid. NMR data were closely similar to those of an authentic sample.

*4.2.6. 3-Phenanthrol (**39b**).* Demethylation of **39a** by the procedure used for preparation of **38b** gave **39b** as a yellow solid. NMR data matched that of an authentic sample.

4.2.7. 4-Phenanthrol. Synthesis of this isomer was carried out by analogous sequence from reaction of 2-bromobenzaldehyde (4.14 g, 22.4 mmol) with 2-methoxyphenylboronic acid (3.04 g, 20 mmol). The adduct was obtained as a yellow oil (381 mg, 90%) whose NMR data were in good agreement with that reported.[27] Wittig reaction of the adduct followed by the acid-catalyzed cyclization gave 4-methoxyphenanthrene, and demethylation by treatment with BBr_3 furnished 4-phenanthrol as a yellow solid. The NMR data were in good agreement with those of an authentic sample.

4.2.8. 2-Phenanthrol. To a solution of 2-acetylphenanthrene (440 mg, 2.0 mmol) in $CHCl_3$ (15 mL) was added *m*-CPBA (1.7 g, 9.8 mmol), and the resulting mixture was stirred at room temperature overnight. A saturated solution of sodium metabisulfite (30 mL) was added, and the mixture was stirred for 30 min and extracted with CH_2Cl_2 (25 mL ×3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and evaporated to dryness under vacuum. Chromatography of the residue on a silica gel column eluted with EtOAc/hexanes (1:10) gave 2-acetoxyphenanthrene as a white solid (220 mg, 47%). This was deacetylated by treatment with KOH (400 mg, 3.0 mmol) in refluxing EtOH (20 mL). 2-Phenanthrol was obtained as a pale

yellow solid (120 mg, 81%). NMR data matched those of an authentic sample.

4.2.9. Other phenol isomers. 1- and 2-Anthrol,[28] benz[*a*]anthracen-7-ol (**24**),[29–31] and pyrene-1- and -2-ol (**25** and **26**)[32–34] were synthesized by the modifications of the published methods.

4.2.10. Phenol isomers of benzo[a]pyrene. Benzo[*a*]pyren-1-, 3-, and 9-ol were prepared by the methods recently reported.[16] Benzo[*a*]-pyren-8-ol was synthesized by the published method.[14a] Benzo[*a*]pyren-7-ol (**42b**) was synthesized from 9,10-dihydrobenzo[*a*]pyrene -7(8H)-one (**40**) by conversion to the enol acetate (**41**), dehydrogenation with *o*-chloranil, and hydrolysis (Scheme 3) by the published procedure.[22] Benzo[*a*]pyren-10-ol (**46b**) was synthesized from **40** by the sequence depicted in Scheme 3.

*4.2.11. 7,8,9,10-Tetrahydrobenzo[a]pyrene (**43**).* Compound **40** was deoxygenated to **43** by indium-catalyzed reduction with Me_2SiClH.[23] To a solution of **40** (270 mg, 1 mmol) in CH_2Cl_2 (1 mL) under argon was added a solution of $InCl_3$ (22 mg, 0.1 mmol) and Me_2SiClH, 0.27 mL, 3 mmol) in CH_2Cl_2 (1 mL). The solution was stirred overnight, then EtOAc (10 mL) and silica gel (10 g) were added, and the solvent was evaporated. Chromatography of the product on a silica gel column eluted with EtOAc/hexanes (1: 25) afforded **43** as a white solid (84.5 mg, 33%), mp 91–93 °C (lit.[35] 92–93 °C).

*4.2.12. 7,8-Dihydrobenzo[a]pyrene-10(9H)-one (**44**).* Oxidation of **43** with DDQ and H_2O by the method of Lee and Harvey[24] furnished **44** as a red solid (87 mg, 75%), mp 174–175 °C (lit.[24] 173–175 °C).

