

407. *Hydroxy-carbonyl Compounds. Part XII.*
5 : 7-Dihydroxycoumarin.

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IN the course of some unsuccessful experiments on the syntheses of 2 : 2-dimethylchromans from coumarins undertaken in connection with studies on toxicarol and xanthoxyletin (this vol., p. 627) we were led to investigate the synthesis of 5 : 7-dihydroxycoumarin and its naturally occurring dimethyl ether, citropten or limettin (Tilden and Burrows, J., 1902, **81**, 508). According to Herzig and Wenzel (*Monatsh.*, 1903, **24**, 864) application of the Perkin reaction to phloroglucinolaldehyde gave only 2 : 4 : 6-triacetoxybenzylidene diacetate, but Gattermann (*Annalen*, 1907, **357**, 345) claims to have obtained 5 : 7-diacetoxycoumarin by the same procedure. In their paper on the acetylation of *o*-hydroxy-aldehydes Malkin and Nierenstein (*J. Amer. Chem. Soc.*, 1931, **53**, 239) direct attention to the contradictory results described by these authors, but appear to have overlooked the statement of Schmidt (*Arch. Pharm.*, 1904, **242**, 294), who claims to have synthesised citropten, thereby confirming the views of Tilden and Burrows (*loc. cit.*) regarding the nature of this substance. Further, Malkin and Nierenstein apparently consider that the failure on the part of Herzig and Wenzel to obtain the coumarin from phloroglucinolaldehyde lies in the facile formation of the benzylidene diacetate, which they regard as inhibiting coumarin formation.

It has now been found that, on being heated with sodium acetate and acetic anhydride, phloroglucinolaldehyde and 2 : 4 : 6-triacetoxybenzylidene diacetate severally gave excellent yields of 5 : 7-diacetoxycoumarin, which on deacetylation yielded 5 : 7-dihydroxycoumarin. The dimethyl ether of the latter was identical with citropten and with a specimen obtained from 2-hydroxy-4 : 6-dimethoxybenzaldehyde (a) by means of the Perkin reaction and (b) by the cyanoacetic acid method.

The facile production of 2 : 4 : 6-triacetoxybenzylidene diacetate and its conversion into 5 : 7-diacetoxycoumarin make it clear that, in the present instance at least, this compound is an intermediate in the coumarin synthesis and hence the formation of

benzylidene diacetates is not necessarily a retarding influence in the synthesis of coumarins by the Perkin reaction. It may well be that under certain conditions the production of a benzylidene diacetate is the preliminary step in the Perkin reaction (compare Perkin, *J.*, 1886, **49**, 318).

EXPERIMENTAL.

5:7-Dimethoxycoumarin-3-carboxylic Acid.—A mixture of 2-hydroxy-4:6-dimethoxybenzaldehyde (5 g.), 20% aqueous sodium hydroxide (8 c.c.), and aqueous cyanoacetic acid (16.3 c.c. of a solution prepared according to the directions of Phelps and Tillotson, *Amer. J. Sci.*, 1908, **26**, 267) was agitated for 2 hours; the sodium derivative which originally separated slowly dissolved. Next day the brown solution was acidified (Congo-red) with hydrochloric acid and the yellow amorphous precipitate of 4:6-dimethoxysalicylidencyanoacetic acid (6.5 g.) was collected, washed, and purified by the aid of aqueous sodium bicarbonate. On being heated with dilute hydrochloric acid (50 c.c.) for $\frac{1}{2}$ hour, this compound, m. p. 205° (decomp.), gave rise to the *acid* (4 g.), which formed pale yellow needles, m. p. 249° (decomp.), from acetone (Found: C, 57.9; H, 4.1. $C_{12}H_{10}O_6$ requires C, 57.7; H, 4.0%).

5:7-Dimethoxycoumarin (Citropten).—The foregoing acid (0.2 g.) was boiled with quinoline (10 c.c.) containing copper-bronze (0.5 g.) for 40 minutes, the filtered solution mixed with an excess of dilute hydrochloric acid and extracted with ether (5 × 20 c.c.), and the combined extracts washed with aqueous sodium bicarbonate, dried, and evaporated. The residual coumarin (0.14 g.) separated from methyl alcohol or a small volume of acetone in elongated rectangular prisms, m. p. 147°, having properties identical with those of citropten, including the intense fluorescence in alcoholic solution (Found: C, 64.4; H, 4.9. Calc. for $C_{11}H_{10}O_4$: C, 64.1; H, 4.9%).

Vigorous acetylation of 2-hydroxy-4:6-dimethoxybenzaldehyde (2 g.) with acetic anhydride (20 c.c.) and sodium acetate (5 g.) at 180–190° for 18 hours gave rise to the same compound (0.4 g.), m. p. and mixed m. p. 147°, after purification.

Application of the Pechmann reaction to phloroglucinol dimethyl ether and malic acid did not yield citropten.

5:7-Dihydroxycoumarin.—A mixture of phloroglucinolaldehyde (8 g.), sodium acetate (8 g.), and acetic anhydride (40 c.c.) was heated (oil-bath at 185–190°) for 12–14 hours. On isolation, 5:7-diacetoxycoumarin separated from methyl alcohol and then ethyl alcohol (charcoal) in slender colourless prisms, m. p. 140° (Gattermann, *loc. cit.*, gives m. p. 138°) (Found: C, 59.6; H, 4.0. Calc. for $C_{13}H_{10}O_6$: C, 59.5; H, 3.8%).

When the aldehyde was replaced by 2:4:6-triacetoxycoumarin, a similar yield of the coumarin diacetate was obtained, m. p. and mixed m. p. 140°, after purification (Found: C, 59.6; H, 3.8%).

10% Aqueous sodium hydroxide was added to the diacetate (5 g.) in warm alcohol, and the mixture heated on the steam-bath until a homogeneous solution was obtained. More aqueous sodium hydroxide (30 c.c.) was then added, the mixture was kept for 15 minutes and acidified with hydrochloric acid, the greater part of the alcohol was evaporated, and the dihydroxycoumarin which separated from the cooled solution was recrystallised from dilute acetic acid, forming elongated colourless prisms, m. p. 285–286° (Found: C, 60.7; H, 3.6. Calc. for $C_9H_6O_4$: C, 60.7; H, 3.4%). Methylation of this compound (0.4 g.) in boiling acetone (20 c.c.) with an excess of methyl iodide and potassium carbonate gave rise to citropten, m. p. and mixed m. p. 147° (Found: C, 63.9; H, 5.0%).

An alcoholic solution of 5:7-dihydroxycoumarin does not fluoresce, but the colourless solution of the compound in sulphuric acid, which is non-fluorescent in diffuse daylight, exhibits a faint bluish-green fluorescence in bright sunlight (compare Gattermann, *loc. cit.*).