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A Simple Synthesis of Phenanthrene

Jeffrey J. Gilbertson, Robert W. Allen, and Gordon W. Gribble 

Department of Chemistry, Dartmouth College, Hanover, New Hampshire

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In continuation of polycyclic aromatic hydrocarbons (PAH) synthesis via an aryne Diels-Alder cycloaddition and bridge extrusion methodology,^{1–5} we now describe a simple phenanthrene (**1**) synthesis using this strategy.

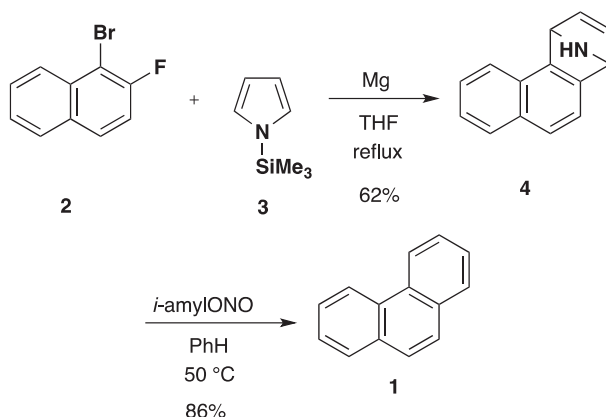
Phenanthrene is an ubiquitous combustion product in the environment found in coal tar,⁶ cigarette smoke,⁷ motor vehicle exhaust,⁸ green coffee beans,⁹ sunflower oil,¹⁰ and other sources.¹¹ Although phenanthrene is not carcinogenic *per se*, it has served as a prototypical molecule for biological studies of the carcinogenic benz[*a*]anthracene, dibenz[*a,h*]anthracene, benzo[*a*]pyrene, and other PAH. For example, the human metabolism of (deuterated) phenanthrene has been used as a marker to measure the potential lung cancer susceptibility in cigarette smokers.¹² Moreover, more than 250 natural phenanthrenes have been described, mostly oxygenated analogues from higher plants.¹³

While myriad syntheses of *substituted* phenanthrenes are known,^{14–16} relatively few syntheses of phenanthrene itself exist. The closest example to the present work is that of Jung and Koreeda, who employed an aryne-furan cycloaddition method to prepare **1** and several polymethylated phenanthrenes.¹⁷

Our synthesis of phenanthrene is shown in *Scheme 1*. The easily synthesized 1-bromo-2-fluoronaphthalene (**2**)^{18,19} is allowed to react with 1-(trimethylsilyl)pyrrole (**3**)²⁰ in the presence of magnesium to afford the Diels-Alder cycloadduct **4** in 62% yield after workup. The trimethylsilyl group is cleaved during the dilute acid workup.^{20,21} Deamination of **4** with iso-amyl nitrile gives phenanthrene (**1**) in 86% yield (78% after sublimation). This simple synthesis of **1**, devoid of column chromatography, should be applicable to the synthesis of ring-substituted and deuterated phenanthrenes given the wide availability of substituted pyrroles.²²

Experimental section

Melting points were obtained on a Thomas-Hoover Mel-Temp capillary apparatus and are uncorrected. Infrared spectra (IR) were recorded on a Perkin-Elmer Model 137 NaCl spectrophotometer. Liquids were measured on NaCl plates (neat), while KBr pellets were used for solids. Nuclear Magnetic Resonance spectra (NMR) were recorded on a Perkin-Elmer R-24 spectrometer using TMS as an internal standard. Thin Layer



Scheme 1 Synthesis of phenanthrene from 2-Bromo-1-fluoronaphthalene.

Chromatography (TLC) was carried out with Silica Gel G plates and developed as noted. Microanalysis was performed by Micro-Tech Laboratories, Skokie, Illinois.

1-Bromo-2-fluoronaphthalene (2)

This was prepared as previously reported from 2-acetylnaphthalene in 42% overall yield,¹⁸ or using the following procedure as adapted from Nakata.¹⁹ To a stirred solution of acetic acid (200 mL) and 2-naphthylamine (100 g, 0.7 mol) was added acetic anhydride (90 mL). The mixture was brought to reflux for 15 min, cooled, and water (5 mL) was added to hydrolyze excess acetic anhydride. The mixture was further refluxed for 10 min and then cooled to 25 °C. A solution of bromine (36.9 mL, 115 g, 0.7 mol) in acetic acid (200 mL) was then added dropwise to the reaction at 25 °C over 1 h. Stirring was continued for an additional 1 h and the resulting product was collected by suction filtration. The solid was then slurried with water (500 mL) and filtered to give *N*-acetyl-1-bromo-2-naphthylamine. This solid was then dissolved in a solution of conc HCl (300 mL) and absolute ethanol (1700 mL) and heated at reflux for 30 min. Upon cooling, cream colored crystals resulted and these were collected by suction filtration. The filtrate was brought to reflux for an additional 1 h, concentrated to approximately one-half its original volume and suction filtered to give a second crop of crystals. The combined solids were then washed with H₂O (100 mL) and air dried to give 152 g (82%) of 1-bromo-2-naphthylamine hydrochloride as a cream colored solid, mp 208 °C dec, which was used directly in the following step. A solution of 1-bromo-2-naphthylamine hydrochloride (50 g, 0.19 mol) in conc HCl (250 mL) was treated portion-wise with NaNO₂ (13.75 g, 0.20 mol). After complete addition of NaNO₂ the mixture was stirred for 30 min and then treated dropwise with HBF₄ (74.1 g, 0.70 mol, 50% in water). The resulting orange-brown slurry was stirred for an additional 30 min and then filtered. The resulting solid was washed with water and ethanol, filtered, and air dried to give the fluoroborate salt as a yellow solid. The salt was then spread on the bottom of a vacuum sublimator, and heated at 90 °C (0.2 Torr) for 1 hr to complete drying. The temperature was then raised to 170 °C at which point decomposition began, resulting in a yield of 20.4 g of 1-bromo-2-fluoronaphthalene (2) (47%). Note: A liquid

