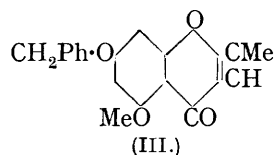
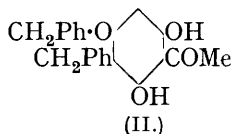
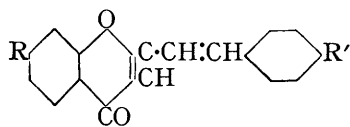


386. *Synthetical Experiments in the Chromone Group. Part XIII.*
Hydroxy-2-styrylchromones.

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IN order to utilise the reaction of Heilbron, Barnes, and Morton (J., 1923, **123**, 2535; Cheema, Gulati, and Venkataraman, J., 1932, 925) for the synthesis of polyhydroxy-2-styrylchromones (I) (Robinson and Shinoda, J., 1925, **127**, 1973), the need for avoiding demethylation was clear at the outset. The action of benzyl chloride on resacetophenone led exclusively to the 4-benzyl ether; we have found this observation of value for the preparation of chalkones and isoflavones involving the use of a ketone in which the *o*-hydroxyl alone is unprotected, the 4-benzyl ether being more accessible than the methyl. From resacetophenone 4-benzyl ether, through the usual stages of the Kostanecki reaction and final debenzylation with hydrobromic acid, 7-hydroxy-2-styrylchromone (I; R = OH, R' = H) and 7 : 4'-dihydroxy-2-styrylchromone (I; R, R' = OH) were prepared.

Benzylation of phloracetophenone yielded a dibenzyl derivative, formulated as (II), since it did not undergo a smooth chalkone or β -diketone condensation. The action of



benzyl chloride on 5 : 7-dihydroxy-2-methylchromone under all conditions gave the 7-benzyl ether, which did not react with benzaldehyde; neither would its 5-*O*-acetyl

derivative nor 5 : 7-diacetoxy-2-methylchromone undergo the styrylchromone condensation. Methylation gave (III), from which the corresponding styrylchromone could not be prepared. The project was to demethylate the latter by means of aluminium chloride (compare Bharadwaj and Venkataraman, *Current Science*, 1933, 2, 50).

Contrary to Sen and Ghosh (J., 1920, 117, 61), no phloracetophenone was isolated from the products of the action of acetic acid and zinc chloride on phloroglucinol; the addition of acetic anhydride to the Nencki mixture (Badhwar and Venkataraman, "Organic Syntheses," 14, 40) did not alter the result.

EXPERIMENTAL.

7-Methoxy-2-styrylchromone (I; R = OMe, R' = H).—7-Methoxy-2-methylchromone (Kostanecki and Rozycki, *Ber.*, 1901, 34, 102) is more conveniently obtained by heating 2-hydroxy-4-methoxyacetophenone (Adams, *J. Amer. Chem. Soc.*, 1919, 41, 260) with sodium and ethyl acetate as in the preparation of 7 : 8-dimethoxy-2-methylchromone (Cheema, Gulati, and Venkataraman, *loc. cit.*). The *styrylchromone* crystallised from alcohol in colourless prisms, m. p. 189—190° (Found : C, 77.7; H, 5.2. C₁₈H₁₄O₃ requires C, 77.7; H, 5.0%).

7 : 4'-*Dimethoxy-2-styrylchromone* (I; R, R' = OMe) formed pale yellow needles, m. p. 144° (Found : C, 73.9; H, 5.5. C₁₉H₁₆O₄ requires C, 74.0; H, 5.2%).

2-Hydroxy-4-benzyloxyacetophenone.—In the preparation of resacetophenone by the Nencki method it is an advantage to use acetic anhydride. A mixture of resacetophenone (30 g.), anhydrous potassium carbonate (54 g.), benzyl chloride (98 g.), and acetone (200 c.c.) was refluxed for 8 hours, the acetone recovered, and the residue steam-distilled to remove benzyl chloride. Two crystallisations of the product from alcohol gave colourless leaflets (25 g.), m. p. 111° (Found : C, 74.3; H, 5.6. C₁₅H₁₄O₃ requires C, 74.4; H, 5.7%). The alcoholic solution is coloured deep brown by ferric chloride.

