A Useful Access to 9-Phenanthrylmethyl Derivatives

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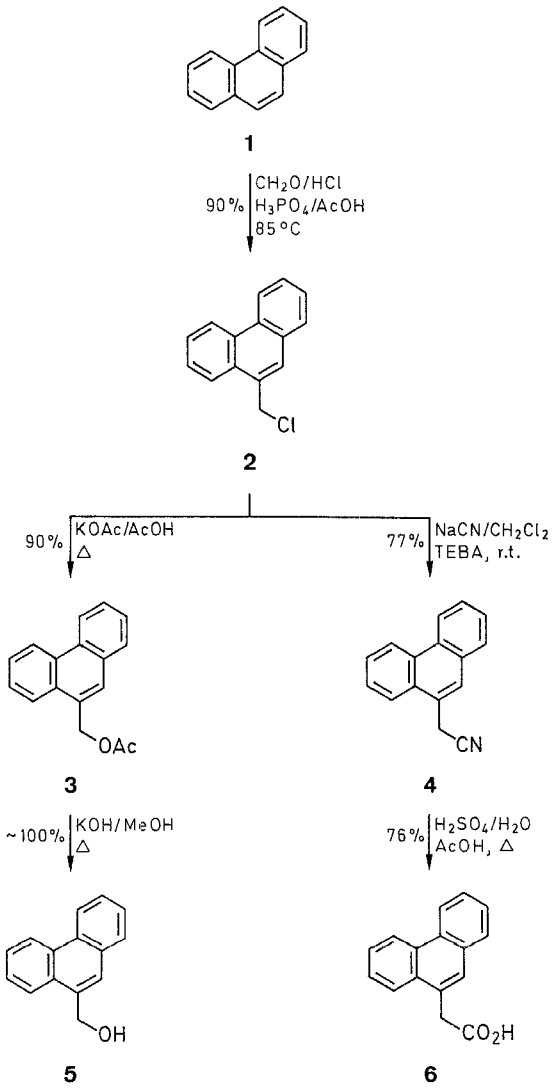
Chloromethylation of phenantrene to give 9-chloromethylphenanthrene and conversions of this compound into other 9-phenanthrylmethyl derivatives in useful yields are described.

9-Phenanthrylmethyl derivatives are among the molecules with a phenanthrene moiety most often seen in theoretical and mechanistic studies[1-6] or otherwise used for diverse synthetic purposes.[7-10] They are generally prepared from 9-bromophenanthrene, which is commercially available or easily obtained by bromination of phenanthrene (**1**).[11] Actual syntheses, however, are far from achieving optimum yields; thus, standard procedure to obtain 9-phenanthrylacetic acid (**6**) from 9-bromophenanthrene makes use of a five-step sequence, with an overall yield[8] of 7%. Availability of 9-phenanthrylmethyl halides by direct halomethylation of **1** would open an improved, practical way to **6** and to other 9-phenanthrylmethyl derivatives.

Reports on the bromomethylation of phenanthrene could not be found in the chemical literature, while those on chloromethylation were both old and disappointing; a very cumbersome working up of the mass of reaction led to 9-chloromethylphenanthrene (**2**) in some mere 15–20% yields.[12-14] Ever since, chloromethylation of phenanthrene is scarcely mentioned in the literature and most often **2** is reported as prepared from 9-phenanthrylmethanol (**5**).[15]



This situation prompted us to reinvestigate the chloromethylation of phenanthrene using modern analytical techniques. Conditions used by Grummitt and Buck to chloromethylate naphthalene[16] were modified until an optimum set was found. The reaction is best run at 85 °C on a very well stirred heterogeneous mixture of phenanthrene, paraformaldehyde and acetic, phosphoric and concentrated hydrochloric acids and, due to the potentially dangerous nature of the hydrochloric acid–formaldehyde system, must be conducted in a good hood. The process leads almost exclusively to the formation of **2**, two minor by-products of retention time close to that of **2** totalled less than 1.5% (by GC) of the final reaction mixture.

High temperatures needed to distill **2** (ca. 200 °C, even at 1.5 mbar), coupled with the presence of traces of moisture and/or acids seem to cause its easy extensive resinification. For synthetic applications, best results were obtained not trying to isolate **2** pure, but after a conventional work-up of the chloromethylation mixture, using the crude material in the next step of the synthesis. Most of the derivatives which one may be interested in, are more polar than the accompanying unreacted **1**, and can be therefore easily purified by column chromatography on silica gel.

