

A New Heterocyclic Structure.
The [1]Benzopyrano[6,5,4-*def*][1]benzopyran. (1,6-Dioxapyrene)

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1,6-Dioxapyrene, the first unsubstituted dioxo-analogue of pyrene was synthesized in good yield from 2-carbomethoxy-6-methoxynaphtho[1,8-*bc*]pyran in a four-step reaction involving a *peri*-heterocyclisation. Its ¹H nmr spectral characteristics were compared with those of native pyrene.

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Although one dithiapyrene is known [1], to our knowledge, none of the nine possible unsubstituted dioxapyrenes have been synthesized up to now. Only a fair amount of functionalized derivatives of the 2,7- and 4,9-dioxapyrenes were prepared.

We describe here a convenient synthesis of 1,6-dioxapyrene **1**, a polyvalent synthon which can provide access to numerous novel heterocyclic structures. Among such structures, heterologues of arenopyrenes are especially interesting since they can be expected to interfere with the metabolisms of carcinogenic arenopyrenes [2-4].

Starting from the recently synthesized 2-carbomethoxy-6-methoxynaphtho[1,8-*bc*]pyran **2** [5], our scheme involves four stages with an overall yield of 58%.

Formylation of compound **2** gives a mixture of the isomeric aldehydes **3**, **4** and **5**. For the most part, the major isomer **3** was isolated by crystallization from toluene. A further preparative hplc carried out on the mother liquor allowed the separation of the two other aldehydes **4** and **5** and provided an additional crop of pure **3**. Demethylation of the aldehyde-ester **3** gave an almost quantitative yield of the *peri*-hydroxylated aldehyde **6**. Compound **6** was het-

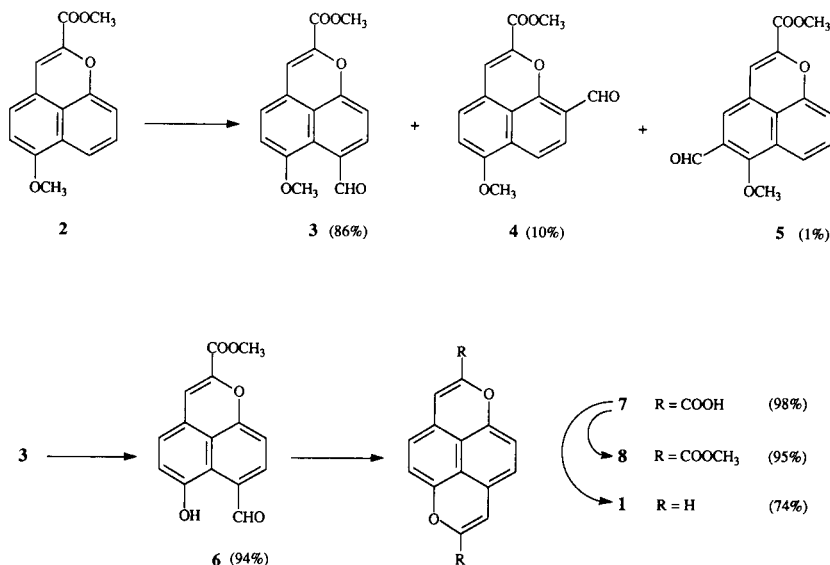
erocyclized by methyl chloroacetate to 1,6-dioxapyrene-2,7-dicarboxylic acid **7** under similar conditions to those we have previously described [5] for the preparation of 2-carbomethoxy-6-methoxynaphtho[1,8-*bc*]pyran **2**. The diacid **7** was decarboxylated by a conventional method to give 1,6-dioxapyrene **1**.

The ¹H nmr spectrum of **1** (deuteriochloroform) exhibited signals at 5.33 (H₃ and H₈), 5.97-6.17 (6H) whose strong fields shifts were 2 ppm above those of pyrene, and higher than those observed for naphtho[1,8-*bc*]pyran itself [5]. This shielding, which was also observed in the spectrum of the diester **8**, suggests that dioxapyrene **1** has less aromatic character than pyrene, analogous to that observed for 1,6-dithiapyrene [1,6].

