Synthesis of 5-Fluoro-7,12-dimethylbenz[a]anthracene-3,4-dione: Nucleophilic Displacement of Fluorine in Polyaromatic Hydrocarbons

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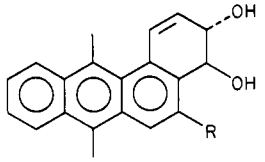
The synthesis of 5-fluoro-7,12-dimethylbenz[a]anthracene-3,4-dione (**24**) from 3-acetyl-1-fluoro-7-methoxynaphthalene (**12**) via 5-fluoro-3-methoxy-7,12-dimethylbenz[a]anthracene (**20**) is described. Unexpectedly reaction of **20** with ethylthio anion and BBr_3/CH_2Cl_2 yielded 5-(ethylthio)-3-hydroxy-7,12-dimethylbenz[a]anthracene and the 5-bromo-3-hydroxy compound. To our knowledge this novel displacement has no precedent in polycyclic aromatic hydrocarbon chemistry.

Metabolism of 7,12-dimethylbenz[a]anthracene (DMBA) by using rat tissue homogenates furnished the DMBA 3,4-dihydrodiol **1** (DMBA-3,4-DHD), shown to be a potent

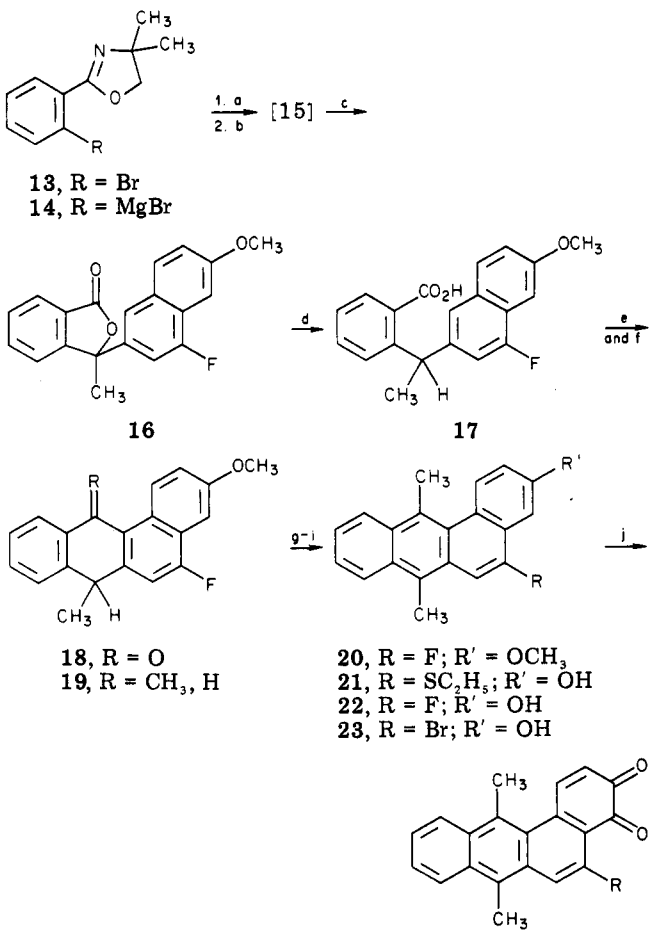


1, R = H
2, R = F

carcinogen and mutagen and a cell-transforming agent both in vitro and in vivo.[1-4] If the qualitative and quantitative aspects of DMBA-3,4-DHD production determine the frequency of carcinogenesis, then the weaker carcinogenic potential[5-7] of 5-F-DMBA may be attributed to the diminished biofunctionalization of the 3,4-double bond. Interestingly, we failed to detect production of the 5-F-DMBA-3,4-DHD (**2**) metabolite[8,9] using a number of induced and uninduced rat liver S-10 fractions. Therefore, we desired a sample of 5-F-DMBA-3,4-DHD (**2**) in order to assess its mutagenic and carcinogenic potential which may provide a partial explanation for decreased carcinogenicity of 5-F-DMBA, reflecting its inability to undergo biotransformation to its 3,4-DHD. In this paper, we report the synthesis of 3,4-dione **24** and our inability to reduce **24** to the 3,4-DHD **2**.

Sukumaran and Harvey[10] previously reported the synthesis of **1**, and the later steps in our synthesis of **24** (**22** → **24**) involving construction of the A-ring DHD are similar. For our purposes, 1-fluoro-7-methoxynaphthalene (**3**) appeared to be a suitable key intermediate.

