Synthesis of 4*H*-Cyclopenta[*def*]phenanthrene from Fluorene Skeleton

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Synopsis. 4-Fluoreneacetic acid was prepared and its chloride was cyclized with $AlCl_3$ to give 4*H*-cyclopenta-[*def*]phenanthren-8-ol accompanied by the 8,9-dione. These were both reduced to 4*H*-cyclopenta[*def*]phenanthrene: the overall yield was 40—50% from diphenic acid. The phenol was converted to acetoxy and amino substrates.

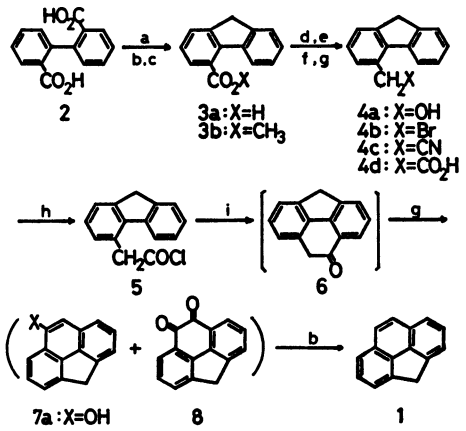
Hydrocarbon 4*H*-cyclopenta[*def*]phenanthrene (**1**) involves an active methylene, a located C_8–C_9 double bond, and strained aromatic rings, and is of interest for carcinogenic screening tests. The characterized aromatic **1** possesses features of naphthalene, fluorene, and phenanthrene, thus **1** is one of the key compounds for studying arenes[1] and annulenes.[2] Reported synthetic pathways of **1** could be classified in three types, according to the ring which is built up at the last step from the component skeleton: (a) formation of the five-membered ring from phenanthrene derivatives;[3] (b) formation of the side six-membered ring from acenaphthene derivatives;[4] (c) formation of the center six-membered ring from fluorene derivatives. The first two methods require many steps, resulting in very low yields, and the third type has not yet succeeded.[5,6]

We wish to report here a convenient preparation of **1** from diphenic acid (**2**) *via* fluorene derivative (Scheme 1). The preparation of 4-fluorenecarboxylic acid (**3a**) in a good yield was reported by one of us.[7] Extension of the carbon chain of **3a** to **4d** has been carried out by means of the Arndt-Eistert reaction;[5] however, no diazomethane is available for mass production. The synthesis of **4d** from **3a** proceeded by the following stepwise sequence: esterification to **3b**, reduction to **4a**, bromination to **4b**, substitution to **4c**, and hydrolysis to **4d**. All these reactions gave very high yields and required only easy treatment.

Ring closures of 4-fluoreneacetic acid (**4d**) and 9-oxo-4-fluoreneacetic acid to the **1** derivatives were attempted unsuccessfully under the conditions which has sufficed to convert biphenyl-2-acetic acid to phenanthrene derivative.[5,8] This may be due to an increase of the distance between C_4 and C_5 of **4d**. This experiment shows that only 4-fluoreneacetyl chloride (**5**) was cyclized under the Friedel-Crafts conditions to 4*H*-cyclopenta[*def*]phenanthren-8-ol (**7a**) accompanied by 4*H*-cyclopenta[*def*]phenanthrene-8,9-dione (**8**). Both **7a** and **8** were reduced to the hydrocarbon **1** with hydriodic acid and red phosphorus[9] in good yields. Also, from the crude products of the ring closure reaction, the hydrocarbon was obtained in a 66% overall yield from **5**.

The phenol **7a** is a tautomer with 4*H*-cyclopenta-[*def*]phenanthren-8(9*H*)-one (**6**), which failed to separate for **6**, probably forming a complex with aluminium, but was confirmed as an intermediate by the NMR spectrum of the reaction mixture in $CDCl_3$ (Fig. 1). The singlets of 4.73 and 4.18 ppm were assigned to the methylene protons of 9- and 4-position of **6**, respectively, by comparison with the spectrum of 9,9-dimethyl-4*H*-cyclopenta[*def*]phenanthren-8(9*H*)-one.[10] Owing to the tautomer with **6**, **7a** may be readily oxidized to dione **8** on exposure to air. So, for storage during a long period, the hydroxyl group of **7a** was protected as the acetate (**7b**: X=OAc) which was hydrolyzed quantitatively to **7a**.