7-Benzyloxy-2-methylchromone was prepared from the above ketone (9 g.) in the manner described for 7 : 8-dimethoxy-2-methylchromone (Cheema, Gulati, and Venkataraman, *loc. cit.*). Two crystallisations from alcohol gave stout colourless needles (3.5 g.), m. p. 137° (Found : C, 76.3; H, 5.3. C₁₇H₁₄O₃ requires C, 76.6; H, 5.2%).

7-Benzyloxy-2-styrylchromone (I; R = CH₂Ph·O, R' = H) formed pale yellow, flat prisms from alcohol and glacial acetic acid, m. p. 161° (Found : C, 80.9; H, 5.1. C₂₄H₁₈O₃ requires C, 81.3; H, 5.1%).

7-Hydroxy-2-styrylchromone (I; R = OH, R' = H).—The ether was not debenzylated by prolonged boiling of the acetic acid solution with concentrated hydrochloric acid, but it was when it was boiled (1.4 g.) in glacial acetic acid (100 c.c.) with hydrobromic acid saturated at 0° (25 c.c.) for 1 hour. The product, collected on cooling, crystallised from alcohol in pale yellow needles (0.6 g.), m. p. 239° (Found : C, 77.3; H, 4.8. C₁₇H₁₂O₃ requires C, 77.4; H, 4.7%).

7 : 4'-*Dibenzyloxy-2-styrylchromone* (I; R, R' = CH₂Ph·O).—Prepared from 7-benzyloxy-2-methylchromone and *p*-benzyloxybenzaldehyde (Rosenmund, *Ber.*, 1913, 46, 1039), this formed pale yellow prisms, m. p. 176°, from alcohol-acetic acid (Found : C, 80.7; H, 5.2. C₃₁H₂₄O₄ requires C, 80.9; H, 5.2%). When debenzylated as in the previous case, it gave 7 : 4'-*dihydroxy-2-styrylchromone* (I; R, R' = OH), which crystallised from alcohol-acetic acid in long, yellow, silky needles, m. p. 332° (Found : C, 73.0; H, 4.1. C₁₇H₁₂O₄ requires C, 72.8; H, 4.2%). This substance is coloured orange by concentrated sulphuric acid and the yellow solution has a bright green fluorescence. The alcoholic solution gives no colour with ferric chloride. The *diacetyl* derivative crystallised from alcohol in colourless needles, m. p. 183° (Found : C, 69.2; H, 4.4. C₂₁H₁₆O₆ requires C, 69.2; H, 4.4%).

Phloracetophenone.—Prepared by the Hoesch method, this crystallised from hot water in very pale cream-coloured needles, m. p. 219° (Found : loss on heating at 120° for 3 hours, 9.5. C₈H₈O₄·H₂O requires H₂O, 9.6%. Found in the dried material : C, 57.3; H, 4.6. Calc. for C₈H₈O₄ : C, 57.1; H, 4.7%). The m. p. after dehydration was 219° (compare Sen and Ghosh, *loc. cit.*). The 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol in bright red needles, m. p. 280° (decomp.) (Found : N, 15.8. C₁₄H₁₂O₇N₄ requires N, 16.1%). The triacetyl derivative, prepared by the Chattaway method, crystallised from alcohol in colourless elongated prisms, m. p. 103° (compare Sonn and Bülow, *Ber.*, 1925, 58, 1691) (Found : C, 57.0; H, 4.6. Calc. : C, 57.1; H, 4.8%).

The product obtained by the action of acetic acid and zinc chloride on phloroglucinol under various conditions, including those described by Sen and Ghosh (*loc. cit.*), crystallised from very dilute alcohol in yellow needles, melting and decomposing above 290° (Found : C, 63.8; H, 4.2).

$C_{16}H_{12}O_6$ requires C, 64.0; H, 4.0%). According to Sen and Ghosh, 5 : 7 : 2' : 4' : 6'-penta-hydroxy-2-phenyl-4-methylenebenzopyran separates from hydrochloric acid as yellow needles with H_2O ; we were unable to prepare a crystalline acetyl derivative. The product obtained by alkaline hydrolysis had the physical properties described by Sen and Ghosh, but it did not yield a dinitrophenylhydrazone.

