JOC Article

Synthesis of Dihydrodiol Metabolites Implicated in the Mechanism of Carcinogenesis of Phenanthro[4,3-*b*][1]benzothiophene and Phenanthro[3,4-*b*][1]benzothiophene, the Polycyclic Sulfur Heterocycles with a "Fjord" Structure

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Dihydrodiols, which are potential proximate carcinogens of phenanthro[4,3-*b*][1]benzothiophene (**3**) and phenanthro[3,4-*b*][1]benzothiophene (**4**) and possess a "fjord" structure, were synthesized. The dihydrodiols synthesized were *trans*-3,4-dihydroxy-3,4-dihydrophenanthro[4,3-*b*][1]benzothiophene (**5**) and *trans*-3,4-dihydroxy-3,4-dihydrophenanthro[3,4-*b*][1]benzothiophene (**6**). The precursors to the dihydrodiols **5** and **6** were 3-methoxyphenanthro[4,3-*b*][1]benzothiophene (**11**) and 3-methoxyphenanthro[3,4-*b*][1]benzothiophene (**16**). Compound **11** was obtained via Suzuki cross-coupling reaction of easily accessible starting materials. However, this synthetic strategy utilizing Suzuki reaction for the preparation of **16** was comparatively less productive than that described previously due to time-consuming synthesis of the starting material(s), and extremely poor yield associated with cyclization of the epoxide **15** to **16**. The methoxy derivatives **11** and **16** were converted to the corresponding dihydrodiols **5** and **6** by a sequence involving demethylation, oxidation, and reduction. The *trans*-stereochemistry of the dihydrodiols was established by ^{1}H NMR, which indicated a large coupling constant between vicinal carbinol protons. The UV spectra of the dihydrodiols **5** and **6** are presented.

Introduction

It is known that polynuclear aromatic hydrocarbons (PAHs) require metabolic activation to display their carcinogenic potential and that the metabolites that have expressed the greatest tumorigenicity are derived from dihydrodiols, especially those in which the isolated double bond is a part of a sterically hindered region (frequently referred to as the bay region).[1−3] Like PAHs, their sulfur analogues (thia-PAHs) are also ubiquitous environmental contaminants, and have been detected in a number of environmental sources including the emission from brown-coal-fired stoves, lubricating oils, coal tar derivatives, exhaust from diesel engines, and cigarette smokes.[4] Despite a number of thia-PAHs being known as carcinogens and mutagens,[4−6] not much is known about their mechanism of carcinogenic/mutagenic action, primarily due to the unavailability of their potential metabolites needed for such studies.

It has been demonstrated that the carcinogenic metabolites of those PAHs which contain a fjord region[7] are generally more tumorigenic than those which contain a bay region, suggesting that additional distortion in the bay region enhances the carcinogenic potential of the metabolite.[1] Previously,[8] I reported the synthesis of *trans*-3,4-dihydroxy-3,4-dihydrophenanthro[3,2-*b*][1]benzothiophene (**2**), a potentially carcinogenic metabolite of phenanthro[3,2-*b*][1]benzothiophene (**1**), which contains an isolated double bond in the bay region. To investigate whether additional steric constraint in the bay region enhances the carcinogenic potential of the dihydrodiol metabolites of thia-PAHs, we have synthesized *trans*-3,4-dihydroxy-3,4-dihydrophenanthro[4,3-*b*]benzothiophene (**5**) and *trans*-3,4-dihydroxy-3,4-dihydrophenanthro[3,4-*b*][1]benzothiophene (**6**), which are the potentially carcinogenic metabolites of phenanthro[4,3-*b*][1]-benzothiophene (**3**) and phenanthro[3,4-*b*][1]benzothiophene (**4**), respectively. **3**, which contains a fjord region, exhibits greater carcinogenic activity than that of its carbon analogue, benzo[*c*]chrysene.[5] However, **4**, which is expected to be more distorted in the bay region than **3** on the basis of the twist angle of their corresponding

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(2) Jerina, D. M.; Chadha, A.; Cheh, A. M.; Schurdek, M. E.; Wood A. W.; Sayer, J. M. *Adv. Exp. Med. Biol.* **1990**, *283*, 533.
(3) Dipple, A.; Moschel; R. C.; Bigger, C. A. H. In *Chemical Carcinogenesis*; Searle, C. E., Ed.; American Chemical Society Monograph 182; American Chemical Society: Washington, DC, 1984; p 41.
(4) Jacob, J. In *Sulfur Analogues of PAHs (Thiaarenes)*; Cambridge University Press: Cambridge, U.K., 1990; see also references therein.
(5) Croisy, A.; Mispelter, J.; Lhoste, J. M.; Zajdela F.; Jacqignon, P. *J. Heterocycl. Chem.* **1984**, *21*, 353.
(6) Warshawsky, D. *Environ. Carcinog. Ecotoxicol. Rev.* **1992**, *C10*, 1.
(7) The fjord region is defined as a bay region with additional steric constraint as exemplified by the region enclosed between positions 1 and 13 of **3** and **4**.
(8) Kumar, S. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1018.

