58. *Synthetical Experiments in the Chromone Group. Part XVIII. Demethylation with Aluminium Chloride.*

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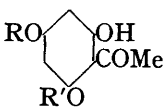
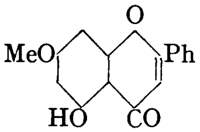
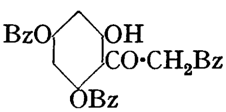
The Friedel–Crafts reaction between phloroglucinol trimethyl ether and acetyl chloride, at a low temperature and in the absence of a solvent, leads to phloracetophenone trimethyl ether; when this is heated with aluminium chloride, the dimethyl ether is formed (Kostanecki and Tambor, *Ber.*, 1899, **32**, 2260). The reaction in benzene or chlorobenzene solution leads, however, to a phloracetophenone monomethyl ether having the properties of one of the two compounds obtained by Sonn and Bülow (*Ber.*, 1925, **58**, 1691) by a Hoesch reaction between phloroglucinol monomethyl ether and acetonitrile; we have confirmed the constitution (I; R = H, R′ = Me) assigned to it by Sonn and Bülow by preparing a *monobenzyl* ether (I; R = CH_2Ph, R′ = Me), since hydroxyl in the *o*-position to a keto-group cannot be benzylated (Gulati, Seth, and Venkataraman, J., 1934, 1765). The monobenzyl ether condenses smoothly with aldehydes to form chalkones (see also Shinoda and Sato, *J. Pharm. Soc. Japan*, 1928, **48**, 220).



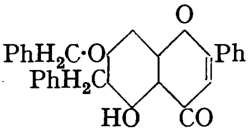
(I.)



(III.)



(IV.)



(V.)

Since the 5-hydroxyl in a flavone resembles the *o*-hydroxyl of a ketone in its resistance to facile methylation, it appeared probable that the ease with which an *o*-methoxy-ketone is demethylated would find a parallel in 5-methoxyflavones. This is so, the action of aluminium chloride on chrysin dimethyl ether (II) in nitrobenzene solution causing partial demethylation to tectochrysin (III). Heating (II) with solid aluminium chloride leads to a mixture of chrysin and tectochrysin, but (II) is the only product of the action of aluminium chloride on 2 : 4 : 6-trimethoxybenzoylacetophenone in nitrobenzene and subsequent treatment with alcoholic sulphuric acid. By the regulated action of hydriodic acid on 2 : 4 : 6-trimethoxybenzoylacetophenone, tectochrysin or chrysin or a mixture of both may be obtained, but apparently not (II).

Since Tasaki (*Acta Phytochim.*, 1925, **2**, 119) gives 115—117° as the m. p. of (II), whereas we find 143°, we have confirmed the constitution of our compound by its synthesis from 2-*benzoyloxy*-4 : 6-*dimethoxyacetophenone* and sodamide (Mahal and Venkataraman, J., 1934, 1767; Bhalla, Mahal, and Venkataraman, J., 1935, 868). Although the action of benzoic anhydride on phloracetophenone leads ordinarily to chrysin (Robinson and Venkataraman, J., 1926, 2344), one experiment, after methylation of the product, gave, in addition to (II), its 3-*benzoyl* derivative; treatment of the latter with aluminium chloride gave tectochrysin. The possibility of 3-acylation during the Robinson reaction has already been indicated (Anderson, *Canadian J. Research*, 1932, **7**, 285; Chadha and Venkataraman, J., 1933, 1074). Another by-product of the condensation of phloracetophenone and benzoic anhydride has been formulated as (IV) (compare Baker, J., 1933, 1381).

The benzylation of chrysin under various conditions gave only 5-hydroxy-7-benzyloxy-6-benzylflavone (V) with the usual properties of a 5-hydroxyflavone.

EXPERIMENTAL.

2 : 4 : 6-*Trimethoxyacetophenone*.—In place of ferric chloride (Kostanecki and Tambor, *loc. cit.*), the condensation between phloroglucinol trimethyl ether (25 g.) and acetyl chloride (26 g.), at − 5° to − 10°, is more conveniently carried out with aluminium chloride (13 g.), added during 3 hours. After 3 hours, ice is added, and the product (19 g.), m. p. 110°, isolated in the usual manner.

2 : 4-*Dihydroxy*-6-*methoxyacetophenone* (I; R = H, R′ = Me).—When a mixture of 2 : 4 : 6-trimethoxyacetophenone (1 g.), aluminium chloride (1 g.), and chlorobenzene (10 c.c.) was refluxed for 1 hour, the solvent removed by steam-distillation, and the residue cooled, cream-coloured needles (from alcohol) were obtained (0·3 g.), m. p. 203° (Sonn and Bülow, *loc. cit.*, give m. p. 205—207°) (Found : C, 59·2; H, 5·5. Calc. for $C_9H_{10}O_4$: C, 59·3; H, 5·5%). The alcoholic solution gave a deep red colour with ferric chloride.

2-*Hydroxy*-4-*benzyloxy*-6-*methoxyacetophenone* (I; R = CH_2Ph, R′ = Me).—Benzylation of the preceding ketone as in the case of resacetophenone (Gulati, Seth, and Venkataraman, *loc. cit.*) and crystallisation from aqueous alcohol gave colourless needles, m. p. 72° (Found : C, 70·5; H, 5·9. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9%).

Chrysin Dimethyl Ether.—(a) The reaction between chrysin (0·2 g.) and methyl sulphate (1 c.c.) in acetone (10 c.c.) and 20% caustic soda solution (2·5 c.c.), first in the cold and then on the water-bath, gave chrysin dimethyl ether (0·1 g.), which formed colourless needles, m. p. 143°, from dilute alcohol (Found : C, 72·1; H, 4·9. Calc. for $C_{17}H_{14}O_4$: C, 72·3; H, 4·9%).