Scheme I[a]



13, R = Br
14, R = MgBr

16

17

18, R = O
19, R = CH_3, H

20, R = F; R′ = OCH_3
21, R = SC_2H_5; R′ = OH
22, R = F; R′ = OH
23, R = Br; R′ = OH

24, R = F
25, R = H

[a] (a) Mg, dry Et_2O; (b) compound **12**; (c) $EtOH/H_2SO_4$, Δ; (d) Zn/KOH, $CuSO_4$, Δ; (e) H_2SO_4, Δ; (f) MeLi/Et_2O; (g) neutral alumina or silica gel; (h) NaSEt/DMF, Δ; (i) BBr_3/CH_2Cl_2, room temperature; (j) PhSe(O)OSe(O)Ph/THF, 75–80 °C (bath).

The key intermediate 1-fluoro-7-methoxynaphthalene (**3**) was synthesized by diazotization[11] of methoxy derivative **7** to afford the diazonium tetrafluoroborate **8** in 80% yield, and this salt smoothly decomposed in boiling xylene

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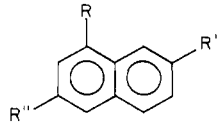

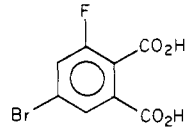

11

3, R = F; R′ = OCH_3; R″ = H
4, R = NH_2; R′ = OH; R″ = H
5, R = $N{\equiv}N^+PF_6^-$; R′ = OH; R″ = H
6, R = F; R′ = OH; R″ = H
7, R = $NH_2{\cdot}HCl$; R′ = OCH_3; R″ = H
8, R = $N{\equiv}N^+BF_4^-$; R′ = OCH_3; R″ = H
9, R = F; R′ = OH; R″ = Br
10, R = F; R′ = OCH_3; R″ = Br
12, R = F; R′ = OCH_3; R″ = $C(O)CH_3$

to yield 66% of intermediate **3**.[12] Demethylation of **3** yielded **6** which upon bromination and subsequent reduction with $SnCl_2$/HCl provided **9**. The ^1H NMR spectra for methoxy derivative **10** and the $KMnO_4$ oxidation product of **9**, namely, **11**, were consistent with the assigned structures (see Experimental Section). However, **10** failed to undergo Grignard formation and subsequent reaction with phthalic anhydride during attempts to construct rings C and D. For these reasons, **3** was converted to **12** by Friedel–Crafts acylation. Acylated product **12** was obtained in good yield and underwent reaction[13] with Grignard reagent **14** to afford **15** (Scheme I). Treatment with aqueous HCl yielded expected lactone **16** in good yield.[14] Lactone **16** was reduced with Zn/KOH, affording **17** which upon cyclization with sulfuric acid[14,15] afforded anthrone **18**. Subsequent reaction with CH_3Li and dehydration of the intermediate carbinol afforded 5-F-3-MeO-DMBA (**20**).

Attempted demethylation by using $NaSCH_2CH_3$[17] in DMF resulted in both demethylation and fluoride displacement to yield **21** in approximately 58% yield. ^1H NMR resonance signals at δ 1.37 (t, J = 7.3 Hz, 3 H) and 3.0 (q, J = 7.3 Hz, 2 H) confirmed the presence of the SCH_2CH_3 moiety. Furthermore, the sharp singlet at δ 8.10 attributable to the C_6H resonance signal established the presence of SCH_2CH_3 substitution at position 5. To our knowledge this observation represents the first reported example of nucleophilic displacement of fluorine in the benzanthracene (BA) nucleus although displacement of F from other aromatic rings has been previously reported.[18,19] Such displacement may have biological consequences since reaction in biological systems with glutathione, cysteine, nucleic acid bases, etc. may lead either to detoxification, formation of compounds with unknown biological activities, or macromolecular binding.

Attempted demethylation of **20** with trimethylsilyl iodide [NaI + $(CH_3)_3SiCl$][20] in acetonitrile failed either at room temperature or under refluxing conditions. However, stirring **20** under N_2 with BBr_3[21] in CH_2Cl_2 at room temperature afforded desired target **22** in approximately 60% yield. Following chromatography of the crude reaction mixture, a trace of bromo compound **23** also was obtained. Both **22** and **23** were shown to be pure by HPLC following their separation by column chromatography. Their ^1H NMR and mass spectra were consistent with the assigned structures. For **23**, base molecular ion peaks of virtually equal intensity at m/e 352 and 350 were particularly diagnostic for the presence of the Br atom.

