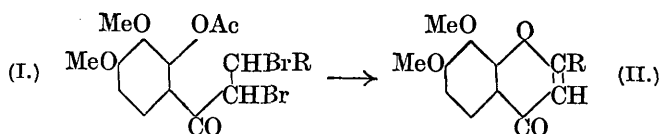


**142.** *Synthetical Experiments in the Chromone Group.*  
*Part VII. Synthesis of 7:8:4'-Trihydroxy-,*  
*7:8:3':4'-Tetrahydroxy-, and 7:8:3':4':5'-,*  
*5:7:3':4':5'-, and 3:7:3':4':5'-Pentahydroxy-*  
*flavones.*

By ISHWAR CHAND BADHWAR, KANWAR SINGH KANG, and  
 KRISHNASAMI VENKATARAMAN.

GALLACETOPHENONE gave poor yields of dark-coloured material when it was heated at 180—185° with anisic, veratric, or trimethylgallic anhydride and the appropriate sodium salt. The methods of von Kostanecki were therefore employed. 2'-Acetoxy-4:3':4'-trimethoxychalkone (von Kostanecki and Schreiber, *Ber.*, 1905, **38**, 2749) was converted into the *dibromide* (I; R = *p*-C<sub>6</sub>H<sub>4</sub>·OMe), which, on treatment with alcoholic potash, gave 7:8:4'-*trimethoxyflavone* (II; R = *p*-C<sub>6</sub>H<sub>4</sub>·OMe). Demethylation with acetic anhydride and hydriodic acid yielded the *trihydroxyflavone*. 7:8:3':4'-*Tetramethoxyflavone* [II; R = C<sub>6</sub>H<sub>3</sub>(OMe)<sub>2</sub> (3:4)] and the corresponding *tetrahydroxyflavone* were similarly prepared from the *dibromide* of 2'-acetoxy-3:4:3':4'-tetramethoxychalkone (von Kostanecki and Rudse, *ibid.*, p. 936). As the interaction of alcoholic potash with 2'-acetoxychalkone dibromides may produce benzylidenecoumaranones, 7:8:3':4'-tetrahydroxyflavone has also been prepared by the prolonged treatment of 2:3:4:3':4'-*pentamethoxy-ω*-benzoylacetophenone with hydriodic acid. 7:8:3':4':5'-

*Pentahydroxyflavone* was made by the demethylation and dehydration of 2 : 3 : 4 : 3' : 4' : 5'-hexamethoxy- $\omega$ -benzoylacetophenone.



For comparison with the last-mentioned flavone in regard to the dyeing and other properties, 5 : 7 : 3' : 4' : 5'- and 3 : 7 : 3' : 4' : 5'-*pentahydroxyflavones* were synthesised by the Robinson reaction, trimethylgallic anhydride and sodium trimethylgallate being heated with phloracetophenone and  $\omega$ -methoxyresacetophenone respectively, and the resulting *tri*- and *tetra*-methyl ethers demethylated in the usual manner.

The colour reactions of the five polyhydroxyflavones have been set forth in detail, so that, in conjunction with our knowledge of the flavones synthesised by von Kostanecki and by Robinson, they may prove helpful in the ready recognition of new flavone pigments isolated from natural sources. From this point of view the synthesis of other polyhydroxyflavones is in progress.

As was expected (compare J., 1929, 2219), 7 : 8 : 3' : 4' : 5'-*penta*-hydroxyflavone proved to be a more powerful dye than the two isomerides. The shades it produced on mordanted wool were similar to, but darker than, those produced by 7 : 8 : 3' : 4'-*tetra*-hydroxyflavone, which in turn were darker than those produced by 7 : 8 : 4'-*tri*hydroxyflavone. The same gradation was observed in regard to other properties, such as the colorations with ferric chloride, with sodium amalgam, and with magnesium and hydrochloric acid.

#### EXPERIMENTAL.

*Gallacetophenone*.—The following method is more convenient than the original process of Nencki (*Ber.*, 1884, 27, 2737) or the modification of Crabtree and Robinson (J., 1922, 121, 1038). To a solution of fused zinc chloride (28 g.) in glacial acetic acid (40 g.) and acetic anhydride (40 g.) at 135–140° (oil-bath), pyrogallol (50 g.) was quickly added, and the whole heated for 45 minutes at 145–150° with occasional shaking. The excess of acetic acid and acetic anhydride was distilled off under reduced pressure, the semi-solid mass poured into water (300 c.c.), and, after cooling, the thick cake collected and crystallised from sulphurous acid; 34 g. of straw-coloured needles, m. p. 168°, were obtained.

