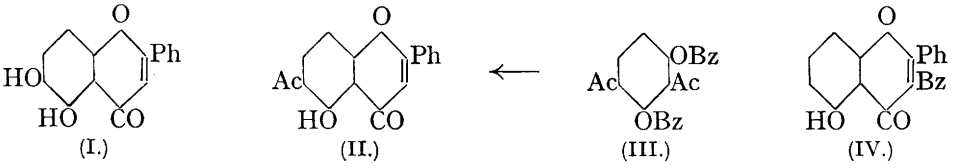
429. *Attempts to Synthesise* 5 : 6-*Dihydroxyflavone* (*Primetin*).

By Wilson Baker.

The author has carried out experiments with the object of preparing derivatives of vicinal tetrahydroxybenzene (J., 1931, 2542; 1932, 2876; this vol., p. 1681), and the synthesis of 5 : 6-dihydroxyflavone (I) (primetin; Hattori and Nagai, *J. Chem. Soc. Japan*, 1930, **51**, 162) provides a closely allied problem, since the substance is a derivative of 2 : 3 : 6-trihydroxyacetophenone. It was hoped to achieve the synthesis of primetin by introducing a hydroxyl group into the appropriate position in either 5- or 6-hydroxyflavone. These experiments were in progress when Sugasawa recorded the synthesis of 5-hydroxyflavone (*Proc. Imp. Acad. Tokyo*, 1934, **10**, 338), though without full experimental details, and in view of this publication the work already done is now described. No account is given of the preparation of 5-hydroxyflavone, since the author's method was apparently the same as that described by Sugasawa, and the properties of the substance and its acetyl derivative agreed completely with Sugasawa's descriptions.



2 : 6-Dihydroxyacetophenone (simplified preparation yielding the substance in 31% yield from resorcinol) was converted into 5-hydroxyflavone by fusion with benzoic anhydride and sodium benzoate, followed by hydrolysis (yield, 17%), and thence into 5-acetoxyflavone. The latter compound yields 5-*hydroxy*-6-*acetylflavone* (II) when treated with aluminium chloride in nitrobenzene, the position of the acetyl group being inferred from the extremely weakly phenolic function of the hydroxyl group, which precludes the assumption of a migration of the acetyl group into position 8. (II) was also obtained (in very small yield) from 2 : 4-*diacetylresorcinol dibenzoate* (III) by boiling with alcohol and potassium acetate (cf. Chavan and Robinson, J., 1933, 368). It was hoped that oxidation of (II) by alkaline hydrogen peroxide would lead directly to primetin, since it has been shown (Baker, Jukes, and Subrahmanyam, this vol., p. 1681) that the Dakin reaction is of general application to hydroxyacetophenones. This expectation, however, was not fulfilled, apparently owing to the abnormally feeble phenolic nature of the 5-hydroxyl group, the substance being unattacked even by hydrogen peroxide in hot alcoholic solution in presence of sodium ethoxide, or by benzoyl peroxide when in the form of its sodium derivative suspended in hot benzene.

The yield of 5-hydroxyflavone obtained by the fusion method from 2 : 6-dihydroxyacetophenone was unsatisfactory, and an alternative route to the compound was sought in the molecular rearrangement of 2 : 6-*dibenzoyloxyacetophenone* in toluene in presence of potassium carbonate (Baker, J., 1933, 1381). The reaction yielded directly 5-hydroxy-3-benzoylflavone (IV) (previously prepared in a different manner by Sugasawa) but in poor yield, and although (IV) may be hydrolysed to 5-hydroxyflavone (conveniently by means of aluminium chloride in nitrobenzene; cf. Baker, this vol., p. 73), the method is inferior to the first. Both benzoyl groups must migrate during the reaction to the ω-carbon atom, whilst in the case of the isomeric 2 : 4-dibenzoyloxyacetophenone only the benzoyl group in the ortho-position migrates (Baker, J., 1933, 1381).

Attempts were made to obtain 6-hydroxy-5-acetylflavone, which should be capable of oxidation to primetin by the Dakin reaction, by molecular rearrangement of 6-acetoxyflavone (Chadha and Venkataraman, J., 1933, 1075). The action of aluminium chloride, either alone or in nitrobenzene, resulted in removal of the acetyl group, a similar behaviour being exhibited by 5-*O*-acetylquinacetophenone.

Further experiments on the synthesis of primetin along other lines are in progress in this laboratory.

Experimental.