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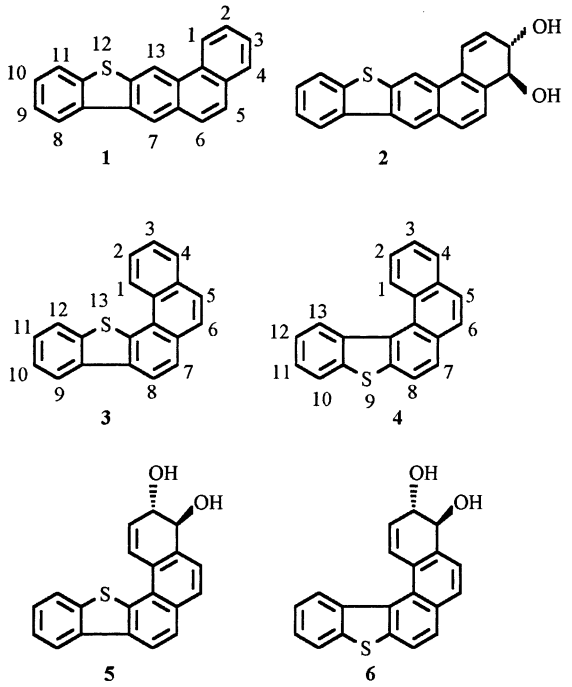
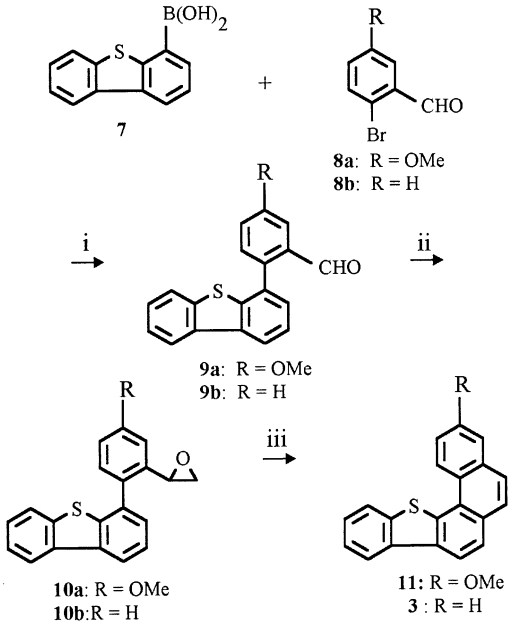
carbon analogues, benzo[*c*]phenanthrene and dibenzo[*c,d*]-phenanthrene,[9] has not been evaluated for its carcinogenic activity.



Results and Discussion

The critical intermediates for preparation of dihydrodiols **5** and **6** are the corresponding methoxy-substituted thia-PAHs **11** and **14** (Schemes 3 and 4)**.** Compound **11** was obtained previously[8] as a major byproduct during the synthesis of **2**, while compound **14** was not previously synthesized. Our approach to the synthesis of **14** was based on our previous observation[10] that a Suzuki cross-coupling reaction[11] of 2-bromo-5-methoxybenzaldehyde (**8b**) with 2-(dihydroxyboryl)benzo[*b*]thiophene provides easy access to the synthesis of analogous 2-methoxy-naphtho[1,2-*b*][1]benzothiophene. The starting boronic acid for the synthesis of **14** was 4-(dihydroxyboryl)dibenzothiophene (**7**), which was prepared according to the published procedure.[12] Suzuki coupling reaction of **7** with **8a** furnished the expected coupling product **9a** in 91% yield (Scheme 1). Modification of the aldehyde functionality of **9a** with trimethylsulfonium iodide and powdered KOH in acetonitrile[13] produced ethylene epoxide derivative **10a** as a thick oil. The ^{1}H NMR of **10a**, which showed the lack of aldehydic proton signal and the presence of four proton signals of equal integration between 2.7 and 2.9 ppm for CH_2 protons of the ethylene epoxide functionality, indicated the formation of **10a** as a 1:1 mixture of diastereomers. The restricted rotation of the aryl−aryl bond and the presence of a chiral center at the benzylic carbon of the ethylene epoxide functionality were, primarily, responsible for **10a** existing as a mixture of diastereomers.[14] Acid-catalyzed cyclization of **10a** with $MeSO_3H$ gave 3-methoxyphenanthro[4,3-*b*][1]-benzothiophene (**11**) in 42% yield. The reaction was carried out the same way as described before[10] except that the solution of epoxide **12a** was added to the solution of $MeSO_3H$. A similar synthetic sequence starting from the Suzuki coupling reaction of **7** and **8b** (Scheme 1) was also successfully applied to the synthesis of the parent thia-PAH, **3**, in overall 69% yield. Compound **3** has been obtained previously by a photochemical method[15] in trace amounts, or by an Elbs reaction[5] in an overall yield of 22%.

