Synthesis of Benzo[1,2]phenaleno[*bc*]thiophenes

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Received October 2, 1981

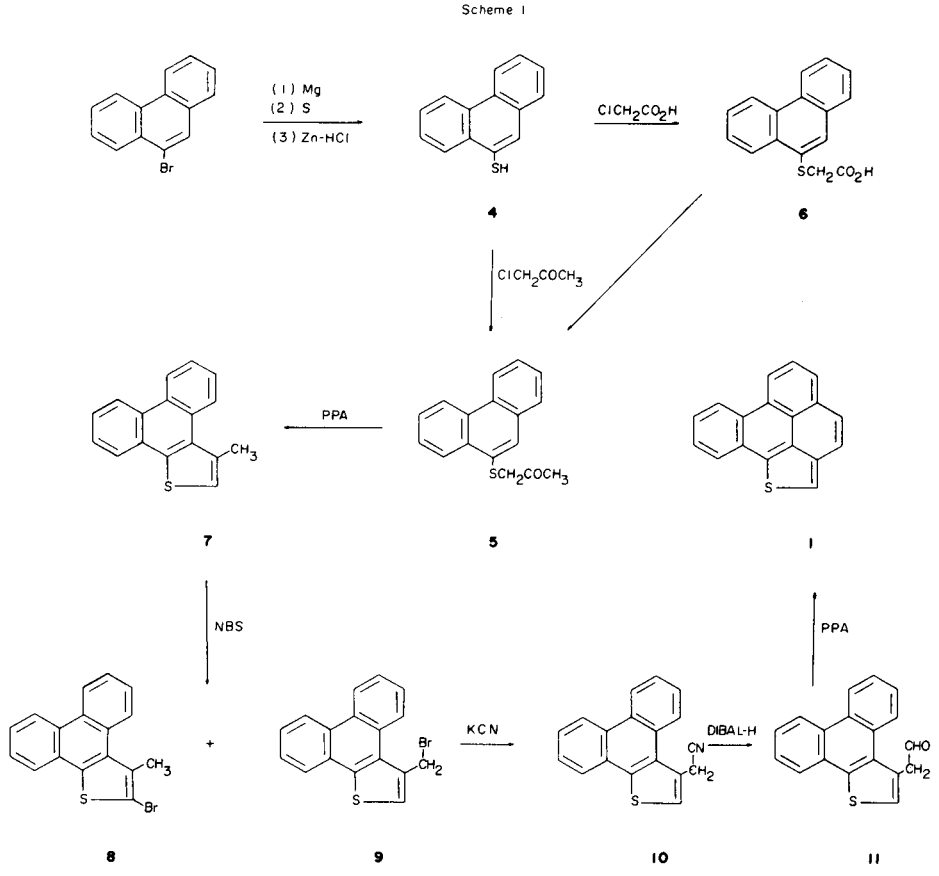
The synthesis of both isomers of benzo[1,2]phenaleno[*bc*]thiophene namely, benzo[1,2]phenaleno[3,4-*bc*]-thiophene and benzo[1,2]phenaleno[4,3-*bc*]thiophene is described.