Consequently, this procedure appears more simple and easier than the methods hitherto available. One of the merits of this facile method is a moderate yield of **1** (40—50% based on **2**). The second is a ready transformation to the 8-derivatives which are difficult to obtain by electrophilic substitution of **1**.[11] **7a** was



a: H_2SO_4. b: HI, P. c: MeOH, H_2SO_4 d: $LiAlH_4$. e: HBr. f: KCN. g: H_3^+O. h: $SOCl_2$. i: $AlCl_3$

Scheme 1.

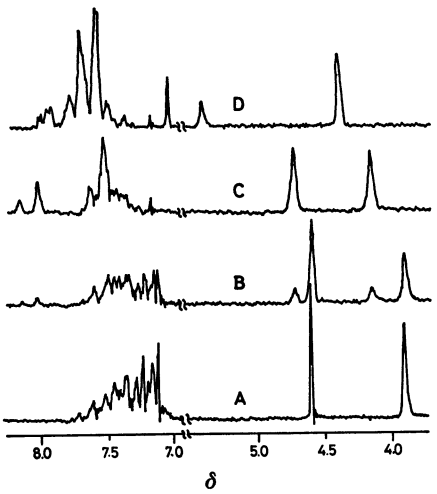


Fig. 1. ^1H NMR spectra on the ring closure reaction of **5** in $CDCl_3$. A: Starting material **5**. B: In the course of the reaction. C: End of the reaction. D: Upon hydrolysis (**7a**).

derived to 4*H*-cyclopenta[*def*]phenanthren-8-amine (**7c**: X=NH_2)[12] which was converted easily into many 8-substituted 4*H*-cyclopenta[*def*]phenanthrenes.

Experimental

All the melting points are uncorrected. The following spectrometers were used: ^1H NMR, JEOL C-60-HL (downfield from internal Me_4Si); IR, JASCO IR-G (KBr pellets); mass spectra, Hitachi RMU-6E or M-80 (direct inlet system). Elemental analyses were determined on a Yanagimoto CHN-corder.

4-(Bromomethyl)fluorene (4b). Dicarboxylic acid **2** was treated with concentrated sulfuric acid at 130—140 °C for 15 min to afford 9-oxo-4-fluorenecarboxylic acid (yield 97%). The keto acid was reduced with hydriodic acid and red phosphorus in acetic acid under refluxing for 20 h to give **3a** (yield 95%).[7] 4-Fluorenemethanol (**4a**) was obtained from methyl 4-fluorenecarboxylate (**3b**) with lithium aluminium hydride in a 99% yield.[13] A solution of **4a** (11.8 g, 60 mmol) in acetic acid (150 ml) was saturated with hydrogen bromide, followed by standing overnight at room temperature. The resulting mixture was extracted with benzene (60 ml) and the extract was washed with water to neutrality. The organic layer was dried and recrystallized from cyclohexane to give **4b** (14.4 g, 93%): mp 126—127 °C (lit,[13] mp 115—118 °C); NMR (CCl_4) δ=3.80 (s, 2H), 4.77 (s, 2H), and 7.02—8.01 (m, 7H). Found: C, 65.19; H, 4.07%.

4-Fluoreneacetonitrile (4c). To a solution of **4b** (4.50 g, 17.3 mmol) in *N,N*-dimethylformamide (100 ml) was added aqueous potassium cyanide (3 normal, 10 ml) and the mixture was refluxed for 4 h. The resulting mixture was poured into water (300 ml) and the precipitate was recrystallized from cyclohexane to give **4c** (3.05 g, 86%): mp 101—102 °C; IR 2270 cm^{-1}; NMR ($CDCl_3$) δ=3.87 (s, 2H), 4.10 (s, 2H), and 7.12—7.76 (m, 7H); MS *m/e* 205 (M^+), 178, and 165. Found: C, 87.94; H, 5.39; N, 6.62%. Calcd for $C_{15}H_{11}N$: C, 87.77; H, 5.40; N, 6.82%.