SCHEME 1[a]



[a] Reagents: i, $Pd(PPh_3)_4$, CsF−DME; ii, $Me_3S^+I^-$, KOH−MeCN; iii, $MeSO_3H-CH_2Cl_2$.

An approach similar to that outlined in Scheme 1 was also investigated for developing a regiospecific synthesis of **16** (Scheme 2**)**, a key intermediate for the synthesis of **6**. However, this approach was not productive compared to that reported earlier by me[8] due to multiple steps involved in the synthesis of the key starting material 1-bromodibenzothiophene (**12**),[16] and also due to extremely poor yield (∼3%) from the cyclization of the epoxide **15** to **16**. Due to scarcity of **15**, no further attempt was made to improve the yield of **16** from this route.

The conversion of **11** to **5** was achieved via an initial demethylation of **11** with BBr_3 to 3-hydroxyphenanthro-[4,3-*b*][1]benzothiophene (**17**) (Scheme 3). The oxidation of **17** with Fremy's salt afforded the dione **18** as a bright red solid in 75% yield. Reduction of **18** with $NaBH_4$ while O_2 was bubbled through the solution took place smoothly with *trans*-stereospecificity in accord with previous findings for reductions of this type[8,10] to afford **5** as one of the target dihydrodiols. The presence of oxygen is absolutely essential for the successful reduction of *o*-quinone

(9) Herndon, W. C. In *Polynuclear Aromatic Compounds*; Ebert, L. W., Ed.; Advances in Chemistry Series 217; American Chemical Society: Washington, DC, 1988; p 1.
(10) Kumar, S.; Kim, T. Y. *J. Org. Chem*. **2000**, *65*, 3883.
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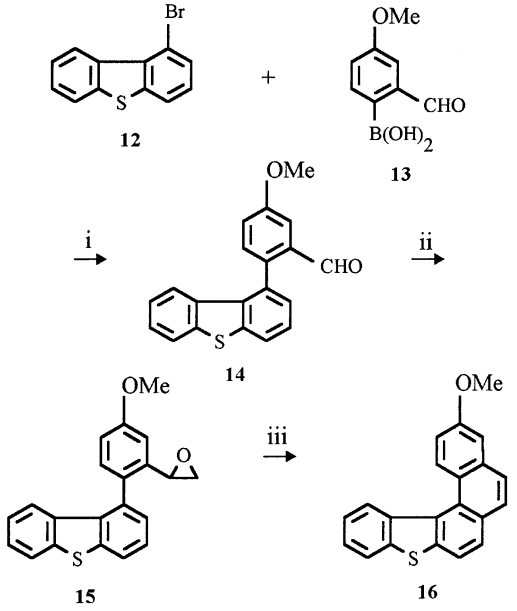
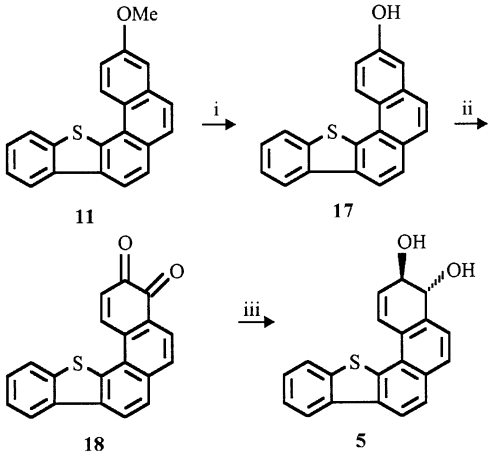
SCHEME 2[a]



[a] Reagents: i, $Pd(PPh_3)_4$, CsF−DME; ii, $Me_3S^+I^-$, KOH−MeCN; iii, $MeSO_3H-CH_2Cl_2$.

SCHEME 3[a]

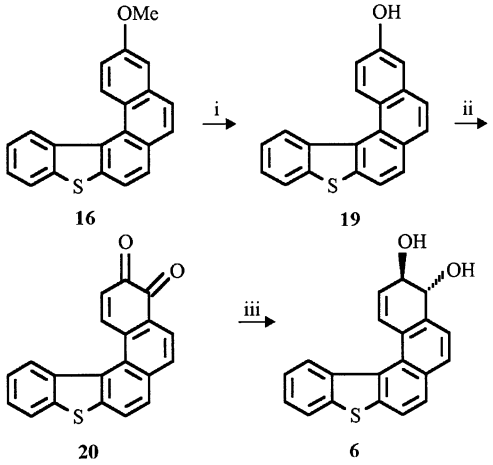


[a] Reagents: i, BBr_3–CH_2Cl_2; ii, Fremy's salt; iii, $NaBH_4$–EtOH.