Attempted oxidation of **20** to 5-fluoro-7,12-dimethylbenz[a]anthracene-3,4-dione (**24**) with Fremy's salt[22] failed. However, **20** was oxidized in poor yield by using Barton's procedure and employing diphenyldiselenic anhydride.[23] Dione **24** exhibited the expected proton resonance signal for the C1 vinyl proton at δ 6.44 (d, 1 H, J = 11 Hz) and for the fluorine-coupled C6 proton at δ 7.92 (d, 1 H, J = 14 Hz). Furthermore, **24** exhibited a UV spectrum similar to that of 7,12-dimethylbenz[a]anthracene-3,4-dione (**25**).[10] Attempted reduction of dione **24** with $LiAlH_4$ in THF did not provide the corresponding 3,4-DHD (**2**). Owing to small quantities, products could not be rigidly characterized, but the characteristic UV spectrum expected for **2** was not observed.

Experimental Section

All melting points are uncorrected and were determined on a Thomas-Hoover capillary melting point apparatus.

Mass spectra were obtained at 70 eV on a low-resolution Du Pont mass spectrometer, Model 21-491, interfaced with a Hewlett-Packard 21605 microprogrammable system computer. Ultraviolet and infrared spectra were recorded on Beckman UV-5260 and IR-4230 instruments. ^1H NMR spectra were determined on a Varian A-60-A or Bruker HX-90E instrument. Purification of compounds was carried out by column chromatography over silica gel 60 (E. Merck) and preparative thin-layer chromatography over precoated silica gel GF plates (E. Merck). The purity of the products was determined by HPLC with an LDC chromatography accessory module containing LDC gradient master constrametric pumps and a UV Spectromonitor III. An LDC Spherosorb ODS column (diameter 5 μm, length 25 cm) and a Whatman precolumn (diameter 4.6 mm, length = 7 cm; packed with CoPell ODS, 10 μm) was employed.

1-Amino-7-hydroxynaphthalene (4; technical grade, Aldrich Chemical Co.) was dissolved in dilute HCl, treated with charcoal, filtered, and precipitated with 30% ammonium hydroxide. The precipitate crystallized from ethyl acetate to furnish white needles of pure 4 which was acetylated, methylated, and deacetylated to give 68% of 1-amino-7-methoxynaphthalene hydrochloride (**7**).[11]

1-Fluoro-7-methoxynaphthalene (3). A cold solution of sodium nitrite (17.5 g, 0.25 mol) in water (60 mL) was added dropwise to a solution (0 °C) of 7 (42 g, 0.24 mol) in water (100 mL) containing concentrated HCl (60 mL). Following stirring for 30 min, urea was added and the mixture filtered. To the clear orange filtrate was added HBF_4 in water (48%, 200 mL). The mixture was allowed to stir at 0 °C for 30 min. The yellow precipitate was collected by filtration and washed with ice-cold water, ethanol, and ether, affording 44 g (80.3%) of diazonium tetrafluoroborate **8**, mp 96–97°C dec. Careful addition of **8** (4.4 g) to 450 mL of boiling dry xylene (refluxed 1 h) yielded, following filtration and distillation, 18.5 g (66%) of **3**: bp 84–85 °C (0.2 mm) [lit.[11] bp 84–86 °C (0.4 mm)]; ^1H NMR ($CDCl_3$) δ 3.82 (s, 3 H, CH_3), 6.84–7.70 (m, 6 H, aromatic); MS, m/e 176 (M^+).

1-Fluoro-7-hydroxynaphthalene (6). A mixture of **3** (6.6 g, 0.038 mol), glacial acetic acid (39.6 mL), and HBr (47–49%; 44 mL) was refluxed for 4 h and poured over crushed ice. The pink-white solid was collected by filtration and subsequently recrystallized from Skellysolve B to yield 5.2 g (86%) of **6**: mp 98–99 °C (lit.[11] mp 96–98 °C); MS, m/e 162 (M^+); IR (KBr) 3350 cm^{-1} (OH); ^1H NMR ($CDCl_3$) δ 5.12 (s, 1 H, OH), 6.9–7.8 (m, 6 H, Ar).

