

**107. The Chemistry of the "Insoluble Red" Woods. Part VII.\***  
*The Synthesis of Coumarino(3' : 4'-3 : 2)coumarones.*

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The synthesis of several coumarino(3' : 4'-3 : 2)coumarones (II), including tri-*O*-methylwedelolactone <sup>1</sup> is described.

IN exploratory experiments on the synthesis of homopterocarpin <sup>2</sup> and its congeners we have synthesised the coumarino(3' : 4'-3 : 2)coumarone system (II).

Demethylation of 4-hydroxy-5 : 7-dimethoxy-3-*o*-methoxyphenylcoumarin (I; R = H) gave the coumarinocoumarone (II; R = H), accompanied by the partially demethylated derivative. Methylation of the lactone (II; R = H) by Canter and Robertson's method <sup>3</sup> gave 2-(2 : 4 : 6-trimethoxyphenyl)coumarone-3-carboxylic acid (III; R = CO<sub>2</sub>H) which could not be correlated with 2-(2 : 4 : 6-trimethoxyphenyl)coumarone <sup>4</sup> (III; R = H) since, in contrast to the 5 : 6-dimethoxy-analogue (tetra-*O*-methylwedelic acid),<sup>1</sup> attempts to decarboxylate it regenerated the parent lactone (II; R = H). Similarly 3-(2 : 4-dimethoxyphenyl)-4-hydroxy-7-methoxycoumarin furnished 6 : 7'-dimethoxycoumarino(3' : 4'-3 : 2)coumarone, which contains the skeletal system of homopterocarpin; and 4-hydroxy-5 : 7-dimethoxy-3-(2 : 4 : 5-trimethoxyphenyl)coumarin (I; R = OMe) gave 5' : 7' : 5 : 6-tetramethoxycoumarino(3' : 4'-3 : 2)coumarone (II; R = OMe), identical with tri-*O*-methylwedelolactone.

\* Part VI, *J.*, 1954, 2794.

<sup>1</sup> Govindachari, Nagarajan, and Pai, *J.*, 1956, 629.

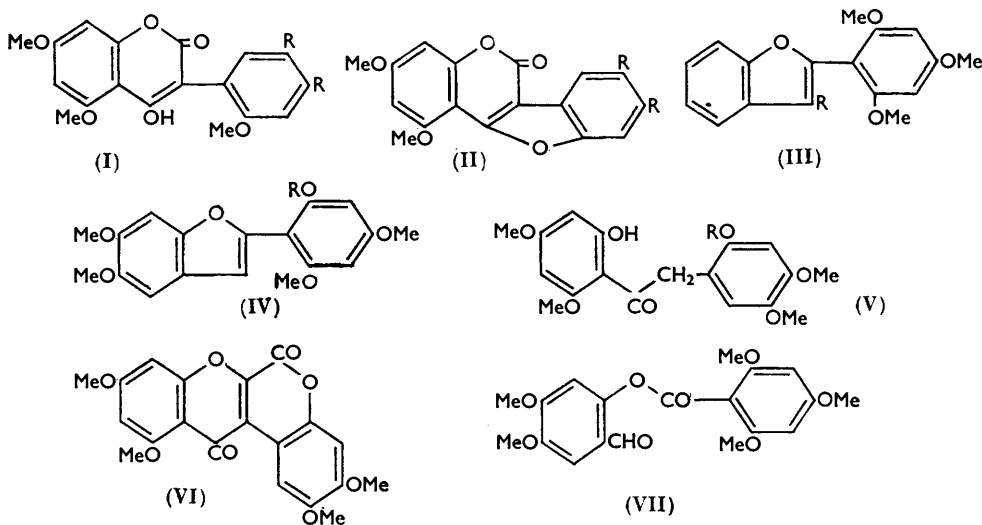
<sup>2</sup> McGookin, Robertson, and Whalley, *J.*, 1940, 787.

<sup>3</sup> Canter and Robertson, *J.*, 1931, 1875.

<sup>4</sup> Whalley and (in part) Lloyd, *J.*, 1956, 3213.

By Whalley and Lloyd's general method<sup>4</sup> 2-hydroxy-4:6:2':4':5'-pentamethoxydeoxybenzoin (V; R = Me) was converted into the chromono(2':3'-3:4)coumarin (VI), and thence into the unstable 2:2'-dihydroxy-4:6:4':5'-tetramethoxydeoxybenzoin (V; R = H) which readily cyclised to 2-(2-hydroxy-4:6-dimethoxyphenyl)-5:6-dimethoxycoumarone (IV; R = H). The methyl ether (IV; R = OMe) of this was identical with the corresponding derivative from tri-*O*-methylwedelolactone.<sup>1</sup>

Condensation of 2:4:6-trimethoxybenzoyl chloride<sup>4</sup> with 2-hydroxy-4:5-dimethoxybenzaldehyde gave 4:5-dimethoxy-2-(2:4:6-trimethoxybenzoyl)benzaldehyde (VII) previously obtained<sup>1</sup> by ozonolysis of the 2-phenylcoumarone (IV; R = Me).