J. Heterocyclic Chem., **19**, 439 (1982).

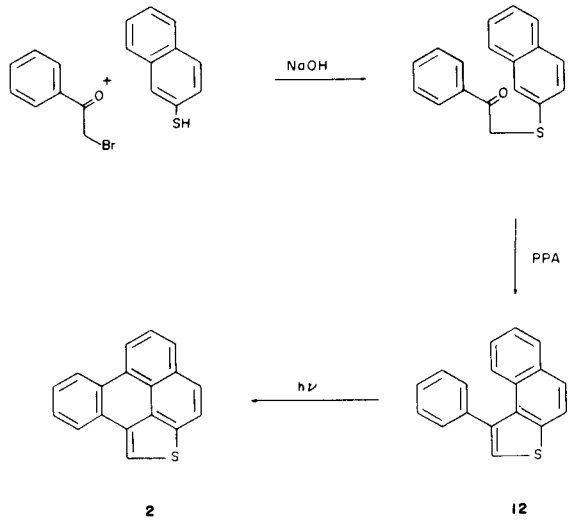
As part of a program to identify the potentially mutagenic and/or carcinogenic components in the sulfur fraction of "coal derived products", we have initiated in this laboratory a synthetic program of obtaining the sulfur analogs of a variety of polycyclic aromatic hydrocarbons. This approach will enable us to distinguish among the many possible isomeric structures as well as to determine their mutagenicity. Benzo[*a*]pyrene was found to be more carcinogenic than benzo[*e*]pyrene (2). In an earlier paper, we reported the synthesis of the sulfur isosteres of benzo[*a*]pyrene (3). Here, we report the synthesis of benzo-[1,2]phenaleno[3,4-*bc*]thiophene (**1**) and benzo[1,2]phen-aleno[4,3-*bc*]thiophene (**2**) which are the sulfur isosteres of benzo[*e*]pyrene.

The synthesis of benzo[1,2]phenaleno[3,4-*bc*]thiophene is outlined in Scheme I. The key intermediate, 3-methyl-phenanthro[9,10-*b*]thiophene (**7**), was prepared by the cyclization of 9-phenanthrylthioacetone (**5**) with polyphosphoric acid. 9-Phenanthrylthioacetone was obtained by the reaction of 9-phenanthrenethiol (**4**) (4) with chloroacetone. Compound **5** can also be prepared from 9-phenanthrylthioacetic acid which is a known compound (4), but in our hands the yield of the acid **6** was very poor. The bromination of 3-methylphenanthro[9,10-*b*]thiophene (**7**) with *N*-bromosuccinimide in carbon tetrachloride solution in the presence of benzoyl peroxide gave 3-bromomethylphenanthro[9,10-*b*]thiophene (**9**) along with a small amount of 2-bromo-3-methylphenanthro[9,10-*b*]thiophene

Scheme I



Scheme II



(**8**). In another experiment with *N*-bromosuccinamide using benzene as the solvent, **8** was obtained exclusively. The reaction of 3-bromomethylphenanthro[9,10-*b*]thiophene with potassium cyanide in a phase-transfer medium gave the corresponding cyano compound **10**. The 3-cyanomethylphenanthro[9,10-*b*]thiophene (**10**) was converted to the aldehyde **11** by reduction with diisobutylaluminium hydride which, without further purification, was cyclized with polyphosphoric acid in *m*-xylene to the desired compound **1**.

The synthesis of benzo[1,2]phenaleno[4,3-*bc*]thiophene (**2**) was accomplished as outlined in Scheme II. The key intermediate, 3-phenylnaphtho[1,2-*b*]thiophene (**12**) was synthesized following the literature procedure (5). The photocyclization of **12** in benzene gave a homogeneous product **2**. The mass spectrum of **2** showed a molecular ion peak at 258 (M^+, 100%) whereas the uncyclized compound **12** showed a molecular ion peak at 260 (M^+, 100%). The elemental analyses of **2** did not correspond to the molecular formula, instead it corresponded to the molecular formula with one mole of benzene of crystallization.

EXPERIMENTAL

The ir spectra were recorded on a Beckmann Acculab-2 spectrometer. The ^1H nmr spectra were obtained on Varian EM 390 and Varian EM 360 spectrometers in the solvents indicated. Chemical shifts are reported in ppm from TMS as an internal reference and are given in δ units. Mass spectra were recorded on a Hewlett Packard model 5980 A mass spectrometer. Elemental analyses were performed by MHW Laboratories, Phoenix, Arizona. Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected.

9-Phenanthrenethiol (**4**).

