Synthesis of Benzo[*s*]picene and its Putative Carcinogenic *trans*-3,4-Dihydrodiol and Fjord Region *anti*-Diol Epoxide Metabolites

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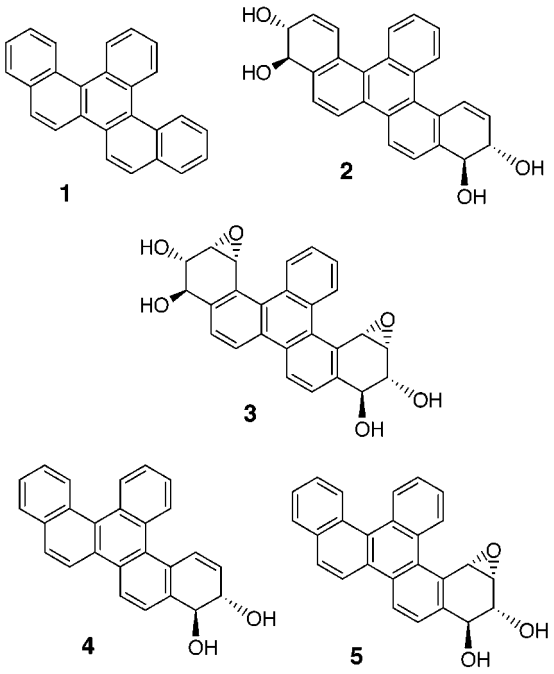
The chemistry of the polycyclic aromatic hydrocarbon benzo[*s*]picene (**1**) has been relatively unexplored as a consequence of its relative synthetic inaccessibility.[1]



Our interest in **1** was stimulated by its potential carcinogenicity; that is, it has two *fjord* regions, a structural feature characteristic of some of the most potent carcinogenic hydrocarbons known (e.g. dibenzo[*def*,*p*]chrysene[2] and benzo[*g*]chrysene[3]). Like both of these polyarenes, **1** is presumed to be distorted from planarity due to steric interference between the *fjord* region atoms.[4]

A practical synthetic route to benzo[*s*]picene was recently reported,[5] making it readily available for chemical and biological investigations. In connection with studies on the metabolic activation and tumorigenicity of benzo[*s*]picene, samples of its potential carcinogenic metabolites were required as authentic standards. Convenient syntheses of the bis-dihydrodiol metabolite (**2**) and the corresponding bis-*anti*-diol epoxide metabolite (**3**) were recently described.[6] We now report a new synthesis of benzo[*s*]picene and efficient syntheses of its 3,4-dihydrodiol, *trans*-3,4-dihydroxy-3,4-dihydrobenzo[*s*]-picene (**4**) and the corresponding *anti*-diol epoxide, *trans*-3,4-dihydroxy-*anti*-1,2-epoxy-1,2,3,4-tetrahydrobenzo[*s*]-picene (**5**), implicated as its proximate and ultimate carcinogenic metabolites, respectively.

Results and Discussion

The successful synthetic route to **1** entails two oxidative photocyclizations (Scheme 1) in the key steps. Wittig reaction of 2-acetylnaphthalene with benzyltriphenylphosphonium chloride and NaH gave the expected olefin **6**, shown by the complexity of its ^{1}H NMR spectrum to be a mixture of *Z*- and *E*-isomers. Although the pure isomers were separable by recrystallization, it was more efficient to employ the mixture directly in the next step because photocatalyzed interconversion of the *Z*- and *E*-isomers occurs with facility.[7] Photocyclodehydrogenation of **6** took place smoothly in the presence of I_2 and epoxybutane[8] to furnish 6-methylbenzo[*c*]phenanthrene (**7a**) arising from regiospecific bond formation in the more reactive 1-position of the naphthalene ring. Bromination of **7a** with *N*-bromosuccinimide and benzoyl peroxide in refluxing CCl_4 provided 6-bromomethylbenzo[*c*]phenanthrene (**7b**). Reaction of **7b** with triphenylphosphine gave the corresponding phosphonium salt 6-(benzo[*c*]-phenanthryl)methyltriphenylphosphonium bromide (**7c**).