#### EXPERIMENTAL

5':7'-Dimethoxycoumarino(3':4'-3:2)coumarone (II; R = H).—Cyclisation of 2-hydroxy-4:6:2'-trimethoxydeoxybenzoin (5 g.) with ethyl carbonate (50 ml.) and sodium dust (2 g.) by Boyd and Robertson's method<sup>6</sup> gave 4-hydroxy-5:7-dimethoxy-3-*o*-methoxyphenylcoumarin, separating in needles (3.5 g.), m. p. 248°, from acetic acid [Found: C, 65.3; H, 5.0; OMe, 27.9. C<sub>15</sub>H<sub>7</sub>O<sub>3</sub>(OMe)<sub>3</sub> requires C, 65.8; H, 4.9; OMe, 28.4%]. A boiling solution of this coumarin (1 g.) in acetic acid (15 ml.) containing 48% hydrobromic acid (12 ml.) deposited, during ½ hr., 5':7'-dimethoxycoumarino(3':4'-3:2)coumarone, forming needles (0.5 g.), m. p. 254°, from acetic acid [Found: C, 68.3; H, 4.3; OMe, 20.6%; M, 267. C<sub>15</sub>H<sub>6</sub>O<sub>3</sub>(OMe)<sub>2</sub> requires C, 68.9; H, 4.1; OMe, 20.9%; M, 296]. Dilution of the cooled, filtered reaction mixture with water furnished a semicrystalline product soluble in 2*N*-aqueous sodium hydroxide, and converted by methylation into the parent coumarinocoumarone (0.35 g.).

This lactone (1 g.) was dissolved on the steam-bath in methanol (25 ml.) and 50% aqueous potassium hydroxide (15 ml.), and kept at 100° whilst 50% aqueous potassium hydroxide (20 ml.) and methyl sulphate (8 ml.) were added alternately in small portions during 2 hr. Next day the turbid mixture was dissolved in water, and the clear solution acidified to yield 2-(2:4:6-trimethoxyphenyl)coumarone-3-carboxylic acid (1 g.) which separated from aqueous acetone in needles, m. p. 216° (Found: C, 66.2; H, 5.5. C<sub>18</sub>H<sub>16</sub>O<sub>8</sub> requires C, 65.9; H, 4.9%).

6:7'-Dimethoxycoumarino(3':4'-3:2)coumarone.—A solution of 3-(2:4-dimethoxyphenyl)-4-hydroxy-7-methoxycoumarin<sup>6</sup> (2 g.) in acetic acid (20 ml.) and 48% hydrobromic acid (10 ml.) was refluxed for 1 hr., cooled, and diluted with water (10 ml.). The alkali-soluble, semicrystalline precipitate was methylated by methyl sulphate-potassium carbonate in boiling acetone during 1 hr. and purification from acetic acid or methanol gave 6:7'-dimethoxycoumarino(3':4'-3:2)coumarone (1.1 g.) in needles, m. p. 197° [Found: C, 69.0; H, 4.0; OMe, 21.0. C<sub>15</sub>H<sub>6</sub>O<sub>3</sub>(OMe)<sub>2</sub> requires C, 68.9; H, 4.1; OMe, 20.9%].

<sup>5</sup> Lloyd and Whalley, *J.*, 1956, 3209.

<sup>6</sup> Boyd and Robertson, *J.*, 1948, 174.

4-Hydroxy-5 : 7-dimethoxy-3-(2 : 4 : 5-trimethoxyphenyl)coumarin (I; R = OMe).—Hoesch condensation of phloroglucinol (10 g.) and 2 : 4 : 5-trimethoxybenzyl cyanide (5 g.) in ether (150 ml.) containing zinc chloride (3 g.) gave 2 : 4 : 6-trihydroxy-2' : 4' : 5'-trimethoxydeoxybenzoin, forming prisms (5 g.), m. p. 207°, from methanol and having an intense red-brown ferric reaction in alcohol [Found : C, 61.0; H, 5.5; OMe, 27.4.  $C_{14}H_9O_4(OMe)_3$  requires C, 61.1; H, 5.4; OMe, 27.8%]. Methylation of this ketone (5 g.) with methyl sulphate-acetone-potassium carbonate gave 2-hydroxy-4 : 6 : 2' : 4' : 5'-pentamethoxydeoxybenzoin, forming prisms (5 g.), m. p. 143°, from alcohol [Found : C, 62.8; H, 5.9; OMe, 43.0.  $C_{14}H_7O_2(OMe)_5$  requires C, 63.0; H, 6.1; OMe, 42.8%].