to dihydrodiol because it reoxidizes the catechol, a major byproduct of such a reaction, back to *o*-quinone.[17] Consequently, the end product of this reduction−oxidation process in the presence of oxygen is pure dihydrodiol. Synthesis of **6** was accomplished by a route similar to that employed for the synthesis of **5**. Thus, the demethylation of **16** with BBr_3 afforded the phenol **19**, which was oxidized with Fremy's salt to produce the dione **18** as a purple solid (Scheme 4). Reduction of the dione **20** with $NaBH_4$ in ethanol while O_2 was bubbled through the solution produced the remaining target dihydrodiol **6** with *trans*-stereospecificity. The UV spectra of dihydrodiols **5** and **6** are shown in Figure 1.

Our preliminary studies have indicated that **6** was nearly 8-fold more mutagenic than **3** in *Salmonella typhimurium* strain TA100 at doses up to 10 nmol/plate. In the same study, **6** showed mutagenic activity similar to that of **3**. A detailed study on the mutagenic activity of these and other thia-PAH derivatives in various strains

SCHEME 4[a]



[a] Reagents: i, BBr_3–CH_2Cl_2; ii, Fremy's salt; iii, $NaBH_4$–EtOH.

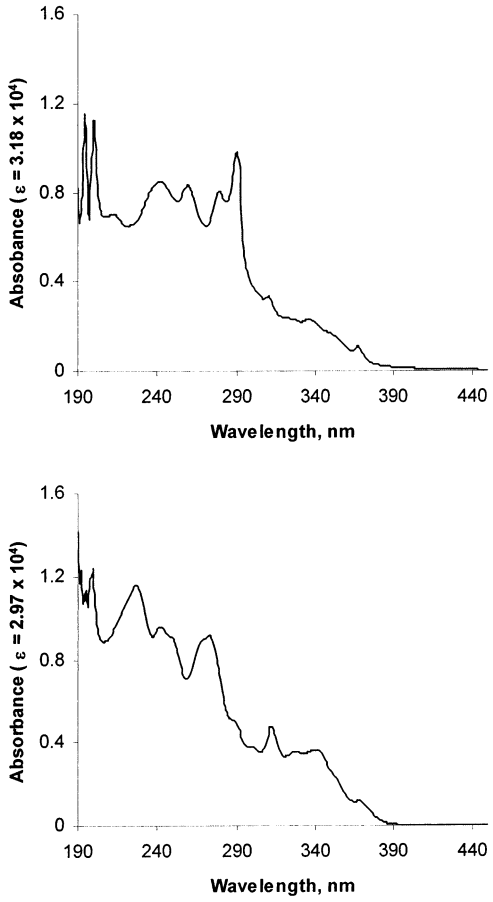


FIGURE 1. UV spectra of dihydrodiols **5** (top) and **6** (bottom) in absolute ethanol.

of *S. typhimurium* are currently under investigation, and will be reported elsewhere.

Experimental Section

All reagents and solvents (anhydrous or otherwise) were used as received without further purification. Dry column grade silica gel (63−200 μm) was used for column chromatog-

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raphy. The ^{1}H and ^{13}C NMR spectra were recorded on a 300 MHz multinuclear NMR spectrophotometer. Chemical shifts are in parts per million relative to that for internal TMS for ^{1}H NMR spectra and relative to solvent signals for ^{13}C NMR spectra. Electron impact (EI) mass spectra were obtained by the mass spectral facility of the Department of Chemistry, State University of New York at Buffalo. All the melting points were uncorrected.

Caution! Phenanthro[b][1]benzothiophenes and their derivatives are potential carcinogens and should be handled in accordance with NIH guidelines for the Laboratory Use of Chemical Carcinogens!

4-(2-Formyl-4-methoxyphenyl)dibenzothiophene (9a). A mixture of **7** (3.0 g, 13.15 mmol),[12] $Pd(PPh_3)_4$ (0.52 g, 0.42 mmol), 2-bromo-5-methoxybenzaldehyde (**8a**; 2.63 g, 12.27 mmol),[18] and anhydrous CsF (4.3 g, 28.25 mmol) in 100 mL of anhydrous DME was stirred under reflux in an argon atmosphere for 20 h. The mixture was cooled to rt, diluted with water, and then extracted with ethyl acetate. The organic phase was washed with water, 5% NaOH, and water successively. After the organic phase was dried over anhydrous Na_2SO_4, the solvent was removed in vacuo to afford an oil, which after chromatography over dry column grade silica gel with 25% CH_2Cl_2 in hexane produced 3.55 g (91%) of colorless oil, which solidified on standing. A small sample of the solid was recrystallized from ethyl acetate−hexane to produce **9a** as light yellow crystals. Mp: 125−127 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.95 (s, 3 H), 7.28 (dd, 1 H, J = 2.9, 8.5 Hz), 7.45−7.62 (m, 5 H), 7.77−7.81 (m, 1 H), 8.18 − 8.23 (m, 2 H), 9.77 (s, 1 H). ^{13}C NMR ($CDCl_3$): δ 191.3 (CHO), 159.6, 140.7, 139.3, 136.8, 135.6, 135.4, 134.4, 132.3, 131.6, 128.4, 126.9, 124.6, 124.5, 122.6, 121.8, 121.6, 121.0, 110.0, 55.5 (OCH_3). MS (EI): m/z 318. Anal. Calcd for $C_{20}H_{14}O_2S$: C, 75.47; H, 4.40. Found: C, 75.31; H, 4.68.

