SUPPORTING INFORMATION

Evaluation of the Enantiomeric Resolution of 7,8-Dihydroxy-7,8-Dihydrobenzo[a]pyrene, its 6-Flouro and 6-Bromo Derivatives on Polysaccharide-Derived Stationary Phases

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Solvents were purified as follows: benzene was distilled from Na, toluene from Na/K alloy and THF from LiAlH₄. NMR spectra were recorded on a Bruker Avance DPX 300 spectrometer, with TMS (¹H) and CCl₃F (¹⁹F) as internal reference. Mass spectra and high-resolution mass measurements were obtained on a VG Analytical Autospec Q spectrometer and CD spectra were obtained on a AVIV Model 62A DS Spectropolarimeter (Aviv Associates, Lakewood, NJ). For column chromatography, Fluka Silica gel 60, 220-440 mesh was used. N-bromosaccharin,¹ 6-bromo-9,10-dihydrobenzo[a]pyrene² and (±)-1,1'-bi-2-naphthol³ were synthesized as reported.

Synthesis of (±)-trans-6-bromo-7,8-dihydroxy-7,8-dihydrobenzo[a]pyrene is outlined in the Scheme and the experimental details follow.
(±)-trans-6-Bromo-7,8-dibenzoyloxy-7,8,9,10-tetrahydrobenzo[a]pyrene (2)

Anhydrous silver benzoate (151.3 mg, 0.661 mmol) was suspended in dry benzene (5 mL) and finely powdered iodine (84 mg, 0.330 mmol) was added. The reaction mixture was protected from light and stirred at room temperature for 2 h. 6-Bromo-9,10-dihydrobenzo[a]pyrene (1, 100 mg, 0.30 mmol) was added along with 1 mL of benzene, the stirring was continued for 24 h at room temperature and then for another 24 hours under reflux. The reaction mixture was filtered through Celite while hot, the Celite washed with hot benzene, and the filtrate was evaporated. The product was purified by preparative tlc (SiO₂, 2 mm, mobile phase 20% n-hexane in benzene) to yield (±)-trans-6-bromo-7,8-dibenzoyloxy-7,8,9,10-tetrahydrobenzo[a]pyrene (2) as a yellow solid (73 mg, 42%). 1H NMR (CDCl₃) (': C-7 benzoyloxy; ': C-8 benzoyloxy): δ 8.57 (d, 1 H-5, J = 9.3 Hz), 8.36 (d, 1 H-11, J = 9.3 Hz), 8.29 - 8.20 (m, 3 H-1, H-3, H-12), 8.13 (d, 1 H-4, J = 9.3 Hz), 8.10 - 8.02 (m, 3 H-2', H-6', H-2), 7.90 - 7.82 (m, 2 H-2", H-6"), 7.59 - 7.51 (m, 1 H-4'), 7.49 - 7.36 (m, 3 H-4", H-3', H-5'), 7.33 - 7.24 (m, 2 H-3", H-5'"), 6.86 (dd, 1 H-7, J = 2.9, 1.1 Hz), 5.94 - 5.89 (m, 1 H-8), 3.77 (ddd, 1 H-10, J = 17.6, 6.3, 1.8 Hz), 3.56 (ddd, 1 H-10, J = 17.6, 12.2, 6.1), 2.75 - 2.63 (m, 1 H-9), 2.57 - 2.42 (m, 1 H-9); 13C NMR (CDCl₃) δ 165.34 (CO"), 165.15 (CO'), 133.18 (C-6a), 133.16 (C-4'), 133.04 (C-4''), 131.27 (C-3a), 131.16 (C-12a), 129.93 (2 C-6', C-2'), 129.79 (2 C-1', C-1''), 129.68 (2 C-6", C-2''), 129.24 (C-5a), 128.84 (C-10a), 128.68 (C-4), 128.38 (2 C-3', C-5'), 128.27 (2 C-3", C-5'"), 128.19 (C-12), 128.16 (C-10b), 126.84 (C-2), 126.68 (C-5), 125.97 (C-1), 125.86 (C-12c), 125.81 (C-3), 125.23 (C-6), 123.83 (C-12b), 122.67 (C-11), 71.24 (C-7), 69.09 (C-8), 22.19 (C-9), 21.90 (C-10); HRMS m/e calcld for C₃₄H₂₃O₄Br 574.0780, found 574.0783.

