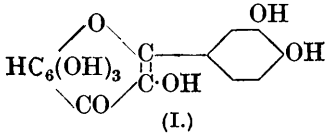
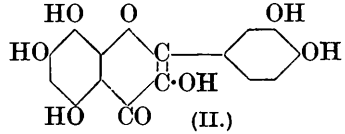
XIV.—*Anthoxanthins. Part X. The Synthesis of Gossypetin and of Quercetagetin.*

By Wilson Baker, Ryuzaburo Nodzu, and Robert Robinson.

Quercetagetin, a colouring matter of the flowers of the African marigold. *Tagetes patula*, was isolated by Latour and Magnier de la Source (*Bull. Soc. chim.*, 1877, **28**, 337) and closely examined by A. G. Perkin (P., 1902, **18**, 75; J., 1913, **103**, 209); the isomeric gossypetin was isolated by Perkin in 1899 from the flowers of the Indian cotton plant, *Gossypium herbaceum* (J., **75**, 826), and a more complete study was published in 1913 (Perkin, J., **103**, 650). Perkin was able to show that the structures of both substances must conform to the formula (I), but it was not possible to determine the situation of the hydroxyl groups in the tetrahydroxybenzene nuclei. The probability that these flavonols are nearly related to quercetin and are indeed hydroxyquercetins (II and III) was commented on, but this attractive view had to be abandoned in the case of one at least of the two colouring matters on account of the synthesis of

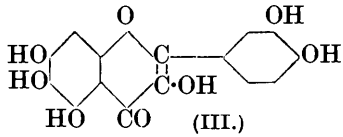


(I.)



(II.)

(II) by Nierenstein (J., 1917, **111**, 872), who employed an apparently unambiguous method. The hydroxyquercetin so obtained was stated to be identical with that previously derived from quercetone

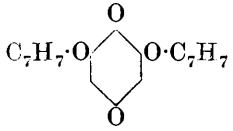


(III.)

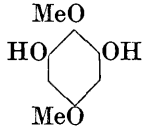
by reduction (Nierenstein and Wheldale, *Ber.*, 1911, **44**, 3487) and comparisons of derivatives confirmed this identity, but it was quite different from gossypetin and from quercetagetin. A remarkable property of this hydroxyquercetin was its ability to yield *iso*-quercetone on oxidation by means of *p*-benzoquinone (Nierenstein, J., 1915. **107**, 869); thus two isomeric quinones corresponded to a single polyhydric phenol. Our results confirm the work of Perkin in all details, but are irreconcilable with that of Nierenstein (the reference is to the paper of J., 1917, **111**, 872), since we find (*a*) that gossypetin has the formula (II); (*b*) that both gossypetin and quercetagetin are derivatives of 1 : 3 : 4 : 5-tetrahydroxybenzene

(hydroxyphloroglucinol), and that consequently (*c*) quercetagetin must be represented by the formula (III).

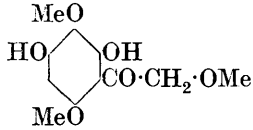
The synthesis of gossypetin was effected in the following manner. The *tribenzyl* ether of pyrogallol, $C_6H_3(O\cdot CH_2Ph)_3$ (IV), was oxidised by means of nitric acid to 2 : 6-*dibenzyloxy*-p-*benzoquinone* (V), this was reduced to the *quinol*, $C_6H_2(OH)_2(O\cdot CH_2Ph)_2$ (VI), which was methylated with formation of 2 : 6-*dibenzyloxy*-1 : 4-*dimethoxybenzene*, $C_6H_2(OMe)_2(O\cdot CH_2Ph)_2$ (VII). Benzyl ethers



(V.)



(VIII.)



(IX.)

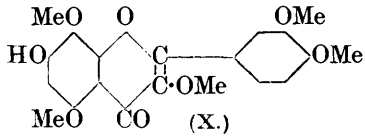
being much more readily hydrolysed than methyl ethers, 2 : 5-*dimethoxyresorcinol* (VIII) was obtained by the action of a mixture of hydrochloric and acetic acids on (VII) at about 65°.