7 : 8 : 4'-*Trimethoxyflavone* (II; R = *p*-C<sub>6</sub>H<sub>4</sub>·OMe).—2'-Acetoxy-4 : 3' : 4'-*trimethoxychalkone* was treated with a 7.25% solution of

bromine in carbon disulphide (25 c.c.), and after 12 hours the solvent was removed. The residual *dibromide* (I; R = *p*-C<sub>6</sub>H<sub>4</sub>·OMe) crystallised from benzene–light petroleum in yellow irregular plates, m. p. 133° (Found: Br, 30.9. C<sub>20</sub>H<sub>20</sub>O<sub>6</sub>Br<sub>2</sub> requires Br, 31.0%). A suspension of the dibromide (5 g.) in alcohol (20 c.c.) was shaken with 40% aqueous caustic potash (4.3 g.); the *trimethoxyflavone*, which separated after some time, crystallised from alcohol in yellow woolly needles (1.8 g.), m. p. 189–190° (Found: C, 69.1; H, 5.1. C<sub>18</sub>H<sub>16</sub>O<sub>5</sub> requires C, 69.2; H, 5.1%).

7 : 8 : 4'-*Trihydroxyflavone*.—The trimethyl ether (1.3 g.) was suspended in acetic anhydride (25 c.c.), hydriodic acid (*d* 1.7; 25 c.c.) slowly added, and the mixture heated for 2 hours (oil-bath at 140–145°) and poured into an ice-cold saturated solution of sodium bisulphite. The *trihydroxyflavone* crystallised from aqueous alcohol in yellow needles (0.3 g.), m. p. 299–300° (decomp.), after sintering at 279° (Found: C, 66.7; H, 3.9. C<sub>15</sub>H<sub>10</sub>O<sub>5</sub> requires C, 66.7; H, 3.7%).

The *triacetate*, prepared by boiling the trihydroxyflavone with excess of acetic anhydride and a drop of pyridine during 2 hours and pouring the solution into water, formed white woolly needles, m. p. 183° (Found: C, 63.2; H, 4.4. C<sub>21</sub>H<sub>16</sub>O<sub>8</sub> requires C, 63.6; H, 4.1%).

7 : 8 : 3' : 4'-*Tetramethoxyflavone* [II; R = C<sub>6</sub>H<sub>3</sub>(OMe)<sub>2</sub> (3 : 4)].—The *dibromide* of 2'-acetoxy-3 : 4 : 3' : 4'-tetramethoxychalkone crystallised from benzene–ligroin in yellow irregular plates, m. p. 118° (Found: Br, 28.9. C<sub>21</sub>H<sub>22</sub>O<sub>7</sub>Br<sub>2</sub> requires Br, 29.3%). The treatment with alkali already described converted it into the *tetramethoxyflavone*, which crystallised from alcohol in bright yellow needles (2.3 g.), m. p. 198–199° (Found: C, 66.8; H, 5.4. C<sub>19</sub>H<sub>18</sub>O<sub>6</sub> requires C, 66.7; H, 5.3%).

7 : 8 : 3' : 4'-*Tetrahydroxyflavone*.—(a) Demethylation of the ether (1.8 g.) gave the *tetrahydroxyflavone*, which crystallised from dilute alcohol (charcoal) in yellow needles (0.4 g.), m. p. 309–310° (decomp.) (Found: C, 63.0; H, 3.6. C<sub>15</sub>H<sub>10</sub>O<sub>6</sub> requires C, 62.9; H, 3.5%).

(b) The following β-diketone (0.3 g.) was demethylated with hydriodic acid (*d* 1.7; 10 c.c.) at 140–145° during 3 hours. The product obtained by pouring the reaction mixture into cold saturated sodium bisulphite solution crystallised from dilute alcohol in yellow needles, m. p. 309–310° (decomp.), not lowered by admixture with the substance obtained in (a).

The *tetra-acetate* crystallised from alcohol in white woolly needles, m. p. 218° (Found: C, 61.0; H, 4.2. C<sub>23</sub>H<sub>18</sub>O<sub>10</sub> requires C, 60.8; H, 4.0%).