This way we prepared pure (> 99% by GC) 9-phenanthrylmethyl acetate (**3**) from **1** in a 81% overall yield. Acetate **3** had not been previously reported in the literature and, apart being analytically and spectroscopically characterized, it was saponified to the alcohol **5**. 9-Phenanthrylmethyl cyanide (**4**) was also obtained pure (99.5% by GC) from **1** in an overall yield of 69%, what represents a significant improvement in time, simplicity of operation and cost from the only procedure of preparation of **4** hitherto reported.[17,18] Finally **4** was hydrolized to the acid **6** in 76% yield. Altogether, preparation of **6** from **1** was achieved in a 52% yield, thus notably improving previous standard synthesis of **6**.

Yields obtained here in the preparation of the chloromethyl, hydroxymethyl and cyanomethyl derivatives from phenanthrene are better than those reported for the preparation of analogous derivatives from biphenyl, making use of a longer method via the Einhorn reaction.[19] However, attempts to chloromethylate 9-chlorophenanthrene under similar conditions were unsuccessful, the starting material being always recovered unchanged.

Melting points are determined on a Kofler Thermopan Reichert apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 681 spectrophotometer and ^{1}H-NMR spectra on a Varian FT-80A spectrometer. Silica gel 230 mesh (Merck) was used for column chromatography. GC were carried out on a Hewlett Packard HP-5710A instrument with a FID detector and equipped with an HP-33805 integrator. Column: 10% OV-101 on chromosorb W-HP (2 m × ⅛″), carrier gas: N_2, 20 mL/min, oven temperature: 250 °C.

Chloromethylation of Phenanthrene: 9-Chloromethylphenanthrene (2):
A mixture of **1** (35.65 g, 0.2 mol), paraformaldehyde (11 g, 0.37 mol), glacial AcOH (36 mL), 12 N HCl (110 mL) and 85% H_3PO_4 (16.5 mL) is vigorously stirred in a flask fitted with a reflux condenser and kept on a water bath at 85 °C in a good hood. The reaction is monitored by GC analysis of aliquots withdrawn at regular intervals and the heating bath taken off once the ratio of **2**:**1** is higher than 10 (ca. 40 h). The mixture is then poured over crushed ice and extracted with ether (2 × 300 mL). The combined organic layer is washed with H_2O until neutral, dried

(Na_2SO_4), and the solvent is removed *in vacuo* to leave a crude dark paste, which is used as such in the next synthetic steps; yield: 43.1 g (90%). A small amount of this material in cold hexane separates some crystals, which after two recrystallizations from hexane is analytically pure (> 99.7% by GC); mp 101–102°C (Lit.[12,13,15] mp 101–102°C).

9-Phenanthrylmethyl Acetate (3):
Crude **2** from the preceding reaction (4.31 g, equivalent to 20 mmol of the starting **1**) in glacial AcOH (9 mL) is refluxed for 7 h with KOAc (3.45 g, 35.1 mmol), then the mixture is poured on ice and extracted with Et_2O (2 × 60 mL). The organic extracts are washed with sat. $NaHCO_3$ (2 × 30 mL) and H_2O (2 × 20 mL), dried (Na_2SO_4), and the solvent is removed *in vacuo* to leave a dark viscous residue (4.71 g), which is chromatographed on silica gel (110 g), eluting by benzene (15 × 100 mL). Fractions 2–3 give only **1** (0.34 g), while fractions 4–11 afford virtually pure (> 99% by GC) **3**; yield: 3.68 g (90%). Overall yield: 81% over unrecovered phenanthrene. A small amount is recrystallized from hexane to give an analytical sample of **3** as white needles, mp 79–80°C.

$C_{17}H_{14}O_2$ (250.3) calc. C 81.58 H 5.64 found 81.46 5.78

IR (KBr): $\nu = 1730\ cm^{-1}$ (C=O).

^{1}H-NMR ($CDCl_3$/TMS): $\delta = 2.14$ (s, 3H, CH_3); 5.62 (s, 2H, CH_2); 7.58–7.75 (m, 4H, 2,3,6,7-H); 7.83 (s, 1H, 10-H); 7.83–7.95 (m, 1H, 1-H); 8.00–8.12 (m, 1H, 8-H); 8.62–8.80 (m, 2H, 4,5-H).