The monomethyl ether of iretol described by de Laire and Tiemann (*Ber.*, 1893, **26**, 2034) should be represented by one of the formulæ (VIII) and (XII). The latter is the 4 : 5-dimethoxyresorcinol of Chapman, Perkin, and Robinson (J., 1927, 3015) and this substance is certainly different from iretol monomethyl ether. We have not, however, been able to satisfy ourselves that the phenol (VIII) is identical with the iretol derivative, and this matter requires further investigation; the present position is explained in the experimental section.

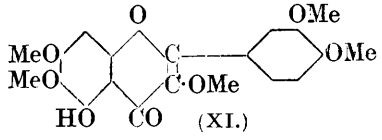
An application of the Hoesch reaction, using methoxyacetonitrile (compare Slater and Stephen, J., 1920, **117**, 309), led to the formation of a *trimethoxyresacetophenone* (IX) and the veratroylation of this ketone gave a *hydroxypentamethoxyflavone* (X). The hexahydroxyflavone obtained on demethylation in the usual manner was proved to be identical with gossypetin (II). The various stages of this synthesis can proceed in one direction only and consequently the structure of the final product is established. For example, the oxidation product of tribenzyloxybenzene might have been 2 : 3-dibenzyloxy-*p*-benzoquinone; this, however, is definitely excluded by the success of the flavone synthesis, which proves that there is a hydroxyl group in the *o*-position to carbonyl in the dihydroxytrimethoxyacetophenone of the series. In contrast with quercetagetin pentamethyl ether (XI) (see below) the substance (X) is readily soluble in aqueous alkalis and exhibits a very weak ferric chloride reaction.

The synthesis of quercetagetin proceeds from 4 : 5-dimethoxyresorcinol (XII) by a similar series of reactions and since the final

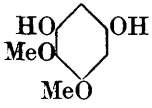
product, a hexahydroxyflavone, is different from gossypetin it must have the constitution (III), the only alternative to (II) under the conditions. This substance proved to be identical with quercetagetin.



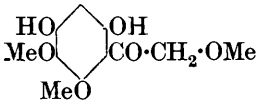
(X.)



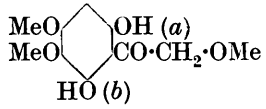
(XI.)



(XII.)



(XIII.)



(XIV.)

The preparation of a dihydroxytrimethoxyacetophenone from 4 : 5-dimethoxyresorcinol and methoxyacetonitrile was carried out by Chapman, Perkin, and Robinson (*loc. cit.*) and the formula (XIII) was attributed to the ketone on grounds of analogy. Had this view been correct, the hydroxypentamethoxyflavone derived from the substance by veratroylation would have been a 7-hydroxyflavone. The product actually obtained had, however, the characteristics of a 5-hydroxyflavone; it gave a ferric chloride reaction and the phenolic function was very feebly exhibited. The properties of the substance were indeed identical with those of Perkin's quercetagetin pentamethyl ether (*loc. cit.*) obtained by the methylation of quercetagetin and it is well known that it is the hydroxyl in position 5 that offers the greatest resistance to methylating agents. These considerations prove that the methoxyacetyl derivative of 4 : 5-dimethoxyresorcinol has the constitution (XIV) and the orientation phenomenon thus brought to light is a very interesting one. The pyrone ring formed in the course of the veratroylation of (XIV) might be closed in the direction (*a*) or (*b*) in the formula; but it is evidently the hydroxyl (*a*) that is involved, because otherwise the flavonol obtained on demethylation would be gossypetin. This is in agreement with Bargellini's view of the direction of ring-closure occurring in his syntheses of baicalein and scutellarein (*Gazzetta*, 1915, **45**, i, 69; 1919, **49**, ii, 47), where the alternatives are analogous, the orientation of groups in the benzene nucleus being identical in all the cases under consideration.

We are greatly indebted to Professor A. G. Perkin, F.R.S., who has kindly sent us specimens of hexa-acetylgossypetin, gossypetin, and quercetagetin which have rendered possible a comparison of the natural and the synthetic products. All the analyses recorded

were carried out by micro-methods, the majority of them by Dr. Ing. A. Schoeller of Berlin-Schmargendorf; substances with many methoxyl groups were burned slowly at a specially high temperature.

EXPERIMENTAL.