The Grignard reagent was prepared by the reaction of 9-bromophenanthrene (6) (20.4 g, 0.08 mole) with magnesium (1.94 g, 0.08 g-atom) in a mixture of benzene and ether. The reaction mixture was refluxed for 10 hours. Sublimed sulfur (2.8 g, 0.08 g-atom) was added in small portions. To the viscous reaction mixture additional benzene was added and refluxed for an additional 5 hours, cooled and hydrolyzed with 10% hydrochloric acid (60 ml). Zinc dust (22 g, 0.3 g-atom) was added followed by concentrated hydrochloric acid (50 ml) and the reduction was allowed to proceed overnight. The organic layer was separated and the aqueous layer was again extracted with benzene. The combined benzene extracts were washed with water and then extracted with 10% sodium hydroxide solution. The basic extract was filtered and then used in the next step without further purification.

9-Phenanthrylthioacetone (**5**).

The sodium salt of 9-phenanthrenethiol (**4**) from above was cooled in an ice-bath and then chloroacetone (15 g, 0.08 mole) was added drop-wise with stirring. The product separated as a yellow solid. The stirring was continued for another half hour and then the solid was filtered and crystallized from boiling ethanol, yield 8 g (38%), mp 105-106°; ir (potassium bromide): 1690 cm^{-1} (C=O) nmr (deuteriochloroform): 7.4-8.8 (m, 9H, Ar*H*), 3.75 (s, 2H, C*H*$_2$), 2.3 (s, 3H, C*H*$_3$); ms: 266 (M^+, 100%).

Anal. Calcd. for $C_{17}H_{14}SO$: C, 76.65; H, 5.29; S, 12.03. Found: C, 76.38; H, 5.38; S, 12.00.

3-Methylphenanthro[9,10-*b*]thiophene (**7**).

9-Phenanthrylthioacetone (2 g, 7.5 mmoles) and polyphosphoric acid (20 g) was heated at 130-140° (bath-temperature) with occasional stirring for 20 minutes and then the reaction mixture was poured onto ice and extracted with ether. The ether solution was washed with water and dried over sodium sulfate. Removal of the solvent gave a solid which was chromatographed on a silica gel column using hexane as the eluent. The analytical sample was crystallized from hexane, yield 0.66 g (36%), mp 125-126°; nmr (deuteriochloroform): 8.5-8.8 (m, 2H, H-7, H-8), 8.2 (m, 1H, H-11) 7.5-7.7 (m, 5H, H-4, H-5, H-6, H-9, H-10), 7.2 (s, 1H, H-2); 2.9 (s, 3H, C*H*$_3$); ms: 248 (M^+, 100%).

Anal. Calcd. for $C_{17}H_{12}S$: C, 82.21; H, 4.87; S, 12.91. Found: C, 82.32; H, 4.84; S, 13.02.

3-Bromomethylphenanthro[9,10-*b*]thiophene (**9**).

A mixture of *N*-bromosuccinamide (1.0 g, 4 mmoles) 3-methylphenanthro[9,10-*b*]thiophene (0.8 g, 4 mmoles), benzoyl peroxide (0.1 g) in carbon tetrachloride was refluxed for 45 minutes. The succinamide was filtered while the solution was hot and upon cooling the filtrate gave the required product which was crystallized from a benzene-cyclohexane mixture to give 0.4 g (60%) of light brown crystals, mp 185-190°; nmr (DMSO-d_6): 7.4-9.0 (m, 9H, aromatic), 5.3 (s, 2H, C*H*$_2$-Br).

Anal. Calcd. for $C_{17}H_{11}BrS$: C, 62.39; H, 3.38; S, 9.79. Found: C, 62.46; H, 3.60; S, 10.00.

2-Bromo-3-methylphenanthro[9,10-*b*]thiophene (**8**).

This compound was prepared from *N*-bromosuccinamide (1.4 g, 7.8 mmoles) and 3-methylphenanthro[9,10-*b*]thiophene (**7**) (2.0 g, 8.0 mmoles) using the above procedure except benzene was used as the solvent, yield 15 g (60%), mp 135-136°; nmr (deuteriochloroform): 7.4-9.0 (m, 8H, aromatic), 2.8 (s, 3H, C*H*$_3$).