EXPERIMENTAL

Melting points were measured on an Electrothermal digital melting-point apparatus and are uncorrected. The proton nuclear magnetic resonance spectra were recorded at 90 MHz using a Varian EM 390 spectrometer, with tetramethylsilane as the internal standard. The ir spectra were recorded on a Perkin-Elmer 1720 spectrometer, the uv spectra were measured with a Varian-

Scheme



Techtron 635 and the mass spectra were obtained with a Ribermag R10-10 C apparatus. The hplc was conducted with a Gilson chromatograph. The starting material **2** was prepared according to the previously described procedure [5]. Commercially available reagents and solvents were used without further purification.

2-Carbomethoxy-7-formyl-6-methoxynaphtho[1,8-*bc*]pyran (**3**), 2-Carbomethoxy-9-formyl-6-methoxynaphtho[1,8-*bc*]pyran (**4**) and 2-Carbomethoxy-5-formyl-6-methoxynaphtho[1,8-*bc*]pyran (**5**).

A solution of the compound **2** [5] (2.56 g, 10 mmoles) in dichloromethane (50 ml) was slowly added at 0°, with stirring, to a solution of titanium tetrachloride (4.1 g, 22 mmoles) and α,α -dichloromethylmethylether (1.25 g, 11 mmoles) in dichloromethane (100 ml). The mixture was stirred at 0° for 45 minutes then at room temperature for two hours. After quenching by water (200 ml), the organic layer was separated, then carefully washed with water and dried (sodium sulfate). Evaporation of the solvent left a mixture of the three isomers which was dissolved in boiling toluene (250 ml). After cooling, only the aldehyde **3** crystallized as yellow crystals, mp 244-245° (1.82 g, 64%); ¹H nmr (deuteriochloroform): δ 3.91 and 3.98 (2s, CO₂CH₃ and OCH₃), 6.76-7.05 (m, H₄, H₅, H₉), 7.25 (s, H₃), 8.05 (d, H₈, J_{H8-H9} = 8.2 Hz), 11.05 (s, CHO); ir (deuteriochloroform): ν 1728 (CO₂), 1667 cm⁻¹ (CHO); uv (ethanol): λ max (log ϵ) 241 nm (4.42).

Anal. Calcd. for C₁₆H₁₂O₅: C, 67.60; H, 4.25. Found: C, 67.55; H, 4.28.

The mother liquors were evaporated under reduced pressure. The solid residue obtained was chromatographed (hplc, Microsorb SI 60 Merck). Elution with ethyl acetate-hexane 1/1 gave successively the following:

a) The *ortho*-methoxylated aldehyde **5** (27 mg, 1%), yellow crystals had mp 202-203° (ethanol); ¹H nmr (deuteriochloroform): δ 3.92 and 3.98 (2s, CO₂CH₃ and OCH₃), 7.03 (s, H₃), 7.06-7.75 (m, H₇, H₈, H₉), 8.03 (s, H₄), 10.36 (s, CHO); ir (deuteriochloroform): ν 1731 (CO₂), 1676 cm⁻¹ (CHO); uv (ethanol): λ max (log ϵ) 236 (4.38), 272 nm (4.32).

Anal. Calcd. for C₁₆H₁₂O₅: C, 67.60; H, 4.25. Found: C, 67.66; H, 4.30.

b) The aldehyde **4** (275 mg, 10%), yellow crystals had mp 215-216° (ethanol); ¹H nmr (deuteriochloroform): δ 3.90 and 3.96 (2s, CO₂CH₃ and OCH₃), 6.83 (d, H₅, J_{H5-H4} = 8 Hz), 7.00 (d, H₄), 7.16 (s, H₃), 7.55 (d, H₇, J_{H7-H8} = 9 Hz), 7.73 (d, H₈), 10.56 (s, CHO); ir (deuteriochloroform): ν 1729 (CO₂), 1775 cm⁻¹ (CHO); uv (ethanol): λ max (log ϵ) 239 (4.31), 273 nm (4.42).

Anal. Calcd. for C₁₆H₁₂O₅: C, 67.60; H, 4.25. Found: C, 67.32; H, 4.22.

c) A second crop of aldehyde **3** (0.62 g, 22%) was obtained bringing up the overall yield of **3** to 86%.

2-Carbomethoxy-7-formyl-6-hydroxynaphtho[1,8-*bc*]pyran (**6**).