The phosphonium salt **7c** was employed as the starting compound for the synthesis of benzo[*s*]picene (**1**) and its 3,4-dihydrodiol (**4**) and diol epoxide (**5**) derivatives. Wittig reaction of **7c** with benzaldehyde furnished *β*-(6-benzo[*c*]phenanthryl)styrene (**8**) as a mixture of *E*- and *Z*-isomers in approximately 1:1 ratio. Photocyclization of **8** in the presence of I_2 and epoxybutane took place smoothly to furnish **1** in good overall yield. Wittig reaction of **7c** with 2,3-dimethoxybenzaldehyde furnished the dimethoxy-substituted derivative of the olefin **8** (**9**), predominantly as the *Z*-isomer with only a trace of the *E*-isomer detectable by NMR analysis. The strong preference for formation of the *Z*-isomer in the Wittig reaction of 2,3-dimethoxybenzaldehyde versus benzaldehyde accords with previous observations.[9] Although direct evidence concerning the reason for this difference is lacking, it is reasonable to suggest that the methoxy group may interact with the positively charged phosphorus atom in the reaction intermediate to favor elimination to form this isomer.

(1) Harvey, R. G. *Polycyclic Aromatic Hydrocarbons*, Wiley-VCH: New York, 1997.

(2) Higginbotham, S.; Ramakrishna, N. V. S.; Johansson, S. I.; Rogan, E. G.; Cavalieri, E. L. *Carcinogenesis* **1993**, *14*, 875. Dibenzo-[*def*,*p*]chrysene is the name for this hydrocarbon in the widely employed IUPAC nomenclature, cf Harvey, R. G. *Polycyclic Aromatic Hydrocarbons*, Wiley-VCH: New York, 1997. It is commonly referred to as dibenzo[*a*,*l*]pyrene in the biological literature.

(3) Szeliga, J.; Lee, H.; Harvey, R. G.; Page, J. E.; Ross, H. L.; Routledge, M. N.; Hilton, B. D.; Dipple, A. *Chem. Res. Toxicol.* **1994**, *7*, 420.

(4) Deviation from planarity is associated with carcinogenicity, and it has been proposed that this effect may have its basis in increased binding of the active diol epoxide metabolites to deoxyadenosine sites in DNA; see, Dipple, A. In *DNA Adducts: Identification and Biological Significance*; Hemminki, K.; Dipple, A.; Segerbäck, D.; Kadlubar, F. F.; Shuker, D.; Bartsch, H., Eds.; IARC: Lyon, France, 1994; pp 107−129; Szeliga, J.; Lee, H.; Harvey, R. G.; Page, J. E.; Ross, H. L.; Routledge, M. N.; Hilton, B. D.; Dipple, A. *Chem. Res. Toxicol.* **1994**, *7*, 420.

(5) Tang, X.-Q.; Harvey, R. G. *J. Org. Chem.* **1995**, *60*, 3568.

(6) Zhang, F.-J.; Harvey, R. G. *J. Org. Chem.* **1998**, *63*, 1168.

(7) Mallory, F. B.; Mallory, C. W. *Org. Reactions* **1984**, *30*, 1.

(8) Epoxybutane serves to prevent competing secondary reactions, principally reduction of the olefin by HI, by scavenging the HI produced; see, Liu, L. B.; Yang, B. W.; Katz, T. J.; Poindexter, M. K. *J. Org. Chem.* **1991**, *56*, 3769.

(9) Zhang, J.-T.; Dai, W.; Harvey, R. G. *J. Org. Chem.* **1998**, *63*, 0000.

