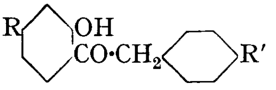
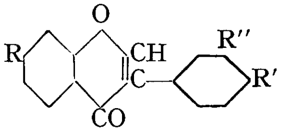
388. *Synthetical Experiments in the Chromone Group. Part XV. A Synthesis of Formononetin, Daidzein, and ψ-Baptigenin.*

By Harbhajan S. Mahal, Harcharan S. Rai, and Krishnasami Venkataraman.

By the method already described (this vol., pp. 513, 1120), namely, the action of sodium on a solution of an *o*-hydroxyphenyl benzyl ketone (I) in ethyl formate at a low temperature, the naturally occurring *iso*flavones formononetin, daidzein, and ψ-baptigenin have now been synthesised in excellent yields (for previous syntheses, see Wessely, Kornfeld, and Lechner, *Ber.*, 1933, **66**, 685; Baker, Robinson, and Simpson, J., 1933, 274; Späth and

(I.)





(II.)

Lederer, *Ber.*, 1930, **63**, 745). The formation of an intermediate oxymethylene ketone, ring closure of which to the *iso*flavone is effected by mineral acid, has been postulated by Späth and Lederer, but it is now clear that the reaction proceeds directly to the *iso*flavone.

EXPERIMENTAL.

2-*Hydroxy*-4-*benzyloxyphenyl* 4-*Methoxybenzyl Ketone*.—A mixture of 2 : 4-dihydroxyphenyl 4-methoxybenzyl ketone (Baker and Eastwood, J., 1929, 1902) (1 g.), benzyl chloride (1 g.), anhydrous potassium carbonate (1·2 g.), and acetone (10 c.c.) was refluxed on the water-bath for 8 hours and poured into water. After 12 hours, the precipitate was collected and crystallised from alcohol, forming colourless needles (0·5 g.), m. p. 103°, which gave a deep red colour with alcoholic ferric chloride (Found : C, 75·7; H, 5·8. $C_{22}H_{20}O_4$ requires C, 75·9; H, 5·8%).

O-*Benzylformononetin* (II; R = O·CH₂Ph, R′ = OMe, R″ = H).—The above ketone (6·3 g.) in ethyl formate (150 c.c.) was gradually added to sodium dust (4 g.) cooled by ice–salt. After 12 hours, the pasty mass was added to ice, ethyl formate distilled, and the aqueous residue extracted repeatedly with ether. The extract was washed with ice-cold caustic soda solution, then with water, dried (magnesium sulphate), and evaporated. The residual oil solidified in contact with alcohol and three successive crystallisations from alcohol, glacial acetic acid, and ethyl acetate gave colourless, thin, elongated, hexagonal plates (3·0 g.), m. p. 182° (Found : C, 76·9; H, 5·1. $C_{23}H_{18}O_4$ requires C, 77·0; H, 5·0%). The pale yellow solution in sulphuric acid exhibited no fluorescence.

Formononetin (II; R = OH, R′ = OMe, R″ = H).—Debenzylation of *O*-benzylformononetin gave colourless triangular plates, m. p. 257° (Found : C, 71·5; H, 4·5. Calc. for $C_{16}H_{12}O_4$: C, 71·6; H, 4·5%). Wessely, Kornfeld, and Lechner (*loc. cit.*) record the same m. p. The substance gave a yellow solution but no fluorescence in sulphuric acid, and no coloration with alcoholic ferric chloride. The acetyl derivative crystallised from alcohol in prismatic needles and colourless elongated rectangular plates, m. p. 170° (Found : C, 69·7; H, 4·8. Calc. for $C_{18}H_{14}O_5$: C, 69·7; H, 4·5%). Hemmelmayr (*Monatsh.*, 1902, **23**, 133) gives m. p. 164—165° for the acetyl derivative prepared from natural ononin.