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Anal. Calcd for $C_{10}H_7F$: C, 74.07; H, 4.32; F, 11.7. Found: C, 73.91; H, 4.11; F, 11.60.

3-Bromo-1-fluoro-7-hydroxynaphthalene (9). Bromine (6.4 g, 0.08 mol) in glacial acetic acid (40 mL) was added dropwise to a solution of **6** (3.2 g, 0.02 mol) in glacial acetic acid (40 mL). The mixture was heated for 1 h on a stem bath, stirred overnight at room temperature, and poured onto ice–water. The precipitated solid was collected by filtration and treated with a mixture of glacial acetic acid (24 mL), stannous chloride (9.6 g), and concentrated HCl (24 mL). The mixture was heated on a steam bath for 1 h and then poured over ice–water. The precipitate was collected by filtration and crystallized several times from a mixture of dichloromethane and petroleum ether to furnish 0.42 g of **9** as white needles: mp 126–127 °C; MS, *m/e* 240, 242 (M^+); ^1H NMR ($CDCl_3$) δ 5.64 (s, 1 H, OH), 6.9–7.3 (m, 3 H, aromatic), 7.46–7.72 (m, 2 H, aromatic).

Anal. Calcd for $C_{10}H_6BrFO$: C, 49.79; H, 2.49. Found: C, 49.57; H, 2.53.

The supernatant furnished 1.35 g of uncharacterized solid (MS, *m/e* 240 M^+).

Characterization of 9. Potassium permanganate (1.2 g) in water (7.5 mL) was added to a solution of **9** (0.3 g, 0.0012 mol) in sodium hydroxide (0.5 N, 2.5 mL). The mixture was refluxed with vigorous stirring for 3.5 h and filtered. The filtrate was acidified with concentrated HCl, concentrated, and extracted with ether. Evaporation of the ether extract and subsequent crystallization from ether–petroleum ether furnished 5-bromo-3-fluorophthalic acid (**11**): mp 176–177 °C; MS, *m/e* 264, 262 (M^+). NMR analysis ruled out the other regioisomers for the bromine atom: ^1H NMR (trifluoroacetic acid) δ 7.20 (dd, 1 H, J_{H4-H6} = 1 Hz, J_{H4-F3} = 8.5 Hz, C6 H), 8.10 (br s exhibiting small coupling with H4 and F3, 1 H, C4 H).

3-Bromo-1-fluoro-7-methoxynaphthalene (10). Dimethyl sulfate (0.24 g, 0.001 mol) was added to a solution of **9** (0.24 g, 0.001 mol) and sodium hydroxide (0.08 g, 0.002 mol). The mixture was heated 1 h on a steam bath, stirred 1 h at room temperature, and poured over ice. The solid was collected by filtration and crystallized from ethanol–water to yield **10**: 0.19 g (40%); mp 70.5–71.5 °C; ^1H NMR ($CDCl_3$) δ 3.93 (s, 3 H, CH_3), 7.12–7.3 (m, 3 H, aromatic), 7.6–7.7 (m, 2 H, aromatic).

Anal. Calcd for $C_{11}H_8BrFO$: C, 51.76; H, 3.14; F, 7.45. Found: C, 51.95; H, 3.27; F, 7.45.

3-Acetyl-1-fluoro-7-methoxynaphthalene (12). To a mixture of **3** (26.0 g, 0.148 mol) and acetyl chloride (16.02 g, 0.20 mol) in 240 mL of dry nitrobenzene was added portionwise anhydrous aluminum chloride (31.2 g, 0.22 mol) with stirring. The reaction mixture was stirred at 0 °C for 1 h and poured onto a mixture of ice and dilute HCl. The organic layer was separated and steam distilled. The residue was purified by chromatography on silica gel with a 1:1 mixture of petroleum ether and ether. Recrystallization from ether yielded **12**: 12.4 g (38%); mp 97–98 °C (lit.[11] mp 97 °C); IR (KBr) 1680 cm^{-1} (C=O); UV (MeOH) λ_{max} 306 nm (ϵ 1.1 × 10^5), 249 (3.13 × 10^5), 241 (3.15 × 10^5); IR (KBr) 1680 (C=O), 1020 cm^{-1} (C—O—C); ^1H NMR ($CDCl_3$) δ 2.65 (s, 3 H, CH_3CO), 3.90 (s, 3 H, OCH_3), 7.0–8.2 (complex, 5 H, aromatic); MS, *m/e* (relative intensity) 218 (88, M^+), 203 ($M^+ - CH_3$, 100), 189 (20), 175 (54), 160 (29), 146 (22), 144 (18), 132 (33), 131 (19).

