

Short Communication

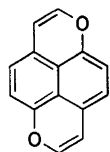
A Convenient Synthesis of 1,6-Dioxapyrene-2,7-dicarboxylic Acid Diethyl Ester

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Polycyclic heteroaromatic hydrocarbons have in recent years attracted attention.¹ 1,6-Dioxapyrene (**1**) has been shown to be highly phototoxic to pro- and eukaryotic cells.² Besides the biological properties, these compounds are also of considerable interest as building blocks for synthetic metals.³



1,6-Dioxapyrene

Fig. 1.

In connection with our own work on conducting molecular solids derived from heterocyclic pyrenes^{4–8} we needed access to large amounts of a 1,6-dioxapyrene-2,7-dicarboxylic acid ester. The dimethyl ester has been described by Buisson and Demerseman⁹ who prepared it by a seven-step synthesis starting from 1,5-naphthalenediol (**2**). The described method proved unsuitable for the preparation of larger amounts (> 100 mg of the ester), and in order to solve this problem the present synthesis, shown in Scheme 1, was developed.

1,5-Naphthalenediol (**2**) was reacted with ethyl chloroacetate in DMF with anhydrous K₂CO₃ as base to give the ester **3** in 93% yield. Vilsmeier–Haack formylation with POCl₃–DMF as reagent gave only the desired mono aldehyde **4** in 87% yield. The best method for cyclization of compound **4** to the oxaphenylene **5** turned out to be treatment with sodium ethoxide in ethanol, followed by re-esterification with SOCl₂ in ethanol.

The formylation of **5** to compound **6** was affected by reaction with dichloromethyl methyl ether and titanium(IV) chloride in CH₂Cl₂. In addition to **6**, some

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other isomers were formed, but fortunately **6** could be isolated pure by crystallisation from ethanol.

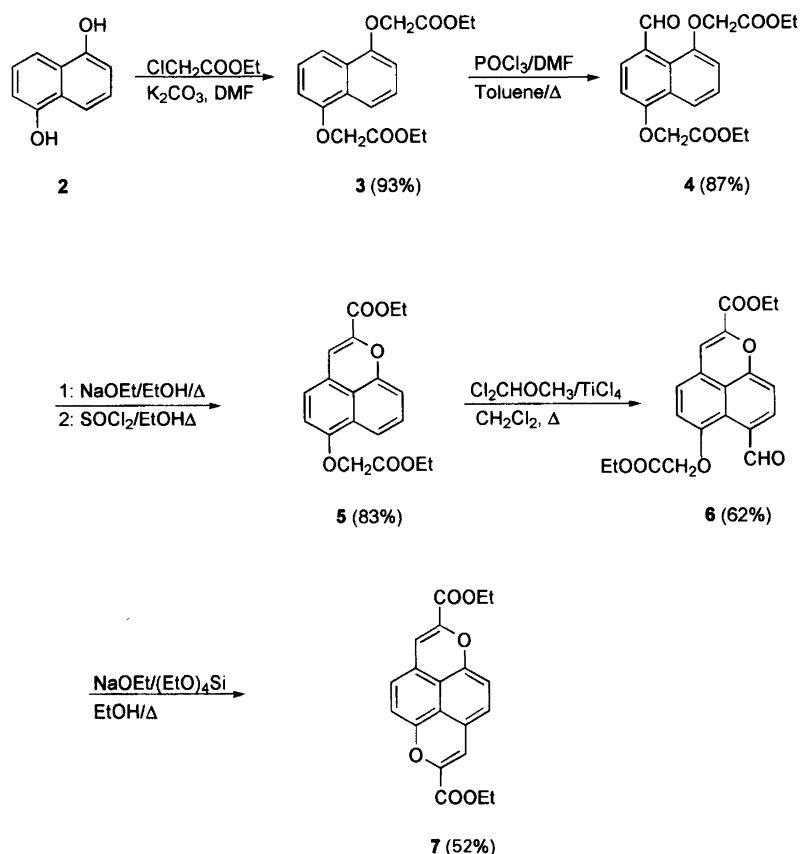
Cyclization of **6** to 1,6-dioxapyrene-2,7-dicarboxylic acid diethyl ester (**7**) was effected by treatment with sodium ethoxide and tetraethoxysilane in ethanol. The tetraethoxysilane presumably acted as a water binding reagent.