1 : 2 : 3-*Tribenzyloxybenzene* (IV).—The following are the best conditions yet found for the benzylation of pyrogallol. A mixture of pyrogallol (50 g.), anhydrous potassium carbonate (240 g.), and dry acetone (300 c.c.) was refluxed in an atmosphere of hydrogen for 30 hours, benzyl chloride (210 g.) being gradually introduced; the mixture was then kept under the same conditions for a further 10 hours. The portion of the reaction product that was insoluble in water was dissolved in ether and washed with aqueous sodium hydroxide, and the solvent and unchanged benzyl chloride were removed by distillation, finally in steam. The residue was crystallised from alcohol (yield, 50 g.) and on recrystallisation the substance was obtained in colourless needles, m. p. 70° (Found: C, 82·4; H, 6·2. $C_{27}H_{24}O_3$ requires C, 81·8; H, 6·0%). It is readily soluble in benzene, ether, acetone, and chloroform and is moderately readily soluble in alcohol, light petroleum, and acetic acid.

2 : 6-*Dibenzyloxy*-p-*benzoquinone* (V).—Nitric acid (40 c.c.; *d* 1·19) was added to a solution of 1 : 2 : 3-tribenzyloxybenzene (80 g.) in acetic acid (800 c.c.) at 40°. After the mixture had been kept for 4 hours at room temperature, the liquid was filtered; the solid residue (15 g.), which consisted chiefly of 5-*nitro*-1 : 2 : 3-*tribenzyloxybenzene* (oriented by analogy only), crystallised from acetone in long colourless needles, m. p. 139° (Found: N, 3·2. $C_{29}H_{23}O_5N$ requires N, 3·2%). A second quantity of nitric acid (40 c.c.; *d* 1·19) was added to the reddish-brown filtrate and on the following day the *quinone* that had separated was isolated (30 g.); addition of much water precipitated a further small quantity of the same substance. This crystallised from acetone in long yellow needles, m. p. 201—202° (Found: C, 75·0; H, 5·3. $C_{20}H_{16}O_4$ requires C, 75·0; H, 5·0%), sparingly soluble in most organic solvents but readily soluble in chloroform.

2 : 6-*Dibenzyloxyquinol* (VI).—Sulphuric acid (60 c.c. of 25%) was gradually added during 3 hours to a gently boiling, well-stirred mixture of dibenzyloxybenzoquinone (40 g.), alcohol (400 c.c.), and zinc dust (80 g.). When the yellow quinone had disappeared, the liquid was filtered hot. Addition of dilute sulphurous acid to the filtrate caused the separation of lustrous pearly-white plates (40 g.). The *quinol*, after recrystallisation by the addition of aqueous sulphurous acid to an alcoholic solution, had m. p. 116—117°

(Found : C, 74·5; H, 5·7. $C_{20}H_{18}O_4$ requires C, 74·5; H, 5·6%). It is readily soluble in alcohol, acetone, ether, and chloroform, moderately readily soluble in hot water, and sparingly soluble in benzene, light petroleum, and cold water.

Reoxidation to the quinone occurs readily in the presence of moisture and is accelerated by alkalis; the crystals develop a fine green coloration in contact with concentrated aqueous potassium hydroxide. Ferric chloride oxidises the quinol very rapidly and smoothly with formation of the quinone.

2 : 6-*Dibenzyloxy*-1 : 4-*dimethoxybenzene* (VII).—Aqueous sodium hydroxide (12 g. of a solution of 60 g. of sodium hydroxide in 150 c.c. of water) and then methyl sulphate (16 g.) were added to a vigorously agitated mixture of 2 : 6-dibenzyloxyquinol (12 g.) and alcohol (120 c.c. of 90%) contained in a vessel from which air was excluded by hydrogen. A further quantity (7 g.) of the sodium hydroxide solution was introduced in the course of 9 hours in order to keep the solution weakly alkaline; the temperature was then raised to about 45° for 1 hour and, after 12 hours, water (50 c.c.) was added and the deposited crystals were collected (12 g.). The substance separated from acetone in massive colourless crystals, m. p. 82—83° (Found : C, 75·5; H, 6·3. $C_{22}H_{22}O_4$ requires C, 75·4; H, 6·3%). It is readily soluble in most organic solvents but is sparingly soluble in cold alcohol and boiling light petroleum.

