341. *Synthesis of 5-Hydroxycoumarin.*

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5-Hydroxycoumarin has been synthesised by a series of reactions starting from methyl 2-hydroxy-4-methoxy-3-formylbenzoate (Shah and Laiwalla, preceding paper) and ethyl malonate.

5-Hydroxy-4-methylcoumarins are readily available through the condensation of methyl β-resorcylate and resacetophenone with ethyl acetoacetate in presence of anhydrous aluminium chloride (Sethna, Shah, and Shah, this vol., p. 228). *5-Hydroxycoumarin*, which obviously cannot be prepared by this method, has now been synthesised from methyl 2 : 4-dihydroxy-3-formylbenzoate (Shah and Laiwalla, *Current Science*, 1936, 197; preceding paper).

Methyl 2 : 4-dihydroxy-3-formylbenzoate gave an unsatisfactory result in the Perkin reaction. It was therefore condensed with ethyl malonate. Hydrolysis of the product afforded *5-hydroxycoumarin-3 : 6-dicarboxylic acid*, which was also obtained by the condensation of 2 : 4-dihydroxy-3-formylbenzoic acid (Shah and Laiwalla, *loc. cit.*) with cyanoacetic acid (cf. Heyes and Robertson, J., 1936, 1836). Attempts to decarboxylate the acid were unsuccessful.

γ-Resorcylaldehyde (Shah and Laiwalla, *loc. cit.*), which was expected to give 5-acetoxycoumarin directly in the Perkin reaction, gave only a resinous unworkable mass. On condensation with cyanoacetic acid, the aldehyde gave *5-hydroxycoumarin-3-carboxylic acid*, decarboxylation of which afforded a substance, m. p. 195—210°. This was possibly 5-hydroxycoumarin, but the amount obtained was too small for further investigation.

5-Hydroxycoumarin-3 : 6-dicarboxylic acid and its methyl ethyl ester could not be methylated.

Methyl 2-hydroxy-4-methoxy-3-formylbenzoate (Shah and Laiwalla, *loc. cit.*), now obtained in much improved yield, afforded, on condensation with ethyl malonate, *ethyl 5-methoxy-8-carbomethoxycoumarin-3-carboxylate*, which on hydrolysis gave *5-methoxycoumarin-3 : 8-dicarboxylic acid*. This acid was smoothly decarboxylated to *5-methoxycoumarin*, demethylation of which with aluminium chloride afforded *5-hydroxycoumarin*, from which 2 : 6-*dimethoxycinnamic acid* was obtained.

Experimental.

5-Hydroxycoumarin-3 : 6-dicarboxylic Acid.—(i) A suspension of ethyl 5-hydroxy-6-carbomethoxycoumarin-3-carboxylate (Shah and Laiwalla, preceding paper) (2 g.) in 4% sodium hydroxide solution (60 c.c.) was left for 8 hours at room temperature. The clear solution obtained was acidified with dilute hydrochloric acid, and the precipitated *acid* purified by means of sodium hydrogen carbonate. It crystallised from alcohol in tiny yellow needles (1·2 g.), m. p. 265—267° (efferv.) (Found: C, 53·4; H, 3·0. $C_{11}H_6O_7$ requires C, 52·8; H, 2·4%). (ii) 2 : 4-Dihydroxy-3-formylbenzoic acid (Shah and Laiwalla, preceding paper) (1 g.), 20% sodium hydroxide solution (10 c.c.), and an aqueous solution of cyanoacetic acid (0·5 g.) were stirred together for 3 hours and kept at room temperature for 24 hours; the mixture was then

acidified with dilute hydrochloric acid. The pale yellow precipitate, on being boiled with 4% hydrochloric acid (40 c.c.), afforded the dicarboxylic acid, which crystallised from dilute alcohol in small needles (0·8 g.), m. p. and mixed m. p. with the acid from (i), 265—267°.

5-Hydroxycoumarin-3-carboxylic acid, prepared from γ-resorcylaldehyde (Shah and Laiwalla, preceding paper) and cyanoacetic acid by method (ii) above, crystallised from nitrobenzene in slender yellow needles, m. p. 272—274° (efferv.) (Found: C, 57·3; H, 2·9. $C_{10}H_6O_5,0{\cdot}25H_2O$ requires C, 57·3; H, 2·9%).