3-Methoxyphenanthro[4,3-*b*][1]benzothiophene (11). A mixture of **9a** (2.7 g, 8.44 mmol), trimethylsulfonium iodide (1.88 g, 9.23 mmol), and powdered KOH (1.40 g, 35.7 mmol) in acetonitrile (100 mL) containing a trace of water was stirred under argon at 65−70 °C for 20 h. The mixture was cooled and extracted with ethyl acetate. The organic phase was washed with water, dried over anhydrous Na_2SO_4, and concentrated in vacuo to yield 2.75 g (100%) of sufficiently pure 4-(2-epoxyethyl-4-methoxyphenyl)dibenzothiophene (**10a**) as a colorless syrupy oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.70−2.77 (m, 1H), 2.90−2.94 (m, 1 H), 3.65 (dd, 1 H, J = 2.7, 4.1 Hz), 3.87 (s, 3 H), 6.91 (d, 1 H, 2.6 Hz), 6.95 (dd, 1 H, J = 0.9, 2.8 Hz), 7.23−7.41 (m, 2 H), 7.43−7.58 (m, 3 H), 7.76−7.82 (m, 1 H), 8.13−8.23 (m, 2 H).

A solution of the epoxide **10a** (1.32 g, 4.33 mmol) in CH_2Cl_2 (25 mL) was added dropwise in 10 min to an ice-cooled solution of CH_3SO_3H (12 mL) in anhydrous CH_2Cl_2 (75 mL) under argon. The solution, which gradually turned dark, was stirred at rt for 12 h. The mixture was diluted with ice-cold water, and the CH_2Cl_2 solution was washed with water, 5% NaOH, and water, successively. After being dried over anhydrous Na_2SO_4, the organic solution was evaporated in vacuo to yield a crude product, which was chromatographed over dry column grade silica gel using 25% CH_2Cl_2 in hexane as eluant to produce 0.55 g (42%) of **11** as a yellow crystalline solid. Mp: 116−118 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.02 (s, 3 H), 7.41 (d, 1 H, J = 2.8 Hz), 7.49 (dd, 1 H, J = 2.8, 9.8 Hz), 7.51−7.61 (m, 2 H), 7.80 (d, 1 H, J = 8.8 Hz), 7.92 (d, 1 H, J = 8.8 Hz), 8.00 (d, 1 H, J = 8.3 Hz), 8.01−8.06 (m, 1 H), 8.30−8.35 (m, 1 H), 8.38 (d, 1 H, J = 8.3 Hz), 9.23 (d, 1 H, J = 9.23 Hz). ^{13}C NMR ($CDCl_3$): δ 157.6, 139.2, 135.1, 134.7, 134.6, 134.2, 131.2, 128.3, 127.7, 126.7, 126.5, 126.4, 126.3, 124.6, 124.2, 122.1, 121.4, 119.1, 116.9, 109.1, 55.4 (OCH_3). MS (EI): m/z 314. Anal. Calcd for $C_{20}H_{14}OS$: C, 80.24; H, 4.46. Found: C, 80.40; H, 4.75.

(18) Fleming I.; Woolias, M. J. *J. Chem. Soc., Perkin Trans. 1* **1979**, 829.

4-(2-Formylphenyl)dibenzothiophene (9b). A mixture of **7** (3.42 g, 15 mmol),[12] $Pd(PPh_3)_4$ (0.6 g, 0.49 mmol), 2-bromobenzaldehyde (**8b**; 2.40 g, 13 mmol), and anhydrous CsF (5.7 g, 37.45 mmol) in 75 mL of anhydrous DME was stirred under reflux in an argon atmosphere for 20 h. The crude product was isolated as described above for **9a** and chromatographed over dry column grade silica gel. The elution of the column with 15% CH_2Cl_2 in hexane gave 3.15 g (84%) of **9b** as colorless crystals. Mp: 92−94 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40 (dd, 1 H, J = 1, 7.3 Hz), 7.45−7.55 (m, 2 H), 7.56−7.66 (m, 3 H), 7.70−7.83 (m, 2 H), 8.10−8.17 (m, 1 H), 8.19−8.28 (m, 2 H), 9.81 (s, 1 H). ^{13}C NMR (300 MHz, $CDCl_3$): δ 191.4 (CHO), 143.8, 140.2, 139.3, 135.7, 135.3, 134.0, 133.4, 132.6, 130.3, 128.6, 128.1, 127.5, 126.9, 124.6, 124.6, 122.6, 121.8, 120.7. MS (EI): m/z 288. Anal. Calcd for $C_{19}H_{12}OS$: C, 78.89; H, 4.49. Found: C, 79.09; H, 4.38.