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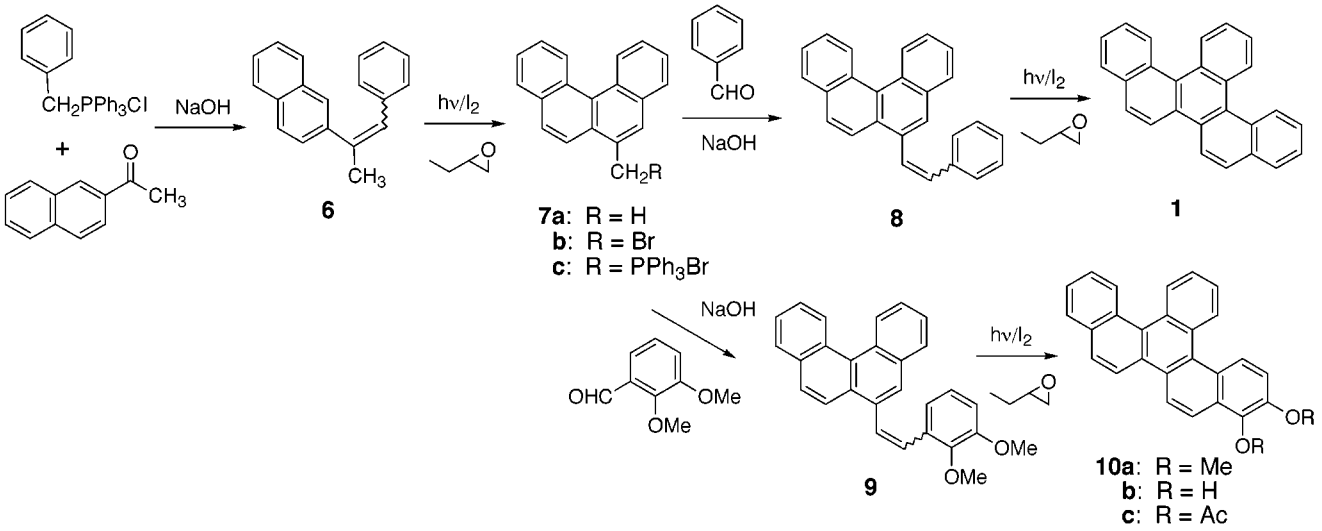
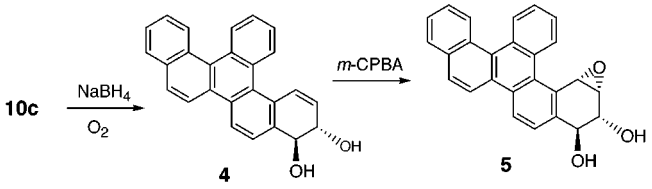
Scheme 1



Scheme 2



Photoreaction of **9** took place readily to afford the cyclized product 3,4-dimethoxybenzo[*s*]picene (**10a**) in excellent yield. As in the synthesis of **7a**, interconversion of the *Z*- and *E*-isomers took place with facility during the photocyclization of both **8** and **9**.

Conversion of **10a** to the 3,4-dihydrodiol (**4**) was accomplished via initial demethylation with BBr_3 to 3,4-dihydroxybenzo[*s*]picene (**10b**). In view of the well-known air sensitivity of polycyclic aromatic hydroquinones, **10b** was isolated and characterized as its diacetate (**10c**).[10] Reduction of **10c** with $NaBH_4$ with O_2 bubbling through the solution (Scheme 2) took place smoothly with concurrent deacetylation to provide *trans*-3,4-dihydroxy-3,4-dihydrobenzo[*s*]picene (**4**) free of the corresponding cis-diastereomer.[11] The coupling constant for the carbinol protons of **4** was 11 Hz, indicating existence of the dihydrodiol in solution predominantly as the trans diequatorial conformer, consistent with previous findings for other sterically unrestricted *trans*-dihydrodiols.[11] Conversion of **4** to the corresponding *anti*-diol epoxide (**5**) took place stereospecifically on treatment with *m*-chloroperbenzoic acid (*m*-CPBA). It was shown in previous studies that epoxidation with *m*-CPBA of *trans*-dihydrodiols free to adopt the diequatorial conformation generally takes place stereoselectively to afford the *anti*-diastereomeric diol epoxides.[11]

As a consequence of their mode of synthesis, the *trans*-dihydrodiol (**4**) and the *anti*-diol epoxide (**5**) are racemic. Although separation of the enantiomers at this stage is possible, it is more convenient to assay the mixture for biological activity prior to attempting their time-consuming separation. If significant activity is found, the isomers may be resolved by the methods devised for the separation of other similar types of compounds, such as resolution on a chiral column,[11] and the individual enantiomers can then be tested for activity.