(±)-trans-6-Bromo-7,8-dibenzoyloxy-7,8,9,10-tetrahydrobenzo[a]pyrene (3)

(±)-Trans-6-bromo-7,8-dibenzoyloxy-7,8,9,10-tetrahydrobenzo[a]pyrene (2, 65 mg, 0.113 mmol) was placed in a three-neck round-bottomed flask, equipped with a thermometer, water condenser and an argon gas inlet. CCl₄ (18 mL) was added, the mixture was stirred and carefully heated with a tungsten halogen lamp (50 W) while argon was bubbled through the solution. When the temperature of the solution reached 60
C, NBS (23.7 mg, 0.1334 mmol) and AIBN (1.5 mg) were simultaneously added to the reaction mixture. The reaction was carefully monitored every few minutes by analytical tlc (SiO$_2$, 25% ethyl acetate in $n$-hexane) and after 15 minutes only a trace amount of the starting compound was visible. The heating was therefore discontinued after a total of 22 minutes and the flask was quickly cooled in ice water. After cooling, a small amount of decolorizing carbon was added, the suspension was filtered through Celite and the Celite washed thoroughly with CCl$_4$. The solvent was carefully evaporated at ambient temperature and the reaction mixture was dried in vacuo. The crude product was dissolved in dry toluene (13 mL), NEt$_3$ (85 µL) and NaHCO$_3$ (340 mg) were added and the mixture heated at reflux under small flux of argon. The reaction was monitored by tlc (SiO$_2$, benzene) and after 6 hours only a trace amount of starting substrate was observed. The heating was discontinued, the reaction mixture was cooled and the suspension was filtered through Celite. The product was purified by preparative tlc (SiO$_2$, benzene) to yield (±)-trans-6-bromo-7,8-dibenzoyloxy-7,8-dihydrobenzo[a]pyrene (3) as a yellow solid (27 mg, 42%). $^1$H NMR (CDCl$_3$) δ 8.59 (d, 1 H, $J = 9.2$ Hz), 8.43 (d, 1 H, $J = 9.4$ Hz), 8.26-8.20 (m, 2 H), 8.17 (d, 2 H, $J = 9.3$ Hz), 8.06 (d, 1 H, $J = 7.6$ Hz), 8.03 - 7.87 (m, 5 H), 7.54 - 7.42 (m, 2 H), 7.39 - 7.26 (m, 4 H), 7.23 (dd, 1 H, $J = 1.8$, 1.1 Hz), 6.67 (ddd, 1 H, $J = 9.9$, 5.7, 0.9 Hz), 5.95 (dd, 1 H, $J = 5.7$, 1.9 Hz); $^{13}$C NMR (CDCl$_3$) δ 165.54 (CO), 165.48 (CO), 133.20, 133.05, 131.31, 131.07, 130.36, 129.95 (2 C), 129.83 (2 C), 129.65, 129.56, 129.45, 128.69, 128.33 (2 C), 128.23 (2 C), 128.04, 127.79, 127.54, 127.04, 126.79, 126.73, 126.65, 126.23, 126.17, 124.61, 124.47, 124.02, 122.00, 71.40, 66.86; HRMS m/e calcd for C$_{34}$H$_{21}$O$_4$Br 572.0623, found 572.0630.