Phenanthro[4,3-*b*][1]benzothiophene (3). Compound **9b** (1.77 g, 6.14 mmol), trimethylsulfonium iodide (1.37, 6.72 mmol), and powdered KOH (1.03 g, 26.2 mmol) in acetonitrile (60 mL) were heated with stirring at 65−70 °C for 16 h. The workup of the reaction mixture produced **10b**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.72−2.81 (m, 1 H), 2.89−2.97 (m, 1 H), 3.67 (dd, 1 H, J = 2.7, 4.1 Hz), 7.30−7.60 (m, 8 H), 7.72−7.83 (m, 1 H), 8.12−8.25 (m, 2 H). Treatment of the crude epoxide **10b** with CH_3SO_3H (15 mL) in CH_2Cl_2 (95 mL) as described for the synthesis of **11** gave a semisolid. The chromatography of the semisolid over dry column grade silica gel using 25% CH_2Cl_2 in hexane as eluant afforded 1.45 g (82%) of **3** as colorless crystals. Mp: 125−126 °C (lit.[5] mp 127 °C). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.51−7.60 (m, 2 H), 7.69−7.74 (m, 1 H), 7.85−8.08 (m, 6 H), 8.32−8.36 (m, 1 H), 8.45 (d, 1 H, J = 8.24 Hz), 9.32 (d, 1 H, J = 8.55 Hz).

1-(2-Formyl-4-methoxyphenyl)dibenzothiophene (14). A mixture of 1-bromodibenzothiophene (**12**)[16] (1.5 g, 5.7 mmol), $Pd(PPh_3)_4$ (0.22 g, 0.18 mmol), 2-(dihydroxyboryl)-5-methoxybenzaldehyde (**13**)[8] (1.14 g, 6.3 mmol), and anhydrous CsF (2.1 g, 13.8 mmol) in 70 mL of anhydrous DME was stirred under reflux in an argon atmosphere for 20 h. The usual workup of the reaction mixture as described for **9a** afforded an oil, which after chromatography over dry column grade silica gel with 50% CH_2Cl_2 in hexane produced 1.7 g (87%) of colorless oil, which solidified on standing in a freezer. A small sample of the solid was recrystallized from CH_2Cl_2–hexane to produce **14** as light yellow crystals. Mp: 146−148 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.99 (s, 3 H), 6.86 (d, 1 H, J = 8.0 Hz), 7.08 (dt, 1 H, J = 1 Hz, 7.2 Hz), 7.25−7.42 (m, 4 H), 7.50 (t, 1 H, J = ∼ 7.5 Hz), 7.64 (d, 1 H, J = 2.6 Hz), 7.84 (d, 1 H, J = 8 Hz), 7.94 (dd, 1 H, J = 1 Hz, 8.0 Hz), 9.67 (s, 1 H). ^{13}C NMR (300 MHz, $CDCl_3$): δ 191.7 (CHO), 159.8, 140.1, 139.8, 137.7, 135.1, 134.9, 134.0, 133.8, 132.1, 127.8, 126.6, 125.7, 124.3, 124.2, 122.8, 121.7, 122.1, 109.7, 55.7 (OCH_3). MS (EI): m/z 318. Anal. Calcd for $C_{20}H_{14}O_2S$: C, 75.47; H, 4.40. Found: C, 75.31; H, 4.68.

3-Methoxyphenanthro[3,4-*b*][1]benzothiophene (16). Compound **14** (0.9 g, 2.81 mmol) was treated with trimethylsulfonium iodide (0.7 g, 3.43 mmol) and powdered KOH (0.3 g, 3.4 mmol) in acetonitrile (40 mL) as described for **10a** to produce sufficiently pure epoxide **15**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.44 (dd, 0.5 H, J = 2.6, 5.6 Hz), 2.50 (dd, 0.5 H, J = 4.1, 5.6 Hz), 2.64 (dd, 0.5 H, J = 2.6, 5.8 Hz), 2.83 (dd, 0.5 H, 4.1, 5.8 Hz), 3.45−3.53 (m, 1 H), 6.60−7.53 (m, 8 H), 7.77−7.91 (m, 2 H). The treatment of the resulting **15** with CH_3SO_3H (1.25 mL) in CH_2Cl_2 (15 mL) as described for the synthesis of **11** gave a semisolid. The chromatography of the semisolid over dry column grade silica gel using 25% CH_2Cl_2 in hexane followed by a preparative TLC using 5% ethyl acetate−hexane as eluant afforded ∼0.03 g (3%) of **16** as light yellow crystals. Mp: 129−130 °C (lit.[8] mp 129−130 °C).