(10) The crude **10a** obtained as a white solid darkened quickly on exposure to air.

(11) The *trans*-stereoselectivity of these reductions is well established; see Harvey, R. G. *Polycyclic Aromatic Hydrocarbons: Chemistry and Carcinogenesis*, Cambridge University: Cambridge, England, 1991; Chapter 13.

Experimental Section

Materials and Methods. Benzyltriphenylphosphonium chloride was purchased from Aldrich. *m*-Chloroperbenzoic acid (Aldrich) was purified by washing with pH 7.4 phosphate buffer and drying under reduced pressure. *N*-Bromosuccinimide (NBS) was purified by recrystallization from water. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. The ^1H NMR spectra were recorded on 400 or 500 MHz spectrometers in $CDCl_3$ with tetramethylsilane as internal standard unless stated otherwise; integration was consistent with the structural assignments. All melting points are uncorrected. ***Caution**: Although benzo[s]picene is not an established carcinogen, it and its dihydrodiol and diol epoxide metabolites are potentially hazardous and should be handled in accordance with "NIH Guidlines for the Laboratory Use of Chemical Carcinogens."*

***β*-Methyl-*β*-(2-naphthyl)styrene (6).** Benzyltriphenylphosphonium chloride (25.20 g, 64.8 mmol) was added in three portions to a stirred suspension of NaH (2.60 g, 65.0 mmol, 60% in mineral oil) under argon. The suspension was stirred for 1 h at room temperature, then 2-acetylnaphthalene (10.00 g, 59 mmol) was added, and the resulting orange mixture was heated at 70 °C for 2 h. The reaction mixture was cooled and poured onto ice, stirred for 1 h, then extracted with ether (3 × 500 mL). The organic layer was washed with water, dried over $MgSO_4$, and evaporated to dryness. Chromatography of the residue on a silica gel column eluted with hexanes−CH_2Cl_2 (9:1) afforded **6** (10.57 g, 83%) as a mixture of *Z*- and *E*-isomers. Recrystallization of this mixture from EtOAc−hexane afforded the pure E-isomer of **6** (7.76 g) as white crystals, mp 144−145 °C (lit.[12] 137−138 °C); recrystallization of the residue from the filtrate from hexane gave an additional 1.25 g of **6** (*E*-isomer with traces of *Z*-isomer). Evaporation of the filtrate gave essentially pure *Z*-isomer (2.93 g) as a white solid, mp 68−70 °C. *E*-isomer: ^1H NMR δ 7.94 (s, 1H), 7.86 (d, J = 8.7 Hz, 1H), 7.84 (d, J = 8.8 Hz, 2H), 7.72 (dd, J = 1.8, 8.6 Hz, 1H), 7.38−7.51 (m, 6H), 7.25−7.28 (m, 1H), 7.01 (s, 1H), 2.39 (s, 3H); Z-isomer: ^1H NMR δ 7.81 (dd, J = 3.4, 6.0 Hz, 1H), 7.76 (dd, J = 3.4, 6.0 Hz, 1H), 7.72 (d, J = 8.9 Hz, 1H), 7.71 (s, 1H), 7.46 (dd, J = 6.2, 6.3 Hz, 2H), 7.28 (dd, J = 1.5, 8.4 Hz, 1H), 7.05−7.09 (m, 3H), 6.98−6.99 (m, 2H), 6.58 (s, 1H), 2.31 (s, 3H).