Daidzein (II; R, R′ = OH, R″ = H).—A mixture of acetylformononetin (0·8 g.), acetic anhydride (16 c.c.), and hydriodic acid (*d* 1·7; 8 c.c.) was heated at 140° for 2 hours, cooled, and poured into saturated sodium bisulphite solution (100 c.c.). The product crystallised from alcohol in long, colourless, prismatic needles (0·5 g.), m. p. 322° after darkening above 310° (Found : C, 70·7; H, 3·6. Calc. for $C_{15}H_{10}O_4$: C, 70·9; H, 3·9%). Daidzein from natural daidzin of *Soja hispida* (Walz, *Annalen*, 1931, **489**, 118) melts at 315—320°, the m. p. also obtained by Baker, Robinson, and Simpson (*loc. cit.*) for their synthetic daidzein. Wessely, Kornfeld, and Lechner record m. p. 323°. The colour reactions with sulphuric acid and with ferric chloride were similar to those of formononetin. The alcoholic solution turned pale orange on treatment with magnesium and hydrochloric acid. The diacetyl derivative crystallised from alcohol in colourless needles and rhombohedral plates, m. p. 187° after sintering at 184° (Found : C, 67·3; H, 4·1. Calc. for $C_{19}H_{14}O_6$: C, 67·4; H, 4·1%). The diacetyldaidzein of Walz melted at 182°. The m. p.'s of synthetic flavones and flavonols are frequently higher than those of the natural substances (Robinson and Venkataraman, J., 1926, 2346).

2-*Hydroxy*-4-*benzyloxyphenyl* 3 : 4-*Methylenedioxybenzyl Ketone*.—ψ-Baptigenetin (Späth and Schmidt, *Monatsh.*, 1929, **53**, 454) (12 g.), benzyl chloride (40 g.), fused potassium carbonate (22 g.), and acetone (120 c.c.) were heated on the water-bath for 8 hours, the acetone recovered, and the residue steam-distilled to remove benzyl chloride. One crystallisation of the product from alcohol gave colourless leaflets (7 g.), m. p. 94° after sintering at 86° (Found : C, 72·5; H, 4·9. $C_{22}H_{18}O_5$ requires C, 72·9; H, 4·9%), which developed a deep red colour with alcoholic ferric chloride.

O-*Benzyl*-ψ-*baptigenin* (II; R = O·CH₂Ph, R′R″ = O₂CH₂).—The above ketone (3 g.) in ethyl formate (50 c.c.) was treated with sodium dust (1·5 g.) (see *O*-benzylformononetin).

The yellow amorphous solid (2·9 g.) obtained after ice treatment was washed with water and crystallised from alcohol–acetic acid and from alcohol, giving colourless prismatic needles, m. p. 168° (Found : C, 74·0; H, 3·9. $C_{23}H_{16}O_5$ requires C, 74·1; H, 4·3%). The crystals were coloured deep brown by sulphuric acid and the pale brown solution exhibited a weak violet fluorescence.

ψ-Baptigenin.—Debenzylation of the benzyl ether (1·6 g.) and two crystallisations of the product from alcohol gave colourless microscopic needles (0·8 g.), m. p. 292—293° (Späth and Lederer; 298—299° in a vacuum) (Found : C, 68·0; H, 3·4. Calc. for $C_{16}H_{10}O_5$: C, 68·1; H, 3·5%). Further crystallisation did not raise the m. p. The substance darkened rapidly above 288° and melted to a dark red liquid. Gorter (*Arch. Pharm.*, 1897, **235**, 494) cites 303—304° as the m. p. of ψ-baptigenin from ψ-baptisin of *Baptisia tinctoria*. The crystals were coloured green by sulphuric acid and the pale yellow solution did not fluoresce. Ferric chloride imparted no colour to the alcoholic solution. The acetyl derivative crystallised from alcohol in small curved needles, m. p. 176° (Gorter, *loc. cit.*, gives 173°) (Found : C, 66·7; H, 3·9. Calc. for $C_{18}H_{12}O_6$: C, 66·6; H, 3·7%).

FORMAN CHRISTIAN COLLEGE, LAHORE.

[*Received, July 23rd,* 1934.]