Methyl 2-Hydroxy-4-methoxy-3-formylbenzoate.—Methyl 2 : 4-dihydroxy-3-formylbenzoate (Shah and Laiwalla, *loc. cit.*) (3 g.), methyl sulphate (6 g.), and fused potassium carbonate (10 g.) in acetone (100 c.c.) were heated under reflux for 24 hours, the solution filtered, and the potassium salt washed thoroughly with acetone (50 c.c.). The solid obtained on evaporation of acetone was washed with 5% sodium hydroxide solution (60 c.c.) and crystallised from benzene–light petroleum; it formed colourless prisms (2·1 g.), m. p. 121—122°.

Condensation of Methyl 2-Hydroxy-4-methoxy-3-formylbenzoate with Ethyl Malonate.—To the foregoing methyl ether (5 g.), dissolved in pyridine (20 c.c.), ethyl malonate (7·5 g.) and piperidine (4 drops) were added. The mixture was heated under reflux for 30 minutes, kept at 100° for 2 hours, and then poured into dilute hydrochloric acid (150 c.c.). *Ethyl 5-methoxy-8-carbomethoxycoumarin-3-carboxylate* crystallised from methanol in small yellow needles (5 g.), m. p. 186—188° (Found: C, 58·8; H, 4·7. $C_{15}H_{14}O_7$ requires C, 58·8; H, 4·6%).

5-Methoxycoumarin-3 : 8-dicarboxylic acid, obtained by shaking the preceding ester (5 g.) with 4% sodium hydroxide solution (100 c.c.) for 3 hours and acidifying the mixture after 12 hours, crystallised from alcohol in needles (4 g.), m. p. 281° (efferv.) (Found: C, 54·6; H, 3·1. $C_{12}H_8O_7$ requires C, 54·6; H, 3·0%).

5-Methoxycoumarin.—The foregoing acid (2 g.) was boiled with quinoline (30 c.c.) containing copper-bronze (4·0 g.) for ¾ hour. The filtered solution was mixed with an excess of dilute hydrochloric acid and extracted with ether, the extract washed with aqueous sodium hydrogen carbonate and evaporated, and the residual *5-methoxycoumarin* (0·9 g.) crystallised from hot water; it formed colourless woolly needles, m. p. 85—87° (Found: C, 68·2; H, 4·8. $C_{10}H_8O_3$ requires C, 68·2; H, 4·6%).

5-Hydroxycoumarin.—A mixture of 5-methoxycoumarin (0·5 g.) and aluminium chloride (1 g.) was heated at 145—150° for 3 hours, ice and hydrochloric acid added, and the insoluble *5-hydroxycoumarin* crystallised from water, forming tiny woolly needles (0·3 g.), m. p. 223—225° (Found: C, 66·5; H, 3·9. $C_9H_6O_3$ requires C, 66·7; H, 3·7%), easily soluble in alcohol and hot water but sparingly in benzene and xylene. It dissolved in alkali with a deep yellow colour, which slowly changed to brown on exposure. Its solutions in alkali and in sulphuric acid were not fluorescent (see Collie and Chrystall, J., 1907, **91**, 1804; Dey, J., 1915, **107**, 1614, 1621).

The *acetyl* derivative, prepared by refluxing the substance (0·2 g.) with acetic anhydride (2 c.c.) and pyridine (2 drops) for 3 hours, crystallised from water in silky needles, m. p. 88—89° (Found: C, 64·7; H, 4·1. $C_{11}H_8O_4$ requires C, 64·7; H, 3·9%).

2 : 6-Dimethoxycinnamic Acid.—5-Methoxycoumarin (0·5 g.) was dissolved in acetone (5 c.c.), and methyl sulphate (5 c.c.) added, followed by 10% sodium hydroxide solution (20 c.c.) in small portions. The mixture was heated on the steam-bath for a few minutes and again for 15 minutes after addition of more of these two reagents. *2 : 6-Dimethoxycinnamic acid*, obtained on acidification with hydrochloric acid after 12 hours, crystallised from water, containing a few drops of alcohol, in stout colourless needles, m. p. 151—153° (Found: C, 63·3; H, 5·8. $C_{11}H_{12}O_4$ requires C, 63·5; H, 5·8%). It decolourised bromine water and alkaline potassium permanganate solution and gave no coloration with ferric chloride.

All the analyses recorded are micro-analyses.

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