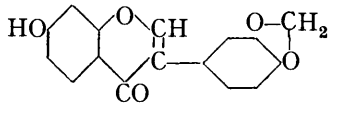
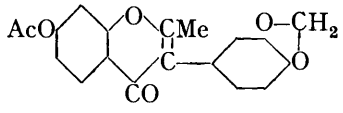
165. *Synthetical Experiments in the* isoFlavone *Group. Part VIII. Note on ψ-Baptigenin.*

By Wilson Baker, Robert Robinson, and N. M. Simpson.

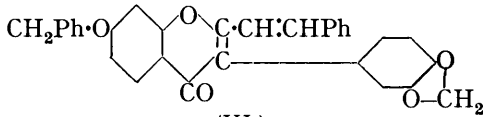
ψ-Baptigenin (I), the aglucone of ψ-baptisin (Gorter, *Arch. Pharm.*, 1897, **235**, 494; Späth and Schmidt, *Monatsh.*, 1929, **53**, 454), has been synthesised by Späth and Lederer (*Ber.*, 1930, **63**, 743), who employed the cyanohydrin method introduced in Part V of this series (Baker, Pollard, and Robinson, J., 1929, 1468). ψ-Baptigenin has also been synthesised by Mahal, Rai, and Venkataraman (J., 1934, 1771), who used a method for the construction of the chromone nucleus (condensation of an *o*-hydroxyacetophenone derivative with ethyl formate in the presence of sodium) which was first employed by Perkin and

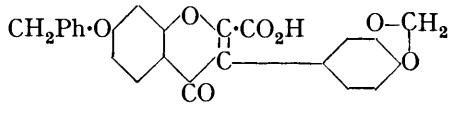
Robinson in the synthesis of anhydrobrazilic acid (J., 1908, **93**, 509). The synthesis herein described (much delayed in publication) is therefore only of interest as an example of the modification of one of the methods available in the series such that phenolic representatives containing groups sensitive to dealkylating agents can be obtained. As in many analogous cases, we have adopted the device of benzylation of the hydroxyl group which must eventually be selectively regenerated from the ether. Protection of this phenolic hydroxyl group is necessary at the stage of the permanganate oxidation (*v. infra*).

(I.) 

 (II.)

ω-Piperonylresacetophenone (ψ-baptigenetin) (Späth and Schmidt, *loc. cit.*) is synthesised by means of the Hoesch reaction and converted by heating with acetic anhydride and sodium acetate into 7-*acetoxy*-3′ : 4′-*methylenedioxy*-2-*methyl*iso*flavone* (II). This substance is hydrolysed, benzylated, and condensed with benzaldehyde, forming 7-*benzyloxy*-3′ : 4′-*methylenedioxy*-2-*styryl*iso*flavone* (III). This is oxidised at the styryl group to 7-*benzyloxy*-3′ : 4′-*methylenedioxy*iso*flavone*-2-*carboxylic acid* (IV). When this acid is heated with acetic and hydrobromic acids, ψ-baptigenin identical with the natural product is obtained; debenzylation and decarboxylation are thus effected in one operation. We are greatly indebted to Prof. E. Späth for the provision of a specimen of the *iso*flavone of natural origin.


(III.)


(IV.)

Experimental.

7-*Acetoxy*-3′ : 4′-*methylenedioxy*-2-*methyl*iso*flavone* (II).—A mixture of ω-piperonylresacetophenone (32 g.), acetic anhydride (110 c.c.), and sodium acetate (28 g.) was refluxed (bath at 180°) for 24 hours, the product mixed with dilute hydrochloric acid, and the solid collected (30 g.). The iso*flavone* crystallised from alcohol in elongated, colourless prisms, m. p. 198·5° after sintering from 195° (Found : C, 67·2; H, 4·2. $C_{19}H_{14}O_6$ requires C, 67·5; H, 4·2%). It is moderately readily soluble in hot alcohol.

7-*Hydroxy*-3′ : 4′-*methylenedioxy*-2-*methyl*iso*flavone*.—This homologue of ψ-baptigenin, readily obtained by the hydrolysis of the foregoing acetate with aqueous alcoholic potassium hydroxide on the steam-bath, crystallised from alcohol in colourless, rectangular plates, m. p. 253—254·5° after sintering at 244° (Found : C, 68·7; H, 4·2. $C_{17}H_{12}O_5$ requires C, 68·9; H, 4·1%), readily soluble in hot alcohol.