Experimental

Melting points were determined on a Büchi 535 apparatus and are uncorrected. The ¹H and ¹³C NMR spectra were recorded on a Varian 400 MHz spectrometer with TMS as an internal standard. C, H analyses were carried out at the Department for General and Organic Chemistry by Preben Hansen and Karin Linthoe, and were within ±0.4% of the theoretical values. All reactions were carried out under a nitrogen atmosphere.

(1,5-Naphthalenedioldioxy) diacetic acid diethyl ester (**3**). 1,5-Naphthalenediol (80.0 g, 0.50 mol) was added to a degassed mechanically stirred suspension of potassium carbonate (170 g, 1.2 mol) in DMF (500 ml) followed by ethyl chloroacetate (120 ml, 1.4 mol). The reaction was allowed to proceed overnight. The mixture was poured into 1.5 l of water, and the crude product isolated by filtration. Crystallization from 6 l of ethanol gave 154.7 g (93%) of white crystals, m.p. 133 × 135 °C. (lit.¹⁰ m.p. 136 °C). ¹H NMR (CDCl₃): δ 7.99 (d, 2 H, J = 8.4 Hz), 7.37 (d, 1 H, J = 7.9 Hz), 7.35 (d, 1 H, J = 8.2 Hz), 6.76 (d, 2 H, J = 7.5 Hz), 4.79 (s, 4 H), 4.29 (q, 4 H, J = 7.1 Hz), 1.30 (t, 6 H, J = 7.1 Hz). ¹³C NMR (CDCl₃): δ 168.8, 153.5, 126.8, 125.1, 115.6, 106.1, 65.9, 61.3, 14.2.

4-Formyl-(1,5-naphthalenedioldioxy) diacetic acid diethyl ester (**4**). Phosphorus oxychloride (50 ml, 0.54 mol) was added dropwise to a vigorously stirred suspension of



Scheme 1.

compound **3** (59.8 g, 0.18 mol) in a mixture of toluene (180 ml) and DMF (37 ml). The temperature was kept between 4 and 8 °C during the addition by cooling with ice-salt mixture. The reaction mixture was stirred and cooled for further 30 min, and finally heated in an oil bath and kept at reflux for 2 h. After being cooled to room temperature, the mixture was poured into 1.8 l saturated, cold aqueous sodium bicarbonate with stirring. We found that filtration of the product went smoothly if the suspension was allowed to stand with stirring overnight. The product was washed with water and dried *in vacuo* over concentrated sulfuric acid. Yield: 56.7 g (87%). A sample crystallized from ethanol had m.p. 122–124 °C. $^1\text{H NMR}$ (CDCl_3): δ 11.18 (s, 1 H), 8.11 (d, 1 H, $J=8.6$ Hz), 8.05 (d, 1 H, $J=8.2$ Hz), 7.45 (d, 1 H, $J=8.2$ Hz), 7.43 (d, 1 H, $J=8.1$ Hz), 6.94 (d, 1 H, $J=7.8$ Hz), 6.79 (d, 1 H, $J=8.2$ Hz), 4.85 (s, 2 H), 4.81 (s, 2 H), 4.29 (m, 4 H), 1.31 (m, 6 H). $^{13}\text{C NMR}$ (CDCl_3): δ 194.5, 168.0, 167.9, 157.3, 154.4, 129.1, 128.7, 127.2, 125.8, 124.9, 116.7, 108.9, 105.0, 65.9, 65.6, 61.7, 61.6, 14.2, 14.1.