9-Phenanthrylmethanol (5):
A mixture of **3** (2.5 g, 10 mmol) and KOH (1.9 g, 34 mmol) in MeOH (10 mL) and H_2O (3 mL) is refluxed for 7 h, then poured into water (100 mL) and extracted with ether (3 × 50 mL). The combined ethereal extract is washed with H_2O (2 × 30 mL), dried (Na_2SO_4) and the solvent is removed *in vacuo* to leave a slightly yellowish solid; yield: 2.08 g (~ 100%). Three recrystallizations from benzene give a sharp melting sample of **5** as white needles, mp 150.5–151°C (Lit. 148–149°C,[15] 149–149.5°C[9,17,20]).

IR (KBr): $\nu = 3200\ cm^{-1}$ (OH).

^{1}H-NMR ($CDCl_3$/TMS): $\delta = 1.79$ (t, 1H, $J = 5.5$ Hz, exchangeable with D_2O, OH); 5.20 (d, 2H, $J = 5.5$ Hz, CH_2); 7.57–7.75 (m, 4H, 2,3,6,7-H); 7.79 (s, 1H, 10-H); 7.82–7.94 (m, 1H, 1-H); 8.10–8.22 (m, 1H, 8-H); 8.62–8.80 (m, 2H, 4,5-H).

9-Phenanthrylacetonitrile (4):
To crude **2** obtained as described above (15.1 g, equivalent to 70 mmol of the starting **1**) in CH_2Cl_2 (20 mL) is added powdered NaCN (4.61 g, 94 mmol) and solid triethylbenzylammonium chloride (1.73 g, 7.6 mmol), and the heterogeneous mixture is stirred at room temperature till complete disappearence (GC) of **2** (88 h), then poured into H_2O (200 mL) and extracted with Et_2O (2 × 150 mL). These extracts are washed with H_2O (2 × 50 mL), dried (Na_2SO_4) and the solvents removed *in vacuo* to leave a brown pasty residue (14.0 g), which is chromatographed on silica gel (325 g), eluent: benzene (9 × 250 mL). Fractions 1–3 consist of mostly (85% by GC) **1** (1.31 g), while fractions 4–7 afford pure **4** (> 99.5% by GC); yield: 9.56 g (77%). Overall yield, 69% based on unrecovered phenanthrene. Residue from fractions 8–9 (1.30 g) still has **4** as the major (85%) component and, after four recrystallizations from benzene/hexane affords an analytical sample of **4**, as white glistening leaflets, mp 101–102°C (Lit.[17] mp 96.5–97°C).

IR (KBr): $\nu = 2250\ cm^{-1}$ (C≡N).

^{1}H-NMR ($CDCl_3$/TMS): $\delta = 4.15$ (s, 2H, CH_2); 7.58–7.76 (m, 4H, 2,3,6,7-H); 7.88 (s, 1H, 10-H); 7.79–7.96 (m, 2H, 1,8-H); 8.60–8.81 (m, 2H, 4,5-H).

9-Phenanthrylacetic Acid (6):
A mixture of **5** (8.04 g, 37 mmol), glacial AcOH (8 mL), conc. H_2SO_4 (8 mL) and H_2O (8 mL) is refluxed for 2 h. The cold mixture is diluted with Et_2O (300 mL), and washed with H_2O (2 × 100 mL). The organic layer is thoroughly extracted with 0.5 N aq. NaOH (3 × 100 mL), and the alkaline extracts are acidified with 12N HCl (15 mL) and re-extracted with Et_2O (300 mL). The combined ether extract is washed with H_2O (3 × 50 mL), dried (Na_2SO_4), and the solvent is removed *in vacuo* to give **6**; yield; 6.64 g (76%). Only one recrystallization from benzene affords a material of mp 220.5–221°C (Lit.[17] 220–221°C).

IR (KBr): $\nu = 1695\ cm^{-1}$ (C=O).

^{1}H-NMR (DMSO-d_6/TMS): $\delta = 4.08$ (s, 2H, CH_2); 7.59–7.75 (m, 4H, 2,3,6,7-H); 7.76 (s, 1H, 10-H); 7.88–8.01 (m, 1H, 1-H); 7.97–8.09 (m, 1H, 8-H); 8.75–8.93 (m, 2H, 4,5-H).

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