(±)-trans-6-Bromo-7,8-dihydroxy-7,8-dihydrobenzo[a]pyrene (4)

(±)-Trans-6-bromo-7,8-dibenzoyloxy-7,8-dihydrobenzo[a]pyrene (3, 27 mg, 0.047 mmol) was suspended in methanol (2.3 mL) and heated to 60°C. Sodium methoxide (128 mg, 2.37 mmol) was added and the suspension immediately became a solution. After 15 minutes, no starting material was detected by tlc, and the reaction mixture was cooled. The mixture was diluted with ethyl acetate and washed sequentially with water, 10% hydrochloric acid and water. The organic layer was dried and the solvent evaporated. The
product was purified by column chromatography (SiO$_2$ in 5% MeOH-PhH) to provide (±)-trans-6-bromo-7,8-dihydroxy-7,8-dihydrobenzo[a]pyrene (4) as a pale yellow solid (16 mg, 93%). The yellow color of this compound in solution intensifies rapidly. $^1$H NMR (CDCl$_3$) δ 8.54 (d, 1 H-5, J = 9.3 Hz), 8.37 (d, 1 H-11, J = 9.4 Hz), 8.24 - 8.18 (m, 2 H-1, H-3), 8.15 (d, 1 H-4, J = 9.3 Hz), 8.13 (d, 1 H-12, J = 9.4 Hz), 8.03 (t, 1 H-2, J = 7.6 Hz), 7.75 (d, 1 H-10, J = 9.9 Hz), 6.55 (ddd, 1 H-9, J = 9.8, 5.7, 1.1 Hz), 5.71 (broad s, 1 H-7), 4.63 (dd, 1 H-8, J = 5.7, 2.1 Hz); $^{13}$C NMR (CDCl$_3$) δ 131.83 (C-6a), 131.28 (C-3a), 131.04 (C-12a), 130.29 (C-5a), 129.40 (C-4), 128.62 (C-12), 128.15 (C-9), 126.93 (C-2), 126.81 (C-10b), 126.69 (C-5), 126.38 (C-12c), 126.22 (C-3), 126.13 (C-1), 125.83 (C-10a), 125.48 (C-10), 124.75 (C-6), 124.08 (C-12b), 121.98 (C-11), 72.38 (C-7), 67.35 (C-8); HRMS m/e calcd for C$_{20}$H$_{13}$O$_2$Br 364.0099, found 364.0109.

**Enantiomeric HPLC Separation of (+)- and (-)-trans-6-Bromo-7,8-dihydroxy-7,8-dihydrobenzo[a]pyrene (4).**

Racemic trans-6-bromo-7,8-dihydroxy-7,8-dihydrobenzo[a]pyrene (4, 6 mg) was separated on a Daicel Chiralcel OG column (0.46 cm x 25 cm) equipped with a precolumn (0.46 cm x 5 cm), using 50% i-propanol in n-hexane as eluent. Column effluent was monitored at $\lambda = 390$ nm. The *early* and *late* isomers eluted at 27 and 35 min, respectively, yielding 1.5 mg of the *early* and 1.4 mg of the *late* isomer. Reanalysis of the enantiomers on the same enantioselective column showed the purities to be 100% for the *early* and 99.3% for the *late* isomer.

**Computational details:** The HyperChem suite of computational programs was utilized for the theoretical treatment of all the molecular systems. Stewart's PM3 semiempirical model$^4$ was applied to calculate the fully geometrically optimized structures. Different starting geometries were chosen to reach local minima of several conformers of interest. Some significant dihedral angles were presented. No attempt was made to find global minimum.
**Figure A.** Circular dichroic spectra (in MeOH, unsmoothed) of (7R,8R) and (7S,8S) 6-Br-BaP-DHD.
Figure B. HPLC traces showing the resolution of (±)-6-Br-BaP-DHD, (±)-6-F-BaP-DHD, and (±)-6-H-BaP-DHD on a Chiralcel OG column, using n-hexane-iso-propanol as the mobile phase, at 30 °C (see Table 1 for details).
REFERENCES