Anal. Calcd for $C_{13}H_{11}FO_2$: C, 71.60; H, 5.00; F, 8.70. Found: C, 71.70; H, 5.06; F, 8.51.

2-[2-[1-(4-Fluoro-6-methoxynaphthyl)-1-hydroxyethyl]-phenyl]-4,4-dimethyl-2-oxazoline (15). The Grignard reagent prepared from oxazoline **13**[14] (10.16 g, 0.04 mol) and sublimed magnesium (1.22 g, 0.051 mol) in 120 mL of dry THF with a few iodine crystals was treated with 3-acetyl-1-fluoro-7-methoxynaphthaline (**12**; 9.0 g, 0.04 mol) dissolved in 20 mL of the dry THF. The reaction mixture was refluxed overnight, cooled, and quenched with 200 mL of 20% aqueous NH_4OH and 200 mL of ether. The organic layer was separated and the aqueous layer repeatedly extracted with ether. The combined ether extracts were dried ($MgSO_4$), and the solvent was removed. The oily residue was washed with cold petroleum ether and on standing solidified, affording 14.1 g (90%) of **15**: mp 131–133 °C (MeOH); IR (KBr) 3280 (OH), 1680 (C=N), 1060 cm^{-1} (C—O—C).

2-[1-Hydroxy-1-(4-fluoro-6-methoxynaphthyl)ethyl]-benzoic Acid Lactone (16). A solution of the oxazoline adduct **15** (6.9 g, 0.018 mol) in 100 mL of 8% ethanolic H_2SO_4 was refluxed for 18 h. Excess ethanol was removed under reduced pressure, and the residue was diluted with water and extracted with ether. The organic layer was washed with cold water and 5% $NaHCO_3$ solution and dried (K_2CO_3). After filtration, the solvent was removed under reduced pressure, affording 5.0 g (85%) of crystalline **16**: mp 142–143 °C (MeOH); IR (KBr) 1750 cm^{-1} (lactone); UV (MeOH) λ_{max} 331 nm, 316, 274, 264; intensity ratio λ_{max} 331/316 = 1.0; λ_{max} 274/264 = 1.0; ^1H NMR ($CDCl_3$) δ 2.15 (s, 3 H, CH_3CO), 3.95 (s, 3 H, OCH_3), 7.00–8.00 (complex, 9 H, aromatic); MS, *m/e* (relative intensity) 322 (M^+, 74), 307 ($M^+ - CH_3$, 100), 263 ($M+ - CO_2 - CH_3$, 27), 220 (17).

Anal. Calcd for $C_{20}H_{15}FO_3$: C, 74.50; H, 4.70; F, 5.90. Found: C, 74.42; H, 4.87; F, 5.90.

2-[1-(4-Fluoro-6-methoxynaphthyl)ethyl]benzoic Acid (17). A mixture of lactone **16** (1.7 g, 5.3 mmol), methanol (20 mL), water (10 mL), zinc dust (5.0 g), KOH (3.0 g), and $CuSO_4$ (50 mg) was refluxed overnight and the hot mixture filtered. After the filter cake was washed with warm water, the filtrate was acidified with dilute HCl and the white precipitate extracted with ether. The ether extract was dried ($MgSO_4$) and the solvent removed under reduced pressure, affording 1.61 g (87%) of **17**: mp 170–172 °C; IR (KBr) 3420, 1700 cm^{-1} (COOH); UV (MeOH) λ_{max} 334 nm (ϵ 1.97 × 10^3), 319 (1.67 × 10^3), 273 (8.2 × 10^3), 262 (8.2 × 10^3); ^1H NMR ($CDCl_3$) δ 1.75 (d, 3 H, *J* = 6.5 Hz, CH_3CH), 3.95 (s, 3 H, OCH_3), 5.7 (q, 1 H, *J* = 6.5 Hz, CH_3CH), 6.80–8.00 (complex, 9 H, aromatic); MS, *m/e* (relative intensity) 324 (M^+, 88), 309 ($M^+ - CH_3$, 14), 306 ($M^+ - H_2O$, 50), 291 ($M^+ - H_2O - CH_3$, 52), 263 ($M^+ - H_2O - CH_3 - CO$, 19), 233 (16), 203 ($M^+ - C_5H_4 - COOH$, 11), 148 (28), 133 (100).