Anal. Calcd. for $C_{17}H_{11}BrS$: C, 62.39; H, 3.38; S, 9.79. Found: C, 62.43; H, 3.19; S, 9.54.

3-Cyanomethylphenanthro[9,10-*b*]thiophene (**10**).

A mixture of **9** (1.0 g, 3 mmoles) and potassium cyanide (2.5 g) in a mixture of benzene (100 ml) and water (15 ml) with 10 drops of Aliquat-336 (tricaprylylmethyl ammonium chloride) was refluxed for 2.5 hours. After the addition of 100 ml of benzene, the benzene layer was separated, washed successively with water, 10% hydrochloric acid and water. After drying over sodium sulfate the benzene was removed under reduced pressure. The residue was crystallized from benzene-ethanol (1:1) giving 0.5 g (60%) of pale yellow needles, mp 192-193°; ir (potassium bromide):

2240 cm^{-1} (C≡N); nmr (DMSO-d_6): 7.3-9.0 (m, 9H, aromatics), 4.7 (s, 2H, CH_2-CN).

Anal. Calcd. for $C_{18}H_{11}NS$: C, 79.09; H, 4.05; N, 5.12; S, 11.73. Found: C, 78.99; H, 4.28; N, 4.95; S, 11.86.

Benzo[1,2]phenaleno[3,4-*bc*]thiophene (**1**).

Diisobutylaluminium hydride (25% solution in toluene, 2 ml, 3 mmoles) was added to a solution of **10** (0.4 g, 1.5 mmoles) in dry benzene (20 ml) under a nitrogen atmosphere. The mixture was stirred at room temperature for two hours. Dilute hydrochloric acid was added and the product was extracted with chloroform. Evaporation of the dried extracts over sodium sulfate, gave the aldehyde as an oil; ir (neat) 1710 cm^{-1} (C=O). A mixture of the above aldehyde, polyphosphoric acid (3 g) and *m*-xylene (10 ml) was heated on a water bath for two hours with occasional stirring of the reaction mixture. The reaction mixture was poured into ice water and extracted with benzene. The benzene extract was washed with water, dried over sodium sulfate and evaporated. The residue was chromatographed on a silica gel column using hexane as the eluant giving pink crystals which were recystallized from hexane, (0.03 g, 8%) mp 153°; ms: 258 (M^+, 100), 226 (M^+-32, 12), 200 (M^+-58, 4.3).

Anal. Calcd. for $C_{18}H_{10}S$: C, 83.68; H, 3.90; S, 12.41. Found: C, 83.49; H, 4.21; S, 12.41.

1-Phenylnaphtho[2,1-*b*]thiophene (**12**).

This was prepared by cyclization of 2-(*S*-benzoylmethyl)thionaphthalene with polyphosphoric acid on a steam bath, yield 75%, mp 86° [lit 5]; ms: 260 (M^+, 100%), 259 (M^+-1, 94.6%), 258 (M^+-2, 66.3%).

Benzo[1,2]phenaleno[4,3-*bc*]thiophene (**2**).

A solution of **12** (0.6 g, 2.3 mmoles) and 30 mg of iodine in 750 ml of benzene was irradiated for 48 hours with a 450 watt medium pressure Hanovia mercury vapor lamp through a corex filter. During the course of the reaction a slow stream of air was passed through the solution. The benzene was removed *in vacuo* and the residue was purified by preparative thin layer chromatography on silica gel (60 F254, E Merck) using 2% benzene in hexane as the mobile phase, yield 0.03 g (5%); mp 165°; ms: 258 (M^+, 100%), 166 (33.6%).

Anal. Calcd. for $C_{18}H_{10}S \cdot C_6H_6$: C, 85.68; H, 4.79; S, 9.52. Found: C, 85.81; H, 4.88; S, 9.39.

Acknowledgement.

This study was supported by the U.S. Department of Energy, Office of the Health and Environmental Research, Contract No. DE-AC02-79EV10237.

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