2 : 5-*Dimethoxyresorcinol* (VIII).—A mixture of 2 : 6-dibenzyloxy-1 : 4-dimethoxybenzene (10 g.), acetic acid (70 c.c.), and hydrochloric acid (30 c.c.; *d* 1·16) was kept at 65—70° for an hour. A large volume of water was then added, the solution was evaporated to a syrup under diminished pressure and extracted with hot water, and the extract was evaporated in a vacuum desiccator over sulphuric acid and sodium hydroxide. Brownish-yellow prisms (3 g.) separated; at the same time a small amount of a different crystalline substance, m. p. 180°, was deposited, but this was not further examined. The main product crystallised from water in faintly brownish-yellow prisms, m. p. 61—62°, and would doubtless be colourless when pure (Found in air-dried material : C, 46·8; H, 6·9; MeO, 29·1; loss at 56° in a high vacuum, 17·7. $C_8H_{10}O_4,2H_2O$ requires C, 46·6; H, 6·9; 2MeO, 30·1; $2H_2O$, 17·5%). 2 : 5-*Dimethoxyresorcinol* is moderately readily soluble in cold water and is readily soluble in most organic solvents; it imparts a purple colour to a pine shaving moistened with concentrated hydrochloric acid. The material dried at 56° in a vacuum had m. p. 86—88°; the hydrated specimen crystallised from benzene unchanged (m. p. 61—62°), but the anhydrous one, on solution in hot benzene and cooling, gave crystals, m. p. 182°. These gave no ferric chloride

reaction, whereas an aqueous solution of the crystals of m. p. 61—62° developed a weak bluish-violet coloration on the addition of ferric chloride.

The benzene mother-liquor from the crystals of m. p. 182° was concentrated to a syrup and on the addition of a little water this gave prisms, m. p. 61—62°.

Iretol monomethyl ether is stated to crystallise from benzene in an anhydrous form, m. p. 87° (de Laire and Tiemann, *loc. cit.*), and to give a deep blue coloration with ferric chloride.

The question of the constitution of this phenol remains an open one and further investigations are in progress.

2 : 4-*Dihydroxy*-ω : 3 : 6-*trimethoxyacetophenone* (IX).—A solution of anhydrous 2 : 5-dimethoxyresorcinol (3·1 g.) and methoxyacetonitrile (2·0 g.) in dry ether (30 c.c.) was saturated with hydrogen chloride and kept over-night at room temperature. The ketimine hydrochloride formed a faintly yellow crust and a further quantity was precipitated in a semi-solid condition on the addition of dry ether. The salt was washed with ether and dissolved in water (50 c.c.), and the solution heated on the steam-bath for 1 hour. On cooling, the crude *ketone* crystallised readily (yield, 3·6 g.); it separated from hot water in long colourless needles, m. p. 150—151° (Found: C, 54·7; H, 6·0; MeO, 38·3. $C_{11}H_{14}O_6$ requires C, 54·5; H, 5·8; 3MeO, 38·4%). Alcoholic ferric chloride produced an intense bluish-brown coloration.

7-*Hydroxy*-3 : 5 : 8 : 3′ : 4′-*pentamethoxyflavone* (O-*Pentamethylgossypetin*) (X).—A mixture of 2 : 4-dihydroxy-ω : 3 : 6-trimethoxyacetophenone (2 g.), potassium veratrate (7 g.), and veratric anhydride (20 g.) was heated (oil-bath at 175—180°) for 4—5 hours, and the melt dissolved in boiling alcohol (150 c.c.). Hydrolysis was effected by means of potassium hydroxide (6·5 g.) dissolved in water (15 c.c.), which was gradually added during 20 minutes to the boiling liquid. The alcohol was removed by distillation under diminished pressure and the residue was dissolved in water and saturated with carbon dioxide; very little of the flavonol was precipitated. The filtrate from this small amount was acidified with hydrochloric acid, the veratric acid that separated was rapidly collected, and the filtrate kept for some hours. Woolly needles were deposited, and more of the same substance was obtained from the mother-liquor after concentration under diminished pressure. The substance, after precipitation from very dilute potassium hydroxide solution by means of carbon dioxide and keeping for a few hours (yield, 0·7 g.), crystallised from aqueous acetic acid in long faintly greenish-yellow needles, m. p. 250—253°, and was then sufficiently pure for most purposes. On recrystallisation from aqueous alcohol, yellow

needles, m. p. 253—254°, were obtained (Found in material dried at 120°: C, 61·9; H, 5·4; MeO, 39·1. $C_{20}H_{20}O_8$ requires C, 61·8; H, 5·2; 5MeO, 40·0%).