Anal. Calcd for $C_{20}H_{17}O_3F$: C, 74.00; H, 5.20; F, 5.90. Found: C, 74.42; H, 4.87; F, 5.92.

3-Methoxy-5-fluoro-7-methylbenz[*a*]anthrone (18). The acid **17** (2.4 g, 7.4 mmol) was treated with 150 mL of concentrated H_2SO_4 with stirring for 1.5 h at room temperature. The mixture was poured onto ice and the precipitate extracted with ether. The organic layer was washed with water and 5% $NaHCO_3$ solution until neutral. After the mixture was dried, the solvent was removed under reduced pressure to yield an oily product (2 g) which was chromatographed on silica gel petroleum ether/ether (1:1), affording 1.5 g (66%) of **18**: yellow crystals; mp 115–117 °C; (ether/petroleum ether); IR (KBr) 1650, 1050 cm^{-1}; UV (MeOH) λ_{max} 313 nm, 298 (sh), 256; λ_{max} 256/313 = 3.00; ^1H NMR ($CDCl_3$) δ 1.60 (d, 3 H, *J* = 7 Hz, CH_3CH), 3.95 (s, 3 H, OCH_3), 4.27 (q, 1 H, *J* = 7 Hz, CH_3CH), 7.5 (d, 1 H, *J* = 11 Hz, C6H), 7.42 (s, 1 H, C_4H), 8.30 (tt, distorted, 1 H, *J* = 3, 9 Hz, C2 H), 9.70 (dd, 1 H, *J* = 3, 9Hz, C1H), 7.30–7.60 (complex, 4 H, aromatic); MS, *m/e* (relative intensity) 306 (m^+), 291 ($M^+ - CH_3$, 88.5), 276 (M^+ – HCHO, 25), 263 ($M^+ - CH_3 - CO$, 33), 248 (31), 233 (35), 220 (36).

Anal. Calcd for $C_{20}H_{15}FO_2$: C, 79.20; H, 4.70; F, 5.90. Found: C, 78.64; H, 4.97; F, 5.97.

3-Methoxy-5-fluoro-7,12-dimethylbenz[*a*]anthracene (20). A solution of anthrone **18** (0.8 g, 2.6 mmol) in 180 mL of dry ether was treated with excess methyllithium (1.3 M, 10 mL) in dry ether. The reaction mixture was refluxed overnight, cooled, and neutralized with 4 N HCl (20 mL). Benzene (75 mL) was added and the mixture refluxed for 1 h. The organic layer was separated and washed with cold water, 5% $NaHCO_3$ solution, and water. After the mixture was dried ($MgSO_4$), the solvent was removed under reduced pressure, affording an oily residue which was chromatographed on neutral alumina with benzene as the eluent. The first 200 mL was combined and the solvent removed under reduced pressure. The product was triturated with petroleum ether, affording 0.7 g (89%) of light yellow crystals of **20**: mp 92–94 °C (hexane); UV (MeOH) λ_{max} 309 nm (sh), 296, 286; λ_{max} 286/296 = 1.12; ^1H NMR ($CDCl_3$ + acetone-d_6) δ 2.76 (s, 3 H, C_7 or C_{12} CH_3), 3.09 (s, 3 H, C_7 or C_{12} CH_3), 3.85 (s, 3 H, OCH_3), 6.8–8.4 (complex, 8 H, aromatic); MS, *m/e* (relative intensity) 304 (M^+, 100), 289 ($M^+ - CH_3$, 23), 258 ($M^+ - CH_3 - OCH_3$, 6), 246 (14).

Anal. Calcd for $C_{21}H_{17}FO$: C, 82.90; H, 5.60; F, 6.30. Found: C, 82.86; H, 5.77; F, 6.11.