4-Fluoreneacetyl Chloride (5). Nitrile **4c** was hydrolyzed with dilute sulfuric acid in acetic acid to give carboxylic acid **4d** in a 96% yield; mp 178—179 °C (lit,[5] mp 178.5—179.0 °C). A mixture of **4d** (2.1 g, 9.4 mmol) in thionyl chloride (10 ml) was gently refluxed for 0.5 h and was dried *in vacuo*. The residue was recrystallized from hexane to afford **5** (2.13 g, 94%): mp 98.0—98.5 °C; IR 1786 cm^{-1}; NMR ($CDCl_3$) δ=3.92 (s, 2H), 4.60 (s, 2H), and 7.11—7.81 (m, 7H); MS *m/e* 244 and 242 (M^+), 206, and 165. Found: C, 74.31; H, 4.51%. Calcd for $C_{15}H_{11}OCl$: C, 74.20; H, 4.57%.

Ring Closure of 5. To a suspension of anhydrous aluminium chloride (0.53 g, 4 mmol) in 1,2-dichloroethane (30 ml), a solution of **5** (485 mg, 2 mmol) in 1,2-dichloroethane (5 ml) was added slowly at 20 °C and stirring was continued for 2 h. The mixture was hydrolyzed with dilute hydrochloric acid and extracted with benzene. The extract was submitted to silica-gel column chromatography to afford **7a** from the first eluate (269 mg, 65%): mp 167—168 °C decomp; IR 3330 and 1126 cm^{-1}; NMR ($CDCl_3$) δ=4.32 (s, 2H), 5.55 (s, 1H, OH), 7.04 (s, 1H), and 7.32—8.00 (m, 6H); MS *m/e* 206 (M^+) and 178. Found: C, 87.21; H, 5.05%. Calcd for $C_{15}H_{10}O$: C, 87.35; H, 4.89%.

The second eluate of the column gave **8** (44 mg, 10%): mp 254—256 °C decomp (lit,[10] mp 256 °C decomp).

4H-Cyclopenta[def]*phenanthrene (1).* Upon the intramolecular Friedel-Crafts reaction of **5** (242 mg, 1 mmol), the mixture containing **7a** and **8** was treated with hydriodic acid (57%, 10 ml) and red phosphorus (1.0 g) in acetic acid (50 ml) to reflux under nitrogen for 90 h. The resulting mixture was poured into aqueous sodium hydrogensulfite (1%, 100 ml) and was extracted with benzene. The organic layer was chromatographed on a silica gel to give **1** from the colorless eluate (126 mg, 66% from **5**): mp 113—114 °C (lit,[14] mp 116 °C).

The reductions of **7a** and **8** were carried out: **1** was obtained in yields of 27, 53, 88, and 78% from **7a** during the reaction times of 16, 24, 48, and 90 h, respectively, by a method similar to that described above. Also, **1** was afforded from **8** in yields of 26, 37, 58, and 80%, respectively.

8-Acetoxy-4H-cyclopenta[def]*phenanthrene (7b).* The mixture of **7a** (721 mg, 3.5 mmol) and acetic anhydride (100 ml) was refluxed for 1 h and was then quenched with cold water. The precipitate was recrystallized from ethanol, affording **7b** (780 mg, 90%): mp 97—98 °C; IR 1758 and 1199 cm^{-1}; NMR ($CDCl_3$) δ=2.48 (s, 3H), 4.31 (s, 2H), 7.50 (s, 1H), and 7.28—7.87 (m, 6H); MS *m/e* 248 (M^+) and 206. Found: C, 82.50; H, 4.96%. Calcd for $C_{17}H_{12}O_2$: C, 82.24; H, 4.87%.

Hydrolysis of **7b** (248 mg, 1 mmol) was carried out in aqueous ethanol (30%, 15 ml) with potassium hydroxide (1.0 g) at 60 °C for 10 min to give 200 mg (97%) of **7a**.

4H-Cyclopenta[def]*phenanthren-8-amine (7c).* A mixture of **7a** (103 mg, 0.5 mmol), sulfur dioxide (3 g), and aqueous ammonia (28%, 40 ml) was heated in an autoclave (50 ml volume) at 150—160 °C at 8.5 kg/cm^2 for 10 h. The resulting product was purified by silica-gel column chromatography to yield **7c** (52 mg, 56%): mp 139.5—140.0 °C decomp (lit,[12] mp 136—138 °C).

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