nitrogen cooled trap was employed to condense the BF_3 gas. Resublimation gave 20.0 g (46%) of **2** as a colorless solid (mp 66–67 °C). Recrystallization from 50% ethanol gave white crystals mp 67–68 °C (lit.²³ mp 69–70 °C). The overall yield from 2-naphthylamine was 38%.

1-(Trimethylsilyl)pyrrole (**3**)²⁰

A stirred mixture of freshly distilled pyrrole (**16**) (115 g, 1.7 mol), 1,1,1,3,3,3-hexamethyldisilazane (**39**) (152 g, 0.94 mol) and a catalytic amount of ammonium sulfate was brought to reflux. After 25 h, the mixture was cooled and washed with water (7 x 150 mL) to remove much of the unreacted pyrrole. The organic phase was then dried over Na_2SO_4 and fractionally distilled to give 121.1 g (51%) of **3** as a colorless liquid, bp 151–152 °C (lit.²⁰ bp 151–152 °C); NMR (CDCl_3) δ 6.79 (broad s, 2), 6.35 (broad s, 2), 0.40 (s, 9); IR (NaCl neat) 2990, 1465, 1257, 1188, 1080, 1045, 943, 835, 725 cm^{-1} .

1,4-Dihydrophenanthrene-1,4-imine (**4**)

To magnesium turnings (1.48 g, 0.061 mol) in dry THF (7 mL) was added a small amount of 1-bromo-2-fluoronaphthalene (**2**) (ca. 0.5 g). To effect Grignard initiation it was necessary to add a few drops of 1,2-dibromoethane. With the Grignard underway and heated to reflux, a mixture of the remaining 1-bromo-2-fluoronaphthalene (**2**) (for a total of 8.01 g, 0.036 mol) and freshly distilled 1-(trimethylsilyl)pyrrole (**3**) (9.92 g, 0.071 mol) in dry THF (40 mL) was added dropwise to the Grignard reaction with stirring and from a pressure-equalizing dropping funnel over 1.5 h. After complete addition, the reaction mixture was stirred at reflux for 8 h, then cooled and the THF was replaced with ethyl ether. This ethereal solution was then extracted with 5% aqueous HCl (7 x 150 mL). The combined aqueous extracts were basified with the addition of conc aqueous KOH and back-extracted with ether (5 x 100 mL). The combined ethereal extract was dried (MgSO_4) and concentrated to dryness to yield 4.28 g (62%) of **4** as brown oil, which was used directly in the next step; NMR (CDCl_3) δ 7.50 (m, 6), 6.99 (s, 2 vinyl protons), 5.35 (s, 1-bridgehead proton), 4.96 (s, 1-bridgehead proton), 3.11 (s, 1-exchangeable NH); HRMS: Calcd for $\text{C}_{14}\text{H}_{11}\text{N}$: 193.0891; Found: 193.0928; Calcd for $\text{C}_{13}^{13}\text{C}_1\text{H}_{11}\text{N}$: 194.0925; Found: 194.0941. A picrate of **4** was prepared in the usual fashion from picric acid,²⁴ and recrystallized from EtOH, mp 203–204 °C dec.

Anal. Calcd for $\text{C}_{20}\text{H}_{14}\text{N}_4\text{O}_7$: C, 56.88; H, 3.34; N, 13.27; Found: C, 56.69, H, 3.43; N 13.44.

Phenanthrene (**1**)

To 1,4-dihydrophenanthrene-1,4-imine (**4**) (0.716 g, 3.72 mmol) in benzene (40 mL) was added iso-amyl nitrite (0.48 g, 4.1 mmol). The mixture was warmed to 50 °C and the progress of the reaction followed by TLC (hexane: EtOAc, 8:2). After complete reaction, the solution was concentrated to dryness and redissolved in CH_2Cl_2 (40 mL). To this solution was added finely ground CaCl_2 (0.90 g, 8.17 mmol) and a small amount of absolute ethanol (0.5 mL) with stirring. After 12 h the solution was filtered and concentrated to yield 0.603 g (86%) of crude **1**. Sublimation at 85 °C (0.3 Torr) afforded 0.546 g

(78%) of **1** as white crystals mp 98–99 °C (lit.²⁵ mp 98.5–99 °C), identical in all respects with a commercial sample.

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ORCID

Gordon W. Gribble  <http://orcid.org/0000-0002-7573-0927>

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