C-Benzylphloracetophenone 4-Benzyl Ether (II).—Phloracetophenone (2 g.), benzyl chloride (9.5 g.), potassium carbonate (5 g.), and acetone (20 c.c.) were heated on the water-bath for 8 hours; the mixture was then poured into water. The oily product was dissolved in ether, washed with 1% aqueous caustic soda and with water, recovered, and crystallised from alcohol, forming colourless rectangular plates (0.2 g.), m. p. 121° (Found : C, 75.4; H, 5.9. $C_{22}H_{20}O_4$ requires C, 75.8; H, 5.7%), which gave a deep red colour with alcoholic ferric chloride.

5 : 7-Dihydroxy-3-acetyl-2-methylchromone and 5 : 7-Dihydroxy-2-methylchromone.—The substance obtained by heating phloracetophenone (10 g.), sodium acetate (10 g.), and acetic anhydride (60 g.) and pouring the product into water (2 l.) was washed and crystallised from alcohol. After two crystallisations, a substance (A) was obtained in colourless needles (5.1 g.), m. p. 131° (Found : C, 60.4; H, 4.7. $C_{16}H_{14}O_7$ requires C, 60.3; H, 4.4%). The mother-liquors, cooled after the separation of (A), deposited a substance (1.1 g.), melting indefinitely above 110° ; dilution with a limited amount of water gave a second impure product (3.5 g.), melting above 120° over a long range. After its removal much water was added and, after 12 hours, the precipitate was collected and crystallised from aqueous alcohol; the colourless needles (B) (0.5 g.), m. p. 252° , were identified as 5 : 7-dihydroxy-3-acetyl-2-methylchromone (Found : C, 61.4; H, 4.3. $C_{12}H_{10}O_5$ requires C, 61.5; H, 4.3%). The diacetyl derivative of (B) had m. p. and mixed m. p. (with A) 131° .

When (A) (3 g.) was boiled with concentrated hydrochloric acid and water (1 : 1) (40 c.c.) for 45 minutes, and the product poured into water, a precipitate was obtained which, after two crystallisations from aqueous alcohol, formed colourless needles (1.1 g.), m. p. and mixed m. p. (with B) 252° .

Treatment of (B) (3.5 g.) with boiling 10% sodium carbonate solution during 2 hours gave a clear solution. The product obtained on acidification crystallised from alcohol in colourless needles (1.3 g.), m. p. 279° (Jochum and Kostanecki, *Ber.*, 1904, **37**, 2099, give 290°), and were identified as 5 : 7-dihydroxy-2-methylchromone (Found : C, 62.2; H, 3.9. Calc. : C, 62.5; H, 4.1%). The acetyl derivative melted at 148° (Jochum and Kostanecki, 149°) (Found : C, 60.9; H, 4.4. Calc. : C, 60.8; H, 4.3%). The preceding results differ from those recorded by Canter, Curd, and Robertson (*J.*, 1931, 1258; see also Shinoda, *J. Pharm. Soc. Japan*, 1928, **48**, 35).

5-Hydroxy-7-benzyloxy-2-methylchromone.—Benzylation of 5 : 7-dihydroxy-2-methylchromone (5.0 g.) and crystallisation of the product from alcohol gave cream-coloured needles (3.1 g.), m. p. 148° (Found : C, 71.9; H, 5.3. $C_{17}H_{14}O_4$ requires C, 72.3; H, 4.9%), which gave a dirty brown colour with alcoholic ferric chloride.

5-Methoxy-7-benzyloxy-2-methylchromone (III).—Methyl sulphate (60 c.c.) and 20% aqueous caustic soda (60 c.c.) were added alternately in small portions to a stirred solution of 5-hydroxy-7-benzyloxy-2-methylchromone (4 g.) in acetone (100 c.c.). Dilution of the pale orange liquid and crystallisation of the precipitate from alcohol gave colourless needles (2.7 g.), m. p. 156° (Found : C, 72.6; H, 5.5. $C_{18}H_{16}O_4$ requires C, 72.9; H, 5.4%). The alcoholic solution developed no colour with ferric chloride.

Interaction of (III) and *p*-benzyloxybenzaldehyde gave a substance which crystallised in stout, bright yellow prisms from alcohol-acetic acid, m. p. 181° (Found : C, 82.9; H, 6.2. $C_{32}H_{26}O_5$ requires C, 78.4; H, 5.3%).