(12) Nagel, D. L.; Kupper, R.; Antonson, K.; Wallcave, L. *J. Org. Chem.* **1977**, *42*, 3626.

6-Methylbenzo[*c*]phenanthrene (7a). Argon was bubbled through a stirred solution of **6** (2.0 g, 8.2 mmol) and I_2 (2.1 g, 8.3 mmol) in 700 mL of Et_2O−cyclohexane (1:1) for 30 min before 12 mL of 1,2-epoxybutane was added. The solution was irradiated by UV light generated from a Hanovia 400-W medium-pressure lamp using a Vycor filter, maintaining the argon flow throughout the procedure. After 4 h, NMR analysis showed consumption of **6** to be complete. Removal of the solvent under reduced pressure and passage of the residue through a short silica gel column eluted with hexane gave **7a** (1.90 g, 96%) as a white solid, mp 76−77 °C (lit.[10] 76.8−77.6 °C): ^{1}H NMR δ 9.11 (d, J = 8.2 Hz, 1H), 9.04 (d, J = 9.4 Hz, 1H), 8.05 (d, J = 8.8 Hz, 1H), 8.03 (d, J = 8.4 Hz, 1H), 7.95 (t, J = 8.8 Hz, 1H), 7.94 (d, J = 9.4 Hz, 1H), 7.75 (s, 1H), 7.58−7.67 (m, 4H), 2.83 (s, 3H).

6-Bromomethylbenzo[*c*]phenanthrene (7b). A solution of **7a** (8.50 g, 35.1 mmol), NBS (6.50 g, 36.5 mmol), and benzoyl peroxide (180 mg) in 250 mL of CCl_4 was heated at reflux for 2 h. The reaction mixture was cooled to room temperature, filtered, and evaporated to dryness. Chromatography of the product on a Florisil column eluted with hexanes−EtOAc (99:1) afforded **7b** (10.27 g, 91%) as a yellow solid, mp 77−79 °C (EtOAc−hexane): ^{1}H NMR δ 9.07 (d, J = 9.2 Hz, 1H), 9.05 (d, J = 9.2 Hz, 1H), 8.19 (d, J = 8.8 Hz, 1H), 8.05 (d, J = 7.7 Hz, 1H), 8.03 (d, J = 8.8 Hz, 1H), 7.99 (t, J = 10.0 Hz, 1H), 7.98 (s, 1H), 7.61−7.70 (m, 4H), 5.09 (s, 2H); MS (*m*/*e*) 320 (M^+, 20), 241 (M^+,-Br 100) (based on Br, 79); HRMS: calcd for $C_{19}H_{13}Br$: 320.0201. Found: 320.0194.

6-(Benzo[*c*]phenanthryl)methyltriphenylphosphonium bromide (7c). A solution of **7b** (4.94 g, 15.4 mmol) and PPh_3 (4.45 g, 17.0 mmol) in 65 mL of toluene was heated at reflux overnight. The usual workup gave **7c** (8.09 g, 90%) as a white solid, mp 284−286 °C: ^{1}H NMR δ 8.87 (d, J = 8.3 Hz, 1H), 8.83 (d, J = 8.5 Hz, 1H), 7.94 (d, J = 4.0 Hz, 1H), 7.78 (d, J = 7.7 Hz, 1H), 7.42−7.75 (m, 21H), 7.34 (d, J = 8.9 Hz, 1H), 6.02 (d, J = 14.0 Hz, 2H). Anal. Calcd for $C_{37}H_{28}BrP$: C, 76.16; H, 4.84; Br, 13.69. Found: C, 76.09; H, 4.83; Br, 13.76.