3-Hydroxy-5-(ethylthio)-7,12-dimethylbenz[*a*]anthracene (21). A solution of **20** (600 mg, 0.002 mol) in DMF (15 mL) was added to a solution of the sodium mercaptide prepared from ethanethiol (2 mL) and hexane-washed sodium hydride (1 g, 50%) in DMF (10.0 mL). The mixture was heated to 155 °C for 3 h

and cooled to room temperature. Water was added and the mixture extracted with ether. The ether layer was extensively washed with water, dried over sodium sulfate, and evaporated to dryness. The brown gummy mass was chromatographed over silica gel and eluted with dichloromethane (R_f 0.30 on silica gel; dichloromethane as the irrigant). The eluant was pooled and following concentration the residue was crystallized from hexane to furnish 400 mg (58%) of **21**: mp 118–121 °C (hexane); IR (KBr) 3340 (OH), 1220 cm^{-1} (C–S–C); UV (MeOH) λ_{max} 323 nm (ϵ 7.3 × 10^3), 308 (1.24 × 10^4), 304 (1.24 × 10^4), 294 (9.96 × 10^3), 277 (8.17 × 10^3); ^1H NMR ($CDCl_3$) δ 1.37 (t, 3 H, J = 7.3 Hz, CH_2CH_3), 3.0 (q, 2 H, J = 7.3 Hz, CH_2CH_3), 3.00 (s, 3 H, C7 or C12CH_3), 3.25 (s, 3 H, C7 or C12CH_3) 7.10 (dd, 1 H, J = 3.0, 7.5 Hz, C2H), 7.60 (d, 1 H, J = 10 Hz, C1H), 7.83 (d, 1 H, J = 3 Hz, C4H), 8.10 (s, 1 H, C6H), 8.20–8.50 (complex, 3 H, aromatic); MS, m/e (relative intensity) 332 (M^+, 100), 317 ($M^+ - CH_3$, 3.4), 304 ($M^+ - C_2H_4$, 5), 271 ($M^+ - SC_2H_5$, 1.0), 286 (33), 259 (57).

Anal. Calcd for $C_{22}H_{20}OS$: C, 79.50; H, 6.02; F, 0.00; O, 4.80; S, 9.60. Found: C, 79.45; H, 6.29; F, 0.07; O, 4.89; S, 9.38.

5-Fluoro-3-hydroxy-7,12-dimethylbenz[*a*]anthracene (22). To a solution of **20** (80 mg, 0.26 mmol) in dichloromethane (20 mL) was added BBr_3 (1.0 mL). The mixture turned violet. The progress of the reaction was followed by TLC over silica gel with dichloromethane as the irrigant. After 6 h, water (10 mL) was added and the mixture vigorously stirred for 10 min. The dichloromethane layer was separated, washed with water, dried over sodium sulfate, and evaporated under reduced pressure to furnish a gummy mass. This gum was chromatographed over silica gel with dichloromethane as the eluent. The fractions containing material with R_f 0.31 (silica gel; dichloromethane) were pooled and evaporated to furnish a pale yellow solid. Crystallization from hexane–dichloromethane provided 35 mg (46%) of **22**: mp 179–180 °C; IR (KBr), 3300 cm^{-1} (OH); UV (MeOH) λ_{max} 308.3 nm (sh, ϵ 4.67 × 10^4), 298 (9.0 × 10^4), 287.2 (9.46 × 10^4); ^1H NMR ($CDCl_3$) δ 3.00 (s, 3 H, C7 or C12 CH_3), 3.30 (s, 3 H, C7 or C12 CH_3), 5.25 (brs, 1 H, OH), 7.18 (dd, 1 H, J = 3, 8 Hz, C2 H), 7.50 (d, 1 H, J = 13 Hz, C4 H), 7.70 (d, 1 H, J = 13 Hz, C6 H), 8.35 (complex, 3 H, aromatic); MS, m/e 290 (M^+, 100), 275 ($M^+ - CH_3$, 38), 247 ($M^+ - CO - CH_3$, 6).

Anal. Calcd for $C_{20}H_{15}OF{\cdot}0.5H_2O$: C, 80.30; H, 5.35; O, 8.02; F, 6.35. Found: C, 80.90; H, 5.00; O, 8.09; F, 6.10.

Forerun dichloromethane fractions from the silica gel column provided <1 mg of material which was homogeneous by HPLC and likely has structure **23**: ^1H NMR ($CDCl_3$) δ 3.00 (s, C7 or C12 CH_3), 3.30 (s, C7 or C12 CH_3), 7.00–8.00 (complex, aromatic); MS, m/e (relative intensity) 352, 350 (M^+, base peaks of equal intensity), 337, 335 ($M^+ - CH_3$, 16 each), 271 (M^+ – Br, 15), 270 (M^+ – HBr, 19), 256 (M^+ – Br – CH_3, 32), 255 (M^+ – HBr – CH_3, 23).