3-Hydroxybenzo[*b*]phenanthro[4,3-b][1]benzothiophene (17). To a stirred solution of **11** (0.14 g, 0.44 mmol) in anhydrous CH_2Cl_2 (35 mL) at 0−5 °C under argon was added a 1 M solution of BBr_3 (0.9 mL, 0.9 mmol) over a period of

2−3 min. After being stirred for 12 h at rt, the mixture was hydrolyzed with ice-cold water. The organic layer was separated, washed with water, dried over anhydrous Na_2SO_4, and then evaporated to afford a solid. The solid was triturated with hexane and filtered to yield 0.13 g (98%) of sufficiently pure **17** as a colorless crystalline solid. A small sample was further purified by preparative TLC (20% ethyl acetate−hexane) to produce **17** as a colorless crystalline solid. Mp: 174−176 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.53 (dd, 1 H, J = 2.8, 10.7 Hz), 7.55−7.68 (m, 3 H), 7.84 (d, 1 H, J = 8.7 Hz), 8.00 (d, 1 H, J = 8.9 Hz), 8.12 (d, 1 H, J = 8.3 Hz), 8.12−8.23 (m, 1 H), 8.47−8.53 (m, 1 H), 8.55 (d, 1 H, J = 8.3 Hz), 9.01 (s, 1 H, exchangeable with D_2O), 9.17 (d, 1 H, J = 8.6 Hz). ^{13}C NMR ($CDCl_3$): δ 155.4, 138.7, 134.7, 134.5, 134.1, 133.5, 130.5, 127.6, 127.1, 126.3, 126.2, 126.0, 124.3, 122.9, 122.5, 121.7, 121.0, 118.4, 117.0, 111.9. MS (EI): m/z 300. Anal. Calcd for $C_{20}H_{12}OS\cdot{}^1/_5H_2O$: C, 79.05; H, 4.10. Found: C, 78.80; H, 4.51.

Phenanthro[4,3-*b*][1]benzothiophene-3,4-dione (18). A solution of **17** (0.13 g, 0.43 mmol) in 100 mL of CH_2Cl_2/benzene (16:84) containing 5 drops of adogen-464 and 0.17 M KH_2PO_4 (30 mL) was stirred at rt while Fremy's salt (0.35 g, 1.3 mmol) was added in one portion with vigorous stirring. After the solution was stirred for 15 h at rt, the organic layer was separated, washed with water, and dried over anhydrous Na_2SO_4. Evaporation of the solvent and the trituration of the residue with 50% CH_2Cl_2/benzene gave 0.1 g (75%) of pure dione **18** as a bright red crystalline solid. Mp: 224−226 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.58 (d, 1 H, J = 10.7 Hz), 7.55−7.62 (m, 2 H), 7.84 (d, 1 H, J = 8.6 Hz), 7.95−8.00 (m, 1 H), 8.03 (d, 1 H, J = 8.4 Hz), 8.18 (d, 1 H, J = 8.3 Hz), 8.22−8.27 (m, 1 H), 8.30 (d, 1 H, J = 8.6 Hz), 9.03 (d, 1 H, J = 10.7 Hz). ^{13}C NMR (300 MHz, $CDCl_3$): δ 180.4, 179.2, 142.4, 139.0, 137.8, 136.0, 134.8, 134.4, 132.5, 131.6, 131.1, 128.2, 127.5, 127.2, 126.9, 126.8, 125.3, 124.8, 123.2, 122.1, 121.8. HRMS (EI): m/z calcd for $C_{20}H_{10}O_2S$ (M^+) 314.0401, found 314.0378.

***trans*-3,4-Dihydroxy-3,4-dihydrophenanthro[4,3-*b*]benzothiophene (5).** To a well-stirred suspension of quinone **18** (0.07 g, 0.23 mmol) in ethanol (50 mL) was added $NaBH_4$ (0.2 g, 5.55 mmol). The mixture was stirred at rt while a stream of oxygen was bubbled through the solution. After 48 h of stirring, the resulting light yellow solution was concentrated at rt in vacuo to 25 mL, diluted with water, and extracted with ethyl acetate. The ethyl acetate solution was dried over anhydrous Na_2SO_4 and evaporated under vacuum to yield a solid, which was triturated with cold ether to give 0.04 g (56%) of **5** as a light yellow solid. Mp: 179−182 °C. ^{1}H NMR (300 MHz, acetone-d_6 + D_2O): δ 4.51−4.59 (m, 1 H), 4.88 (d, 1 H, J = 12 Hz), 6.42 (dd, 1 H, J = 1.9, 10.3 Hz), 7.54−7.69 (m, 2 H), 7.80 (dd, 1 H, J = 2.4, 10.3 Hz), 7.92−8.20 (m, 4 H), 8.39 (d, 1 H, J = 8.6 Hz), 8.41−8.52 (m, 1 H). HRMS (EI): m/z calcd for $C_{20}H_{14}O_2S$ (M^+) 314.0714, found 314.0713. UV (5% THF−EtOH): λ_{max} (ϵ) 199 (36200), 228 (34300), 242 (28500), 250 (26500), 272 (27200), 290 (14400), 312 (14200), 328 (10600), 340 (10800).