***β*-(6-Benzo[*c*]phenanthryl)styrene (8).** To a solution of the phosphonium salt **7c** (1.50 g, 2.6 mmol), benzaldehyde (285 mg, 2.7 mmol), and a catalytic amount of 18-crown-6 in 45 mL of CH_2Cl_2 was added to 4.7 mL of a 50% aqueous solution of NaOH, and stirring was continued overnight. The usual workup followed by chromatography on a silica gel column eluted with hexane gave **8** (762 mg, 91%) as a mixture of *Z*- and *E*-isomers (~1:1). *Z*-isomer, white semisolid: ^{1}H NMR δ 9.14 (d, J = 8.4 Hz, 1H), 9.10 (d, J = 8.5 Hz, 1H), 8.15 (d, J = 8.8 Hz, 1H), 8.03 (dd, J = 1.6, 8.0 Hz, 1H), 7.91 (t, J = 8.8 Hz, 1H), 7.83 (d, J = 7.9 Hz, 1H), 7.78 (s, 1H), 7.62−7.71 (m, 3H), 7.56 (t, J = 7.4 Hz, 1H), 7.03−7.16 (m, 6H), 6.93 (d, J = 12 Hz, 1H). Anal. Calcd for $C_{26}H_{18}$: C, 94.51; H, 5.49. Found: C, 94.55; H, 5.49. *E*-isomer, white semisolid: ^{1}H NMR δ 9.10 (d, J = 8.2 Hz, 1H), 9.05 (d, J = 9.0 Hz, 1H), 8.21 (d, J = 8.8 Hz, 1H), 8.11 (s, 1H), 8.03−8.06 (m, 2H), 7.95 (d, J = 8.8 Hz, 1H), 7.93 (d, J = 16 Hz, 1H), 7.61−7.70 (m, 6H), 7.43 (t, J = 7.4, 7.8 Hz, 2H), 7.34 (t, J = 7.4 Hz, 1H), 7.25 (d, J = 16 Hz, 1H). Anal. Calcd for $C_{26}H_{18}$: C, 94.51; H, 5.49. Found: C, 94.61; H, 5.45.

Benzo[*s*]picene (1). Photocyclization of **8** (232 mg, 0.74 mmol) was carried out by the procedure employed for the synthesis of **7a** (reaction complete in 2 h by NMR). Chromatography of the product on a short Florisil column furnished **1** (220 mg, 95%) as a white solid, mp 204−205 °C (EtOAc) (lit.[5] 198−199 °C): ^{1}H NMR δ 9.02 (d, J = 8.3 Hz, 2H), 8.97 (dd, J = 6.2, 6.2 Hz, 2H), 8.65 (d, J = 9.0 Hz, 2H), 8.06 (d, J = 8.8 Hz, 2H), 8.04 (dd, J = 1.3, 7.8 Hz, 2H), 7.61−7.71 (m, 6H).

***β*-(6-Benzo[*c*]phenanthryl)-2,3-dimethoxystyrene (9).** Wittig reaction of the phosphonium salt **7c** (4.95 g, 8.5 mmol) with 2,3-dimethoxybenzaldehyde (1.42 g, 8.5 mmol), was conducted by the procedure employed for the preparation of **8**. The usual workup and chromatography on a column of silica gel eluted with hexanes−EtOAc (95:5) gave a yellow semisolid product identified as the *Z*-isomer of **9** (3.12 g, 94%) with only a trace amount of the *E*-isomer: ^{1}H NMR δ 9.13 (d, J = 8.7 Hz, 1H), 9.08 (d, J = 8.5 Hz, 1H), 8.16 (d, J = 8.7 Hz, 1H), 8.03 (d, J = 7.8 Hz, 1H), 7.92 (d, J = 8.8 Hz, 1H), 7.80 (d, J = 7.9 Hz, 1H), 7.72 (s, 1H), 7.69 (t, J = 7.0, 8.4 Hz, 1H), 7.61−7.65 (m, 2H), 7.54 (t, J = 7.2, 7.7 Hz, 1H), 7.20 (d, J = 3.2 Hz, 2H), 6.65 (dd, J = 6.3, 6.2 Hz, 1H), 6.47−6.49 (m, 2H), 3.91 (s, 3H), 3.84 (s, 3H). Anal. Calcd for $C_{28}H_{22}O_2$: C, 86.12; H, 5.68. Found: C, 85.95; H, 5.70.