2 : 6-*Dihydroxyacetophenone*.—Resorcinol (220 g.) was converted into 7-hydroxy-4-methylcoumarin (230 g.) by the method of Pechmann and Duisberg (*Ber.*, 1883, **16**, 2122), and thence by boiling with twice its weight of acetic anhydride for 1 hour into the acetyl derivative (250 g.). The dry acetyl derivative (40 g.) and powdered aluminium chloride (90 g.) were placed in an oil-bath at 120° and the temperature was raised to 170° during 1½ hours. After the product had been heated with dilute hydrochloric acid, the crystalline 7-hydroxy-8-acetyl-4-methylcoumarin was collected, washed, and heated on the water-bath for 4 hours with a solution of sodium hydroxide (40 g.) in water (200 c.c.) in an atmosphere of coal gas. The solution was cooled and acidified, and the precipitated 2 : 6-dihydroxyacetophenone crystallised from water (1½ l.; charcoal). The total yield from the 250 g. of the acetyl derivative was 95 g. of pale yellow, sandy crystals, m. p. 156—157° (cf. Limaye, *Ber.*, 1932, **65**, 375; Sugasawa, *loc. cit.*). The *dibenzoyl* derivative, obtained by heating 2 : 6-dihydroxyacetophenone (3 g.), pyridine (6 c.c.), and benzoyl chloride (5·6 g.) for 15 minutes on the steam-bath and subsequent treatment with dilute hydrochloric acid, separated from alcohol in blunt-ended prisms, m. p. 105° (Found : C, 73·2; H, 4·5. $C_{22}H_{16}O_5$ requires C, 73·3; H, 4·4%).

5-*Hydroxy*-3-*benzoylflavone* (IV).—2 : 6-Dibenzoyloxyacetophenone (5 g.) in toluene (50 c.c.) was stirred with anhydrous potassium carbonate on the steam-bath for 6 hours. The solids were collected, washed with benzene, dried, stirred into water, again collected, and dried. The product was then extracted with boiling benzene and precipitated therefrom in the crystalline condition (1 g.) by the addition of light petroleum. It separated from alcohol in fine, pale yellow prisms, or from a small quantity of benzene in hexagonal plates, m. p. 177° (Found : C, 77·5; H, 4·5. Calc. for $C_{22}H_{14}O_4$: C, 77·2; H, 4·1%). Sugasawa (*loc. cit.*) describes the substance as yellow prisms, m. p. 173—174°. Its alcoholic solution gives a deep purplish-brown colour with ferric chloride.

2 : 4-*Diacetylresorcinol Dibenzoate* (III).—2 : 4-Diacetylresorcinol (2 g.; Baker, this vol., p. 1684) in pyridine (5 c.c.) was heated with benzoyl chloride (2·9 g.) on the steam-bath for 15 minutes. The product, isolated in the usual way, separated from methyl alcohol in colourless prisms, m. p. 123° (Found : C, 71·8; H, 4·6. $C_{24}H_{18}O_6$ requires C, 71·6; H, 4·5%).

5-*Hydroxy*-6-*acetylflavone* (II).—(A) 5-Acetoxyflavone (0·4 g.), aluminium chloride (0·8 g.), and a few drops of nitrobenzene were heated for 5 minutes at 140°. After treatment with dilute hydrochloric acid and removal of the nitrobenzene in steam, the remaining solid was crystallised twice from alcohol (charcoal). It formed pale yellow, prismatic needles, m. p. 201° (Found : C, 72·7; H, 4·4. $C_{17}H_{12}O_4$ requires C, 72·9; H, 4·3%). (B) 2 : 4-Diacetylresorcinol dibenzoate (1 g.) was boiled with alcohol (25 c.c.) and potassium acetate (5 g.) for 20 hours, and the mixture diluted and made alkaline with sodium hydroxide. The yellow product was crystallised from alcohol, giving 5-hydroxy-6-acetylflavone (26 mg.), which was directly compared (mixed m. p.) with that prepared under (A). The substance gives a brownish-red colour with alcoholic ferric chloride and is insoluble in hot dilute aqueous sodium hydroxide. The sodium derivative is obtained as a yellow powder by the addition of an alcoholic solution of sodium ethoxide to its hot solution in alcohol.

5-O-*Acetylquinacetophenone*.—Powdered quinacetophenone (5 g.), anhydrous sodium acetate (5 g.), and acetic anhydride (15 c.c.) were stirred for 10 minutes, finally at 50°. After the addition of water the product was collected and crystallised from alcohol; it formed small prisms, m. p. 91° (cf. Klinger and Kolvenbach, *Ber.*, 1898, **31**, 1216).

The Dyson Perrins Laboratory, Oxford University. [*Received, October 6th*, 1934.]