2 : 3 : 4 : 3' : 4'-*Pentamethoxy- $\omega$ -benzoylacetophenone*.—Ethyl veratrate (6 g.) and gallacetophenone trimethyl ether (2 g.) were melted together, finely divided sodium (0.3 g.) added, and the mixture heated at 120° for 2 hours; the semi-solid mass was then poured into ice-cold dilute acetic acid and extracted with ether, and the extract twice shaken with 10% caustic soda solution. From the alkaline solution, carbon dioxide precipitated the *pentamethoxybenzoylacetophenone*, which crystallised from dilute alcohol in pale yellow needles (0.5 g.), m. p. 105° (Found : C, 64.0; H, 6.1.  $C_{20}H_{22}O_7$  required C, 64.2; H, 5.9%). It gave a dark green coloration with alcoholic ferric chloride.

2 : 3 : 4 : 3' : 4' : 5'-*Hexamethoxy- $\omega$ -benzoylacetophenone*, similarly prepared from gallacetophenone trimethyl ether (7.7 g.), ethyl trimethylgallate (26.4 g.), and sodium (1.2 g.), crystallised from dilute alcohol in pale yellow needles (10 g.), m. p. 125° (Found : C, 62.7; H, 6.3.  $C_{21}H_{24}O_8$  requires C, 62.4; H, 5.9%).

7 : 8 : 3' : 4' : 5'-*Pentahydroxyflavone*, obtained by heating the preceding ketone (9 g.) with hydriodic acid (*d* 1.7; freshly distilled over red phosphorus; 150 c.c.) and acetic anhydride (50 c.c.), and repeatedly crystallised from dilute alcohol, formed yellow needles (1.2 g.), m. p. above 345° (Found : C, 59.8; H, 3.5.  $C_{15}H_{10}O_7$  requires C, 59.6; H, 3.3%).

7 : 8 : 3' : 4' : 5'-*Penta-acetoxylflavone* crystallised from alcohol in white woolly needles, m. p. 263° (Found : C, 58.9; H, 4.0.  $C_{25}H_{20}O_{12}$  requires C, 58.6; H, 3.9%).

7-*Hydroxy-3 : 3' : 4' : 5'-tetramethoxyflavone*.—An intimate mixture of  $\omega$ -methoxyresacetophenone (6 g.), trimethylgallate anhydride (70 g.), and potassium trimethylgallate (12 g.) was heated (oil-bath at 180—185°) for 6 hours. The product was cooled, powdered, and then refluxed in alcohol (150 c.c.) for 30 minutes while caustic potash (17.5 g. in 20 c.c. of water) was gradually added and the mixture shaken. After a further 30 minutes' heating, the alcohol was removed under reduced pressure, and the filtered liquid diluted with much water and saturated with carbon dioxide. The precipitate was washed and dried (5.0 g.).

A portion was crystallised from alcohol, giving long white needles, m. p. 246°, of 7-*hydroxy-3 : 3' : 4' : 5'-tetramethoxyflavone* (Found : C, 63.6; H, 5.1.  $C_{19}H_{18}O_7$  requires C, 63.6; H, 5.0%), moderately easily soluble in methyl and ethyl alcohol, readily soluble in glacial acetic acid, sparingly soluble in ether and benzene, and insoluble in light petroleum. The *acetyl* derivative crystallised from methyl alcohol in long, colourless, woolly needles, m. p. 146° (Found : C, 63.4; H, 5.1.  $C_{21}H_{20}O_8$  requires C, 63.0; H, 5.0%).

3 : 7 : 3' : 4' : 5'-*Pentahydroxyflavone*.—The remainder (2 g.) of

the crude tetramethoxyflavone was treated with a boiling mixture of acetic anhydride (30 c.c.) and hydriodic acid ( $d$  1.7; 30 c.c.) during 2 hours, the cooled liquid filtered, and the dark red residue boiled in glacial acetic acid (10 c.c.) and water (10 c.c.) for 5 minutes (charcoal). The filtered solution deposited pale yellow needles, m. p. 310—312° (decomp.) after darkening at 304—305°. The mother-liquor of the hydriodide of the flavone was poured into ice-cold sodium bisulphite solution; more of the *pentahydroxyflavone* was obtained (total yield, 1.0 g.) (Found: C, 59.5; H, 3.4.  $C_{15}H_{10}O_7$  requires C, 59.6; H, 3.3%). The substance resembles its tetramethyl ether in solubility.

3 : 7 : 3' : 4' : 5'-*Pentaacetoxyflavone* crystallised from dilute acetic acid in long, almost colourless needles, m. p. 175—176° (Found: C, 59.0; H, 4.3.  $C_{25}H_{20}O_{12}$  requires C, 58.6; H, 3.9%).