3,4-Dimethoxybenzo[*s*]picene (10a). Photocyclization of **9** (205 mg, 0.53 mmol) was carried out by the procedure employed for the synthesis of **7a** (reaction time 2 h). The usual workup and chromatography through a short Florisil column gave **10a** (196 mg, 96%) as a white solid, mp 211−213 °C (hexanes−EtOAc): ^{1}H NMR δ 9.01 (d, J = 8.4 Hz, 1H), 8.97 (dd, J = 5.2, 7.0 Hz, 1H), 8.92 (dd, J = 5.2, 6.9 Hz, 1H), 8.76 (d, J = 9.3 Hz, 1H), 8.64 (d, J = 9.0 Hz, 2H), 8.38 (d, J = 9.2 Hz, 1H), 8.05 (d, J = 8.8 Hz, 2H), 8.04 (d, J = 7.5 Hz, 1H), 7.68 (t, J = 7.1, 8.3 Hz, 1H), 7.60−7.65 (m, 3H), 7.44 (d, J = 9.3 Hz, 1H), 4.10 (s, 3H), 4.09 (s, 3H). Anal. Calcd for $C_{28}H_{20}O_2$: C, 86.57; H, 5.19. Found: C, 86.51; H, 5.20.

3,4-Dihydroxybenzo[*s*]picene (10b). To a solution of **10a** (210 mg, 0.54 mmol) in 200 mL of CH_2Cl_2 was added in a dropwise manner 5.4 mL of a solution of BBr_3 (1.0 M solution in CH_2Cl_2) at 0 °C. Stirring was continued at this temperature for 40 min, and then the reaction was quenched by addition of water. The solvent was evaporated under reduced pressure, EtOAc was added, and the organic layer was washed with water, dried over Na_2SO_4, and evaporated to dryness to yield **10b** (194 mg) as a white solid that darkened quickly in air: ^{1}H NMR (CD_3-$COCD_3$) δ 9.01 (d, J = 8.5 Hz, 1H), 8.99 (d, J = 9.6 Hz, 1H), 8.97 (d, J = 9.5 Hz, 1H), 8.96 (d, J = 9.5 Hz, 1H), 8.80 (d, J = 9.0 Hz, 1H), 8.72 (d, J = 9.3 Hz, 1H), 8.45 (d, J = 9.1 Hz, 1H), 8.44 (d, J = 9.0 Hz, 1H), 8.15 (d, J = 8.9 Hz, 1H), 8.13 (d, J = 8.0 Hz, 1H), 7.73 (t, J = 7.7 Hz, 1H), 7.64−7.69 (m, 2H), 7.40 (d, J = 9.0 Hz, 1H). In view of the air sensitivity of **10b**, it was isolated and characterized as the diacetate (**10c**).

3,4-Acetoxybenzo[*s*]picene (10c). The crude **10b** was dissolved in 7.0 mL of Ac_2O and 5.0 mL of pyridine, and the solution was stirred overnight at room temperature. The usual workup afforded **10c** (220 mg, 91%) as a white solid, mp 220−222 °C (hexanes−EtOAc): ^{1}H NMR δ 9.02 (d, J = 8.3 Hz, 1H), 8.96−8.97 (m, 1H), 8.92 (d, J = 9.3 Hz, 1H), 8.89−8.91 (m, 1H), 8.70 (d, J = 9.3 Hz, 1H), 8.61 (d, J = 8.9 Hz, 1H), 8.06 (d, J = 8.8 Hz, 2H), 8.05 (d, J = 6.5 Hz, 1H), 7.63−7.71 (m, 4H), 7.53 (d, J = 9.3 Hz, 1H), 2.55 (s, 3H), 2.41 (s, 3H). Anal. Calcd for $C_{30}H_{20}O_4$: C, 81.06; H, 4.54. Found: C, 80.78; H, 4.53.