A solution of the aldehyde **3** (1 g, 3.5 mmoles) in dichloromethane (100 ml) was added dropwise at 20°, with stirring, to a suspension of aluminum chloride (4 g, 30 mmoles) in dichloromethane (100 ml). The mixture was stirred for twenty additional hours, then quenched with water. After separation, the organic layer was thoroughly washed with water, dried (sodium sulfate) and the solvent was evaporated. The crude product (0.95 g) was dissolved in boiling toluene (100 ml). After cooling to 50°, cyclohexane (100 ml) was added. The solution was cooled to -30° to yield 0.89 g (94%) of the aldehyde **6** as red crystals, mp 222-223°; ¹H nmr (deuteriochloroform): δ 3.90 (s, CO₂CH₃), 6.86 (d, H₅, J_{H5-H4} = 8.6

Hz), 7.06 and 7.13 (2d, H₄ and H₉, J_{H4-H5} and J_{H9-H8} = 8.6 Hz), 7.16 (s, H₃), 7.80 (d, H₈), 9.43 (s, CHO), 12.43 (s, OH); ir (deuteriochloroform): ν 1729 (CO₂), 1641 cm⁻¹ (CHO); uv (ethanol): λ max (log ϵ) 240 (4.39), 350 nm (4.03).

Anal. Calcd. for C₁₅H₁₀O₅: C, 66.67; H, 3.73. Found: C, 66.58; H, 3.85.

[1]Benzopyrano[6,5,4-*def*][1]benzopyran-2,7-dicarboxylic Acid (**7**).

A mixture of the aldehyde **6** (1 g, 3.7 mmoles), ethyl chloroacetate (0.5 g, 4.10 mmoles), potassium carbonate (1.12 g, 8.10 mmoles) and dimethylformamide (20 ml) was gently refluxed with stirring for 4 hours. After cooling to about 80°, a solution of potassium carbonate (0.6 g, 4.3 mmoles) in water (40 ml) was added and the solution thus obtained was gently refluxed for 1 hour. After elimination of the solvents under reduced pressure (0.1 Torr), the solid residue was dissolved in water (25 ml), the solution was acidified to pH 2 with hydrochloric acid, then centrifuged. After decantation of the supernatant, the acid **7** was obtained (1.08 g, 98%) as a yellow-green powder which decomposes above 300°.

This acid, particularly insoluble in organic solvents, was characterized as its diester **8** described below.

Anal. Calcd. for C₁₆H₈O₆: C, 64.87; H, 2.72. Found: C, 64.51; H, 2.55.

2,7-Dicarbomethoxy[1]benzopyrano[6,5,4-*def*][1]benzopyran (**8**).

A solution of the above diacid **7** (1 g, 3.40 mmoles) in 100 ml of methanol saturated with gaseous hydrochloric acid was gently refluxed for 12 hours. After usual work up, the crude ester was recrystallized from toluene to yield orange crystals, mp 306-308° (1.04 g, 95%); ¹H nmr (deuteriochloroform): δ 3.84 (s, 6H CO₂CH₃), 6.33 and 6.43 (2d, 4H, J = 8 Hz), 6.51 (s, 2H, H₃, H₈); ir (deuteriochloroform): ν 1724 cm⁻¹ (CO₂); uv (ethanol): λ max (log ϵ) 240 (4.28), 375 nm (3.79); ms: (70 eV) m/z (%) 324 (M⁺, 20), 150 (80).

Anal. Calcd. for C₁₈H₁₂O₆: C, 66.67; H, 3.73. Found: C, 66.79; H, 3.94.

[1]Benzopyrano[6,5,4-*def*][1]benzopyran (**1**).

A mixture of the diacid **7** (0.5 g, 1.7 mmoles), copper powder (1 g) and quinoline (10 ml) was refluxed for 90 minutes. After usual work up, the crude product was dissolved in chloroform, and the solution was filtered through a short silica gel column. After evaporation of the solvent, the 1,6-dioxapyrene (**1**) (0.26 g, 74%) was recrystallized from light petroleum ether to afford fine bright yellow needles, mp 162-163°; ¹H nmr (deuteriochloroform): δ 5.33 (d, H₃ and H₈, J_{H3-H2} and J_{H8-H7} = 6 Hz), 5.97-6.17 (m, 6H); uv (ethanol): λ max (log ϵ) 225 (4.59), 360 (4.03), 395 (3.75), 4.17 nm (3.75); ms: (70 eV) m/z (%) 208 (M⁺, 100), 179 (20), 152 (30).

Anal. Calcd. for C₁₄H₈O₂: C, 80.76; H, 3.87. Found: C, 80.70; H, 3.80.

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