2-Ethoxycarbonylnaphtho[1,8-*bc*]pyran-6-yloxyacetic acid ethyl ester (5). Aldehyde **4** (28.8 g, 0.08 mol) was added with stirring to a solution of 2.0 g (0.09 mol) sodium in 240 ml ethanol. The mixture was heated and

kept at reflux for 2 h, after which it was cooled to room temperature. 25 ml SOCl_2 were then added very cautiously, and refluxing was continued overnight. The reaction mixture was poured into 1 l of water, filtered, washed with water and dried. Yield: 22.7 g (83%). A sample recrystallized from ethanol-activated carbon had m.p. 140–142 °C. $^1\text{H NMR}$ (CDCl_3): δ 7.66 (d, 1 H, $J=8.2$ Hz), 7.35 (d, 1 H, $J=8.1$ Hz), 7.33 (d, 1 H, $J=8.2$ Hz), 6.98 (s, 1 H), 6.95 (d, 1 H, $J=7.9$ Hz), 6.80 (d, 1 H, $J=7.7$ Hz), 6.52 (d, 1 H, $J=7.8$ Hz), 4.75 (s, 2 H), 4.36 (q, 2 H, $J=7.1$ Hz), 4.29 (q, 2 H, $J=7.1$ Hz), 1.39 (t, 3 H, $J=7.1$ Hz), 1.31 (t, 3 H, $J=7.1$ Hz). $^{13}\text{C NMR}$ (CDCl_3): δ 168.4, 161.4, 152.7, 152.2, 141.5, 127.8, 126.8, 124.8, 121.4, 118.3, 114.8, 114.5, 109.5, 106.3, 65.6, 61.6, 61.4, 14.3, 14.2.

7-Formyl-2-ethoxycarbonylnaphtho[1,8-*bc*]pyran-6-yloxyacetic acid ethyl ester (6). A solution of compound **5** (20.5 g, 0.06 mol) in CH_2Cl_2 (300 ml) was added to a stirred solution of titanium(IV) chloride (14.4 ml, 0.13 mol) and dichloromethyl methyl ether (6.0 ml, 0.07 mol) in CHCl_2 (600 ml). The solution was refluxed for 3 h, and poured onto 1 l ice-cold water. The organic phase was separated, washed with water, dried over MgSO_4 , filtered, concentrated *in vacuo* and crystallized from ethanol. Yield: 13.8 g (62%). A sample recrystal-

lized from ethanol had m.p. 194–196 °C (decomp.) ^1H NMR (CDCl_3): δ 11.1 (s, 1 H), 8.07 (d, 1 H, $J=8.4$ Hz), 7.05 (s, 1 H), 6.99 (d, 1 H, $J=8.4$ Hz), 6.92 (d, 1 H, $J=7.9$ Hz), 6.75 (d, 1 H, $J=7.9$ Hz), 4.77 (s 2 H), 4.38 (q, 2 H, $J=7.1$ Hz), 4.30 (q, 2 H, $J=7.1$ Hz), 1.40 (t, 3 H, $J=7.1$ Hz), 1.34 (t, 3 H, $J=7.1$ Hz). ^{13}C (CDCl_3): δ 193.3, 167.6, 160.8, 156.4, 153.8, 141.1, 131.7, 127.6, 125.4, 125.1, 122.2, 119.6, 114.7, 109.9, 109.6, 65.9, 61.9, 61.8, 14.2, 14.1.

1,6-Dioxapyrene-2,7-dicarboxylic acid diethyl ester (7). Finely powdered compound **6** (2.4 g, 6.5 mmol) and tetraethoxysilane (10 ml) were added to a stirred solution of Na (0.20 g, 8.7 mmol) in EtOH (100 ml). The suspension was heated to reflux and kept there for 1 h. After being cooled to room temperature, the mixture was poured into 2 M AcOH (100 ml) and filtered. The crude product was washed with water, dried and sublimed *in vacuo*. Yield: 1.2 g (52%). Orange-red crystals which begin to sublime above 250 °C. ^1H NMR (CS_2): δ 6.47 (s, 2 H), 6.39 (d, 2 H, $J=7.9$ Hz), 6.28 (d, 2 H, $J=7.9$ Hz); 4.27 (q, 4 H, $J=7.1$ Hz); 1.33 (t, 6 H, $J=7.1$ Hz). ^{13}C (CS_2): δ 160.8, 153.4, 142.8, 127.6, 121.6, 121.3, 115.1, 109.6, 61.5, 14.1.

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