***trans*-3,4-Dihydroxy-3,4-dihydrobenzo[*s*]picene (4).** A suspension of **10c** (67 mg, 0.15 mmol) and $NaBH_4$ (200 mg, 5.35 mmol) in 150 mL of EtOH with O_2 bubbling through the solution was stirred at ambient temperature for 24 h. EtOH was removed under reduced pressure, water was added, and the aqueous suspension was extracted with EtOAc−ether. The combined organic extracts were washed with brine, dried over Na_2SO_4, and evaporated to dryness. Chromatography of the product on a short Florisil column eluted with hexane−THF (1:1) gave **4** (47 mg 86%) as a white solid, mp 238−241 °C (triturated with acetone): ^{1}H NMR (DMSO-d_6) δ 8.83 (d, J = 8.3 Hz, 1H), 8.68−8.72 (m, 3H), 8.11 (d, J = 8.6 Hz, 2H), 7.92 (d, J = 8.3 Hz, 1H), 7.71 (t, J = 7.0, 8.3 Hz, 1H), 7.61−7.68 (m, 3H), 7.14 (dd, J = 2.2, 10.0 Hz, 1H), 6.22 (dd, J = 2.2, 10.0 Hz, 1H), 5.71 (d, J = 5.9 Hz, 1H, exchangeable with D_2O), 5.38 (d, J = 5.0 Hz, 1H, exchangeable with D_2O), 4.59−4.61 (m, 1H, after addition of D_2O changed to doublet, J = 11.0 Hz), 4.50−4.53 (m, 1H, after addition of D_2O changed to doublet, J = 11.0 Hz); MS (*m*/*e*) 362 (M^+, 15); HRMS: Calcd for $C_{26}H_{18}O_2$: 362.1307. Found: 362.1312. UV (EtOH) λ_{max} (ϵ): 214 (3.87×10^4), 288 (8.77×10^4) nm.

***trans*-3,4-Dihydroxy-*anti*-1,2-epoxy-1,2,3,4-tetrahydrobenzo[*s*]picene (5).** To a solution of **4** (51 mg, 0.14 mmol) in freshly distilled THF (6 mL) was added *m*-CPBA (242 mg, 1.4 mmol). Stirring was continued for 2 h, then the solution was diluted with THF and ether, and washed with cold aqueous 10% NaOH, water, and dried over Na_2SO_4. The solvent was removed under reduced pressure without heating and triturated with ether to yield **5** (48 mg, 90%) as a white solid, mp 213-215 °C: ^{1}H NMR (DMSO-d_6) δ 8.85 (d, J = 8.5 Hz, 1H), 8.79 (d, J = 8.6 Hz, 1H), 8.75 (dd, J = 3.6, 8.9 Hz, 1H), 8.73 (d, J = 9.0 Hz, 1H), 8.51−8.53 (m, 1H), 8.14 (d, J = 9.0 Hz, 1H), 8.13 (d, J = 7.8 Hz, 1H), 7.98 (d, J = 8.4 Hz, 1H), 7.69−7.74 (m, 3H), 7.66 (t, J = 7.1, 7.6 Hz, 1H), 5.85 (d, J = 6.4 Hz, 0.6H, exchangeable with D_2O), 5.68 (d, J = 5.0 Hz, 0.6H, exchangeable with D_2O), 4.71 (d, J = 4.3

Hz, 1H), 4.67 (t, J = 6.9, 8.4 Hz, 1H), 3.77 (t, J = 5.6, 8.6 Hz, 1H), 3.74 (d, J = 4.4 Hz, 1H), MS (*m*/*e*) 378 (M^+, 5), 154 (11); HRMS: Calcd for $C_{26}H_{18}O_2$: 378.1256. Found: 378.1256. UV (EtOH) λ_{max} (ϵ): 209 (4.96×10^4), 270 (6.61×10^4), 279 (8.07×10^4), 289 (8.14×10^4) nm.

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