5 : 7-*Dihydroxy-3' : 4' : 5'-trimethoxyflavone*.—The chromone synthesis was carried out as in the previous case with phloracetophenone (8 g.), trimethylgallic anhydride (80 g.), and potassium trimethylgallate (16 g.). Hydrolysis was effected with 10% alcoholic potash (175 c.c.). The brown powder (6.5 g.) precipitated from the alkaline solution by carbon dioxide was dissolved in boiling glacial acetic acid; addition of a few drops of concentrated sulphuric acid produced a deep red colour. The mixture was diluted with an equal volume of boiling water, and the whole boiled for a few minutes (charcoal). The filtered liquid deposited yellow woolly needles, m. p. 264—265° (Found: C, 63.0; H, 5.0.  $C_{18}H_{16}O_7$  requires C, 62.8; H, 4.6%), soluble in glacial acetic acid, sparingly soluble in cold methyl and ethyl alcohol, and moderately readily soluble in the hot solvents. The yellow solution in sulphuric acid has a violet fluorescence, and an alcoholic solution gives a greenish-brown colour with ferric chloride.

5 : 7 : 3' : 4' : 5'-*Pentahydroxyflavone*.—Demethylation of the trimethyl ether in the usual way gave a reddish-brown product, which, crystallised from dilute acetic acid (and a few drops of sulphuric acid) in the way described above, formed brownish-yellow needles, decomp. about 310° (Found: C, 56.2; H, 4.1. Calc. for  $C_{15}H_{10}O_7, H_2O$ : C, 56.3; H, 3.8%. Compare Bargellini and Monti, *Gazzetta*, 1915, 45, 65).

The dyeing properties of the three pentahydroxyflavones were studied on mordanted wool.

	5 : 7 : 3' : 4' : 5'.	3 : 7 : 3' : 4' : 5'.	7 : 8 : 3' : 4' : 5'.
Aluminium	Dull yellow	Lemon-yellow	Greenish-yellow
Chromium	Biscuit	Raw sienna	Grey
Iron	Slate-grey	Brownish-grey	Dark grey
Tin	Yellow	Orange	Madder-brown

*Colour Reactions.*—Colorations were given by the polyhydroxy-flavones with the following reagents : (a) sulphuric acid ; (b) glacial acetic acid and a drop of sulphuric acid ; (c) aqueous sodium hydroxide ; (d) alcoholic ferric chloride ; (e) potassium acetate ; (f) lead acetate ; (g) sodium amalgam ; (h) magnesium and hydrochloric acid.

7 : 8 : 4'-*Trihydroxyflavone* : (a) pale yellow, non-fluorescent ; (b) bright yellow ; (c) orange ; (d) dark green, becoming brownish-violet on addition of a drop of aqueous ammonia ; (e) bright yellow ; (f) gelatinous yellow precipitate ; (g) cloudy pale orange, becoming greenish-orange ; (h) bright orange-red. 7 : 8 : 3' : 4'-*Tetrahydroxyflavone* : (a), (b), (d), (e) as above ; (c) orange-red ; (f) gelatinous orange precipitate ; (g) pale yellow, becoming dirty orange ; (h) bright orange. 7 : 8 : 3' : 4' : 5'-*Pentahydroxyflavone* : (a), (d), (e) as above ; (b) bright yellow colour, then brownish-orange crystalline precipitate ; (c) deep orange-red ; (f) gelatinous, deep orange precipitate ; (g) greenish-yellow, becoming dark brown ; (h) deep orange-red coloration, green fluorescence. 7-*Hydroxy-3 : 3' : 4' : 5'-tetramethoxyflavone* : (a) yellow solution, green fluorescence ; (c) pale greenish-yellow ; (d) faint green ; (g) pale green ; (h) rose-red. 3 : 7 : 3' : 4' : 5'-*Pentahydroxyflavone* : (a) pale yellow solution, faint green fluorescence ; (c) pale magenta ; (d) dirty brown ; (f) pale orange precipitate ; (g) intense green, slowly becoming light brown ; (h) pale red. 5 : 7 : 3' : 4' : 5'-*Pentahydroxyflavone* : (a) pale yellow solution, green fluorescence ; (c) orange-red ; (d) dark greenish-brown ; (f) brown precipitate ; (g) orange-red ; (h) yellow.

FORMAN CHRISTIAN COLLEGE,  
LAHORE.

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