3-Hydroxyphenanthro[3,4-*b*][1]benzothiophene (19). Compound **16**[8] (0.5 g, 1.59 mmol) was dissolved in 60 mL of CH_2Cl_2, and 3.2 mL (3.2 mmol) of BBr_3 in CH_2Cl_2 (1 M) was added dropwise at 0 °C under argon. The dark solution was stirred for 18 h at rt. Conventional workup as described for **8** afforded 0.47 g (100%) of **19** as a colorless solid. Mp: 170−172 °C (EtOAc−hexane). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.17 (dd, 1 H, J = 9.0 and 2.6 Hz), 7.41 (d, 1 H, J = 2.6 Hz), 7.41−7.57 (m, 2 H), 7.78 (d, 1 H, J = 8.7 Hz), 7.88 (d, 1 H, J = 8.7 Hz), 7.94 (d, 1 H, J = 8.3 Hz), 8.04 (d, 1 H, J = 8.3 Hz), 8.09 (dd, 1 H, J = 7.8 and 0.7 Hz), 8.69 (d, 1 H, J = 8.7 Hz), 8.86 (d, 1 H, J = 9 Hz), 8.96 (s, 1 H). MS (EI): m/z 300 (M^+, 100). Anal. Calcd for $C_{20}H_{12}OS\cdot{}^1/_5H_2O$: C, 79.0; H, 4.1. Found: C, 78.6; H, 4.4.

Phenanthro[3,4-*b*][1]benzothiophene-3,4-dione (20). Oxidation of **19** (0.18 g, 0.6 mmol) with Fremy's salt (0.49 g, 1.83 mmol) by the procedure employed for the preparation of **9** yielded, after trituraion with CH_2Cl_2−benzene, 0.16 g (87%) of **20** as a purple crystalline solid. Mp: 235−237 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.44 (d, 1 H, J = 10.4 Hz), 7.51−7.62 (m, 2 H), 7.86 (d, 1 H, J = 8.6 Hz), 8.03−8.08 (m, 2 H), 8.10 (d, 1 H, J = 8.6 Hz), 8.17 (d, 1 H, J = 10.6 Hz), 8.15−8.22 (m, 1 H), 8.27 (d, 1 H, J = 8.3 Hz). ^{13}C NMR (300 MHz, $CDCl_3$): δ 181.1, 180.7, 145.2, 142.6, 140.0, 136.2, 136.1, 131.2, 130.7 (2 C), 129.2, 128.1, 127.2, 126.5, 126.0, 124.7 (2 C), 124.5, 124.0, 123.1. HRMS (EI): m/z calcd for $C_{20}H_{10}O_2S$ (M^+) 314.0401, found 314.0400.

***trans*-3,4-Dihydroxy-3,4-dihydrophenanthro[3,4-*b*][1]benzothiophene (6).** Reduction of **20** (0.14 g, 0.45 mmol) with $NaBH_4$ (0.42 g, 11.66 mmol) in the presence of oxygen by the usual procedure as described for **5** gave a crude product. Trituration of the product with 1:1 ethyl acetate−hexane afforded 0.04 g (30%) of pure **6**. Mp: 177−179 °C. ^{1}H NMR (300 MHz, acetone-d_6 + D_2O): δ 4.76 (d, 1 H, J = 10.5 Hz), 4.82 (d, 1 H, 10.5 Hz), 6.18 (d, 1 H, J = 9.7 Hz), 6.84 (d, 1 H, J = 9.7 Hz), 7.47−7.56 (m, 2 H), 7.92−8.11 (m, 5 H), 8.35−8.39 (m, 1 H). HRMS (EI): m/z calcd for $C_{20}H_{14}O_2S$ (M^+) 318.0714, found 318.0683. UV (5% THF−EtOH): λ_{max} (ϵ) 194 (36500), 201 (71400), 212 (44700), 238 (52600, sh), 242 (27100), 260 (26500), 279 (25600), 290 (31300), 310 (10600), 337 (7300, sh), 351 (5300, sh), 367 (3500).

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