Cyclisation of this ketone (4 g.) with ethyl carbonate (80 ml.) and sodium dust (2 g.) during  $\frac{1}{2}$  hr. gave 4-hydroxy-5 : 7-dimethoxy-3-(2 : 4 : 5-trimethoxyphenyl)coumarin which separated from acetic acid in needles, m. p. 289° [Found : C, 61.0; H, 5.3; OMe, 39.7.  $C_{15}H_5O_3(OMe)_5$  requires C, 61.8; H, 5.2; OMe, 39.9%].

Tri-O-methylwedelolactone (II; R = OMe).—When a solution of the previous coumarin (1 g.) in acetic acid (15 ml.), containing 48% hydrobromic acid (8 ml.), was boiled for  $\frac{1}{2}$  hr. and cooled, crystals (0.5 g.) separated. Methylation by methyl sulphate-potassium carbonate in boiling acetone during 1 hr. then gave tri-O-methylwedelolactone, forming needles (0.5 g.), m. p. 247° (from acetic acid), identical with an authentic specimen [Found : C, 63.3; H, 4.4; OMe, 33.4.  $C_{15}H_4O_3(OMe)$  requires C, 64.0; H, 4.5; OMe, 34.8%].

5 : 6-Dimethoxy-2-(2 : 4 : 6-trimethoxyphenyl)coumarone (IV; R = Me).—A solution of 2 : 4 : 6-trihydroxy-2' : 4' : 5'-trimethoxydeoxybenzoin (5.5 g.) in pyridine (100 ml.), containing ethoxalyl chloride,<sup>7</sup> was kept at 10°, and 24 hr. later the semicrystalline product (isolated with chloroform) was refluxed for 30 min. with hydriodic acid (50 ml.; *d* 1.7) and acetic acid (from 25 ml. of anhydride), an orange-coloured microcrystalline solid (4 g.) separating. Methylation of this product (4 g.) during 24 hr. in boiling acetone containing methyl sulphate and potassium carbonate gave 5' : 7' : 6 : 7-tetramethoxychromono(2' : 3'-3 : 4)coumarin, which formed needles (4 g.), m. p. 294°, from acetic acid [Found : C, 62.5; H, 4.5; OMe, 31.8.  $C_{16}H_4O_4(OMe)_4$  requires C, 62.5; H, 4.2; OMe, 32.2%].

A solution of this coumarin (4 g.) in water (25 ml.) and alcohol (25 ml.), containing potassium hydroxide (7 g.), was refluxed for 2 hr., cooled, diluted with water (100 ml.), and acidified. 2 : 2'-Dihydroxy-4 : 6 : 4' : 5'-tetramethoxydeoxybenzoin separated in needles (2.3 g.), m. p. 132°, having an intense red-brown ferric reaction in alcohol. Cyclisation of this occurred during purification from hot alcohol to give 2-(2-hydroxy-4 : 6-dimethoxyphenyl)-5 : 6-dimethoxycoumarone (2 g.) in prisms, m. p. 151°, devoid of a ferric reaction in alcohol [Found : C, 65.7; H, 5.2; OMe, 36.9.  $C_{14}H_8O_2(OMe)_4$  requires C, 65.4; H, 5.5; OMe, 37.6%], and methylated quantitatively to 5 : 6-dimethoxy-2-(2 : 4 : 6-trimethoxyphenyl)coumarone, m. p. 148°, identical with a specimen prepared from tri-O-methylwedelolactone (Found : C, 65.7; H, 5.7. Calc. for  $C_{19}H_{20}O_6$  : C, 66.3; H, 5.9%). 2-(2-Benzoyloxy-4 : 6-dimethoxyphenyl)-5 : 6-dimethoxycoumarone separated from alcohol in prisms, m. p. 133° [Found : C, 71.7; H, 6.1; OMe, 29.8.  $C_{21}H_{12}O_2(OMe)_4$  requires C, 71.4; H, 5.8; OMe, 29.5%]. Debzylation of this compound with acetic-hydrochloric acid on the steam-bath during 20 min. gave a low yield of 2-(2-hydroxy-4 : 6-dimethoxyphenyl)-5 : 6-dimethoxycoumarone, m. p. 151°.

4 : 5-Dimethoxy-2-(2 : 4 : 6-trimethoxybenzoyl)benzaldehyde (VII).—A solution of 2-hydroxy-4 : 5-dimethoxybenzaldehyde (1.2 g.) and of 2 : 4 : 6-trimethoxybenzoyl chloride, prepared from 2 : 4 : 6-trimethoxyphenylglyoxylic acid (2.5 g.) by Lloyd and Whalley's method,<sup>5</sup> in pyridine (20 ml.) was heated on the steam-bath during 2 hr. Isolation of the product 24 hr. later gave 4 : 5-dimethoxy-2-(2 : 4 : 6-trimethoxybenzyl)benzaldehyde which separated from methanol in needles (1 g.), m. p. 161°, having a negative ferric reaction in alcohol (Govindachari *et al.*,<sup>1</sup> record the m. p. 159—160°) (Found : C, 61.1; H, 5.9. Calc. for  $C_{19}H_{20}O_8$  : C, 60.6; H, 5.4%).

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