Benzyl Ether.—A mixture of homo-ψ-baptigenin (7·5 g.), anhydrous sodium carbonate (7·5 g.), sodium iodide (0·5 g.), and acetone (100 c.c.) was refluxed and stirred for 12 hours while benzyl chloride (4·5 g.) was gradually added. The operation was continued for 24 hours more and the product was then precipitated by the addition of water. The solid was collected, washed with water and alcohol, dried (7 g.), and crystallised from alcohol, being so obtained in long, colourless needles, m. p. 186° (Found : C, 74·2; H, 4·7. $C_{24}H_{18}O_5$ requires C, 74·6; H, 4·7%). The *ether* is sparingly soluble in hot alcohol and readily soluble in warm acetic acid.

7-*Benzyloxy*-3′ : 4′-*methylenedioxy*-2-*styryl*iso*flavone* (III).—Benzaldehyde (2·8 g.) was added to a mixture of benzyloxymethylenedioxymethyl*iso*flavone (7 g.) and alcoholic sodium ethoxide (0·5 g. of sodium in 100 c.c.), which was then refluxed for 1 hour. After a few hours the solid was collected and extracted with hot alcohol (50 c.c.), and the insoluble portion crystallised from acetic acid (yield, 6 g.). Recrystallised from acetic acid, the iso*flavone* formed clusters of pale yellow, microscopic prisms, m. p. 199—200·5° (Found : C, 78·5; H, 4·7. $C_{31}H_{22}O_5$ requires C, 78·5; H, 4·7%), very sparingly soluble in hot alcohol and readily soluble in hot acetic acid.

Condensation of benzyloxymethylenedioxy-2-methyl*iso*flavone with nitrosodimethylaniline could not be effected. An analogous series of experiments with 7 : 4′-dimethoxy-2-methyl*iso*flavone was also fruitless.

*7-Benzyloxy-3′ : 4′-methylenedioxy*iso*flavone-2-carboxylic Acid* (IV).—A solution of potassium permanganate (10 g.) in water (200 c.c.) was fairly quickly added to one of benzyloxymethylenedioxystyryl*iso*flavone (8·3 g.) in pure pyridine (300 c.c.). Complete reduction of the permanganate occurred in 20 minutes and 5% permanganate solution (100 c.c.) was then added slowly with stirring during 2 hours. The liquid was heated to boiling, filtered, and mixed with water and an excess of hydrochloric acid. The precipitate was collected, triturated with 50% acetic acid, collected, and crystallised from 90% acetic acid and then from glacial acetic acid (yield, 3·7 g.). The *acid* crystallises from acetic acid (great disparity between solubilities in hot and cold), in pale ochreous needles and from acetone in nearly colourless, stout, microscopic needles, m. p. 179—181° (Found : C, 69·0; H, 3·9. $C_{24}H_{16}O_7$ requires C, 69·2; H, 3·8%). The acid is readily soluble in aqueous sodium carbonate; it is decarboxylated on heating above its m. p. and the product is *O*-benzyl-ψ-baptigenin, m. p. 167° (cf. Mahal, Rai, and Venkataraman, *loc. cit.*).

ψ-Baptigenin (I).—The foregoing carboxylic acid (0·6 g.) was dissolved in boiling acetic acid (10 c.c.), and hydrobromic acid (10 c.c., *d* 1·5) added. The clear solution was raised to the b. p. and then heated in boiling water for 1 hour. The odour of benzyl bromide became apparent and, as a test showed that the products were much more soluble than had been anticipated, the liquid was diluted with ether and washed with water. The green fluorescence of the aqueous solution was greatly enhanced when it was neutralised with sodium carbonate and a milkiness was produced. Eventually a small sandy precipitate was obtained and this was collected centrifugally and combined with the material obtained from the ethereal solution. The latter was washed with aqueous sodium carbonate until the washings were distinctly alkaline and then once again; acidification of this extract afforded no precipitate. Aqueous sodium hydroxide, however, extracted ψ-baptigenin, which was obtained in a crude condition by acidification of the solutions. The material, sublimed in a high vacuum (bath at 220°) and crystallised from alcohol, formed colourless needles, m. p. 293—294° (decomp.). The m. p. was not depressed by admixture with an authentic specimen of natural origin. Direct comparison of the behaviour towards solvents and reagents disclosed no divergence of properties and the crystalline habit was identical in the case of the two specimens.

DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, March 25th*, 1937.]