5-Fluoro-7,12-dimethylbenz[*a*]anthracene-3,4-dione (24). A solution of **22** (28 mg, 0.096 mmol) in THF (5 mL) was added to a suspension of diphenyldiselenic anhydride[23] (160 mg, 0.44 mmol) in THF (10 mL). The mixture was heated at 80 °C under N_2 for 30 min and evaporated to dryness under reduced pressure. The residue was dissolved in dichloromethane (5 mL) and chromatographed over silica gel. The green band eluted with dichloromethane was evaporated to furnish a green solid which proved to be a mixture of three components by TLC. Preparative TLC on dichloromethane washed silica gel plates with dichloromethane as the irrigant furnished **24**: UV (MeOH) λ_{max} 328 nm, 274 (sh), 257, 242 (sh); IR (KBr) 1665 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.00 (s, 3 H, C7 or C12CH_3), 3.20 (s, 3 H, C7 or C12 CH_3), 6.44 (d, 1 H, J = 11 Hz, C1 H), 7.3–8.5 (complex, 6 H, aromatic); MS, m/e (relative intensity) 306 (M^+ + 2 H, 100), 304 (M^+), 302 (M^+ – 2 H). Two samples of **25** standard, one of which was prepared in these laboratories by employing Barton's reagent[23] according to Sukumaran and Harvey[10] and the other of which was prepared by Newman et al.[16] using Fremey's salt, also exhibited the following: MS, m/e (relative intensity) 288 (M^+ + 2 H, 100), 286 (M^+), 284 (M^+ – 2 H); ^1H NMR ($CDCl_3$) δ 6.32 (d, 1 H, J = 11 Hz, C1H).

Anal. Calcd for $C_{20}H_{13}O_2F{\cdot}O{\cdot}5H_2O$: C, 76.6; H, 4.48. Calcd for $C_{20}H_{13}O_2F{\cdot}C_2H_5OH$: C_2H_5OH: C, 75.43; H, 5.43. Found: C, 76.17; H, 5.48.[24]

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(24) For combustion analysis purposes we only had approximately 1 mg of sample left following our chemical studies. Thus, a duplicate analysis could not be obtained. The H content found for **24** was high and may reflect either H_2O or EtOH of crystallization. The mass spectrum and UV data support the assigned structure. It should be noted that **24** was precipitated from EtOH/hexane. Concurrent with submission of this sample for analysis we also submitted a sample of 7,12-dimethylbenz[*a*]anthracene-3,4-dione standard prepared in our laboratory by using methodologies similar to those found in ref 10. That sample analyzed as follows. Anal. Calcd for $C_{20}H_{14}O_2$: C, 83.9; H, 4.96; Found: C, 83.84; H, 5.17.

Notes

$_{\pi}4_s + {}_{\pi}2_s$ Photochemical Cycloaddition of Naphthalene to 1,3-Cyclohexadiene

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Recently Yang and his coworkers reported that there is an excellent correlation between the polarity of [arene*:1,3-diene] exciplexes or the role of eximers of arenes and the orientation of photocycloaddition of 1,3-dienes to arenes.[1,2] They have pointed out two possible pathways for stepwise $_{\pi}4_s + {}_{\pi}2_s$ photocycloaddition. One is tthat the addition may occur via highly polar exciplexes, and the other is the cycloaddition of excimers of arenes to 1,3-dienes. Photochemical cycloaddition of naphthalene to 1,3-cyclohexadiene (CHD) is known to produce the corresponding $_{\pi}4_s + {}_{\pi}4_s$ adducts (**1** and **2**,[3] Chart I), which may be derived from a relatively nonpolar exciplex,[1] and

(1) Yang, N. C.; Srinivasachar, K.; Kim, B.; Libman, J. *J. Am. Chem. Soc.* **1975**, 97, 5006–5008.
(2) Yang, N. C.; Shou, H.; Wang, T.; Masunovi, J. *J. Am. Chem. Soc.* **1980**, *102*, 6652–6654.
(3) (a) Yang, N. C.; Libman, J.; Savitzky, M. F. *J. Am. Chem. Soc.* **1972**, *94*, 9226–9227. (b) Yang, N. C.; Libman, J. *Ibid.* **1972**, *94*, 9228–9229.

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