(b) 2-*Benzoyloxy*-4 : 6-*dimethoxyacetophenone* was prepared by heating 2-hydroxy-4 : 6-dimethoxyacetophenone (1 g.) with benzoyl chloride (1 g.) and pyridine (2 g.) for 15 minutes. Treatment with hydrochloric acid and ether extraction gave colourless needles, m. p. 91° (from alcohol) (Found : C, 68·1; H, 5·3. $C_{17}H_{16}O_5$ requires C, 68·0; H, 5·3%). The benzoate (1 g.) was shaken with sodamide (1 g.) and ether (15 c.c.) and the deep chocolate-brown solid was collected, washed with ether, and treated with ice and acetic acid. The diketone separated as an oil and was converted into the chromone by boiling with 20% alcoholic sulphuric acid (20 c.c.) for 2 hours. Crystallisation from alcohol gave colourless needles (0·4 g.), m. p. 143°, identical with (II).

(c) To a solution of aluminium chloride (1·4 g.) in nitrobenzene (10 c.c.), 2 : 4 : 6-trimethoxybenzoylacetophenone (0·7 g.) was added. After 12 hours, the mixture was treated with ice, and the nitrobenzene removed by steam-distillation. The cooled residue was partly crystalline and contained 2-hydroxy-4 : 6-dimethoxydibenzoylmethane as indicated by the ferric chloride coloration. It was collected, washed with dilute hydrochloric acid, boiled for 2 hours with 20% alcoholic sulphuric acid (20 c.c.), and poured into water. One crystallisation of the product from alcohol gave (II), m. p. 143° (0·5 g.).

Tectochrysin (III).—(a) A solution of aluminium chloride (0·2 g.) and (II) (0·2 g.) in nitrobenzene (5 c.c.) was heated on the water-bath for 1 hour, cooled, and treated with dilute hydrochloric acid and the product was collected after steam-distillation of the solvent. Crystallisation from alcohol gave colourless needles (0·12 g.), m. p. 165° (Found : C, 71·5; H, 4·7. Calc. for $C_{16}H_{12}O_4$: C, 71·6; H, 4·5%). The ferric chloride coloration was deep red. After (II) (0·5 g.) had been heated with a like amount of aluminium chloride at 115° for 30 minutes, treatment with ice–hydrochloric acid and fractional crystallisation from aqueous alcohol gave tectochrysin (0·08 g.) and chrysin (0·15 g.), m. p. 275°. (b) 2 : 4 : 6-Trimethoxybenzoylacetophenone (0·5 g.) was heated with hydriodic acid (*d* 1·7; 5 c.c.) and acetic anhydride (5 c.c.) for 5 minutes and poured into sodium bisulphite solution. Crystallisation of the product from alcohol gave (III) (0·2 g.), m. p. 165°. When the heating was prolonged to 20 minutes, a minute amount of (III) and 0·2 g. of chrysin were obtained.

3-*Benzoylchrysin Dimethyl Ether.*—The crude product (2 g.), in one experiment, of the Robinson reaction with phloracetophenone and benzoic anhydride, obtained by precipitation with carbon dioxide, was treated with acetone (20 c.c.), 10% caustic soda solution (35 c.c.), and methyl sulphate (25 g.) with mechanical stirring during 2 hours. Dilution with water and two crystallisations from acetone gave yellow needles (0·3 g.), m. p. 212° (Found : C, 74·8; H, 4·8. $C_{24}H_{18}O_5$ requires C, 74·6; H, 4·7%). Evaporation of the mother-liquors and recrystallisation of the residue from alcohol gave chrysin dimethyl ether (0·6 g.), m. p. 143°.

In a second experiment, phloracetophenone (5 g.) gave chrysin (2·2 g.), which was twice recrystallised from alcohol. When the mother-liquors were concentrated to small bulk and cooled, cream-coloured needles (0·5 g.), m. p. 157°, of 2-*hydroxy*-4 : 6-*dibenzoyloxy*-ω-*benzoylacetophenone* (IV) separated (Found : C, 72·2; H, 4·4. $C_{29}H_{20}O_7$ requires C, 72·5; H, 4·2%). When the substance was hydrolysed with alkali, the odour of acetophenone became perceptible. The alcoholic solution gave a deep red colour with ferric chloride. Dissolution in sulphuric acid and treatment with ice led to a mixture, which, however, after hydrolysis with 10% alcoholic caustic potash, precipitation with carbon dioxide, and crystallisation from alcohol, gave chrysin, m. p. 275°.

5-*Hydroxy*-7-*benzyloxy*-6-*benzylflavone* (V).—(a) Benzylation of chrysin in the known manner (Gulati, Seth, and Venkataraman, *loc. cit.*) with benzyl chloride, acetone, and potassium carbonate, and crystallisation of the product from acetone, gave yellow needles, m. p. 205° (Found : C, 80·3; H, 5·4. $C_{29}H_{22}O_4$ requires C, 80·2; H, 5·1%). (b) To a solution of caustic potash (0·25 g.) in alcohol, chrysin (0·5 g.) and benzyl bromide (0·4 g.) were added. After being shaken for a few minutes, the mixture was warmed on the water-bath for ½ hour. The orange precipitate was collected and washed with dilute hydrochloric acid, and the product crystallised from acetone, giving pale yellow needles (0·3 g.), m. p 205°, identical with the benzyl ether obtained in (a).

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[*Received, October 22nd,* 1935.]