*4.2.13. 10-Acetoxy-7, 8-dihydrobenzo[a]pyrene (**45**).* To a solution of **43** (108 mg, 0.4 mmol) in isopropenyl acetate (10 mL) was added *p*-toluenesulfonic acid monohydrate (10 mg) and Ac_2O (1 mL), and the solution was heated at reflux for 24 h. The solvents were evaporated by vacuum, and chromatography of the residue on a silica gel column eluted with EtOAc/hexanes (1: 20) afforded **45** as a pale-red solid (184.6 mg, 97%).

*4.2.14. 10-Acetoxybenzo[a]pyrene (**46a**).* To a solution of **45** (75 mg, 0.24 mmol) in toluene (15 mL) was added *o*-chloranil (62 mg, 0.25 mg), and the solution was stirred for 24 h at 80 °C. Following evaporation of the solvent, the residue was chromatographed on a silica gel column eluted with EtOAc/hexanes (1: 10 to 1: 5). Compound **46a** was obtained as a yellow solid (66 mg, 58%).

*4.2.15. 7,8-Benzo[a]pyren-10-ol (**4bb**).* To a solution of **46a** (76 mg, 0.26 mmol) in MeOH (20 mL) was added *p*-toluenesulfonic acid monohydrate (75 mg), and the solution was heated at reflux overnight. Following removal of the solvent under vacuum, the residue was purified by chromatography on a silica gel column. Elution with EtOAc: hexanes (1:5) gave **46b** as a yellow solid (40 mg, 57%), mp 156–157 °C (lit.[36] 155–157 °C). NMR data are in agreement with that reported.[36]

4.3. General procedures for oxidation of PAPs to PAQs

IBX Oxidation. To a solution of the phenol (1 equiv) dissolved in DMF was added solid IBX (1 equiv), and the resulting white suspension was stirred at room temperature. A color change was generally observed within 30 min. Stirring was continued until TLC showed consumption of the starting material was complete, usually evidenced by a clear solution. The reactions were generally complete within one hour. The mixture was extracted with EtOAc, washed with water and brine, and the solvent was removed under vacuum. The residue was purified by chromatography on a silica gel column to furnish the PAQ.

BTI Oxidation. To a solution of the PAP (1 equiv) in DMF and H_2O (2:1) was added dropwise a solution of BTI (2 equiv) in DMF/H_2O at 0 °C, and the resulting mixture was stirred at 0 °C until TLC showed disappearance of the PAP (~2 h). The mixture was extracted with EtOAc, washed with water and brine, and the solvent was removed under vacuum. Chromatography of the residue on a silica gel column provided the pure PAQ.

4.4. Polycyclic aromatic quinones

*4.4.1. Phenanthren-1,2-dione (**3**).* Red solid, mp 201–203 °C (lit.[19] 202–204 °C, red needles). ^{1}H NMR data are in agreement with values reported.[19,37]

*4.4.2. Phenanthrene-1,4-dione (**4**).* Yellow solid, mp 151–152 °C (lit.[19] 152–154 °C, yellow needles). ^{1}H NMR data agree with values reported.[19,37]

*4.4.3. Phenanthren-3,4-dione (**5**).* Mp 131–132 °C (lit.[37] 133 °C). NMR data agree with values reported.[37]

*4.4.4. Anthracen-1,2-dione (**7**).* Mp 170–175 °C (decomp.) (lit.[20] 169–176 °C decomp.). 1H NMR data agree with values reported.[20]

*4.4.5. Anthracen-1,4-dione (**8**).* Mp 219–221 °C (lit.[38] 218–221 °C). NMR data agree with values reported.[38]

The structural assignments of the benzo[*a*]pyrenedione isomers were confirmed by comparison of their ^{1}H and ^{13}C NMR spectra with those of authentic samples and/or with NMR spectral data reported: benzo[*a*]pyren-7,8-dione (**10**),[14] benzo[*a*]pyren-7,10-dione (**11**). [39] benzo[*a*]pyren-9,10-dione (**14**),[16] benzo[*a*]pyren-1,6-dione (**18**),[16] benzo[*a*]pyren-3,6-dione (**21**),[16]

Acknowledgements

This investigation was supported by NIH Grants (P01 CA 92537, R01 CA 039504, R01 ES 015857, and P30 ES 013508).

Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.12.022.

References and notes

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