The flavonol derivative dissolves in concentrated hydrochloric acid and in aqueous alkalis to yellow solutions; it develops no characteristic coloration with ferric chloride in alcoholic solution.

3 : 5 : 7 : 8 : 3′ : 4′-*Hexahydroxyflavone* (*Gossypetin*) (II).—The foregoing pentamethyl ether was boiled with an excess of hydriodic acid (*d* 1·7) for 35 minutes. On addition of dilute sulphurous acid, a yellow solid separated, which crystallised from aqueous alcohol in yellow microscopic needles, m. p. 310—314° (difficult to observe owing to decomposition and blackening of the tube) (Found in material dried at 150°: C, 56·3; H, 3·6. Calc. for $C_{15}H_{10}O_8$: C, 56·6; H, 3·2%).

The substance is readily soluble in cold alcohol and very sparingly soluble in water and gives a bright yellow solution in sulphuric acid. In these respects and also in its behaviour towards ferric chloride and lead acetate in alcoholic solution, the synthetical material agrees exactly with gossypetin (m. p. 311—313°). A specimen of the hexa-acetyl derivative of gossypetin kindly provided by Professor A. G. Perkin was hydrolysed for a comparison of the highly characteristic reactions in alkaline solutions.* When very small quantities were employed it was difficult to reproduce the recorded colour changes because it was hard to avoid the use of too much alkali and the reaction was too rapid. The most trustworthy procedure involved the use of buffered solutions and we have employed those prepared from the "Universal Buffer Mixture" supplied by the British Drug Houses Limited. The natural and the synthetic specimen exhibited an identical behaviour. The flavonol is not dissolved by the solution of p_H 6·2 nor by that of p_H 6·8, but in the latter case reaction proceeds slowly and the solid gradually disappears, the solution becoming pale reddish-brown. Gossypetin dissolves in a solution of p_H 8·0 and the yellow solution slowly changes through brownish-green, brownish-purple and grey-purple to a weak grey; it never exhibits a blue colour.

Oxidation is more rapid in more alkaline solutions and at p_H 8·6 the more characteristic changes become apparent. The most convenient reagent is, however, that of p_H 9·8; this dissolves the flavonol to a yellow solution, and on agitation with air the colour changes to green and then to a fine pure blue, the latter being relatively stable. The further change to brown (and finally loss of colour intensity) is very slow but is more rapid in the more alkaline

* Subsequently the reactions of a different specimen of natural gossypetin were observed with the same results.

solutions; at p_H 11·0 the yellow solution very quickly becomes green and blue and the intensity rapidly diminishes, the liquid becoming slate-blue, grey, and finally almost colourless. When the blue solutions are acidified they become red. The preparation of gossypetone by oxidation of the synthetic gossypetin with *p*-benzoquinone in alcoholic solution was also carried out on a very small scale; the substance separated in the way described by Perkin (*loc. cit.*) and had the recorded appearance and properties.

O-*Hexa-acetyl Derivatives.*—The synthetic gossypetin was acetylated by means of boiling acetic anhydride and a drop of pyridine during 2 hours; the product was isolated and treated again in the same way. The substance then crystallised from alcohol in sparingly soluble, colourless needles; these melted at 229—230°, and at the same temperature when mixed with a specimen of *O*-hexa-acetylgossypetin obtained by re-acetylation and crystallisation of the material of natural origin.

3 : 5 : 7 : 8 : 3′ : 4′-*Hexamethoxyflavone* (O-*Hexamethylgossypetin*).—The hydroxypentamethoxyflavone described above was methylated by means of potassium hydroxide and methyl sulphate in aqueous-alcoholic solution; the derivative crystallised from alcohol in glistening colourless needles, m. p. 170—172° (as stated by Perkin for *O*-hexamethylgossypetin) (Found: C, 62·5; H, 5·7. Calc. for $C_{21}H_{22}O_8$: C, 62·7; H, 5·5%). In this case two analyses by ordinary methods gave low values for carbon. The substance dissolves in concentrated hydrochloric acid to an intensely yellow solution; the colour is partly discharged on addition of water and wholly when, on keeping, the substance separates in very long, slender, colourless needles.

2 : 6-*Dihydroxy*-ω : 3 : 4-*trimethoxyacetophenone* (XIV).—This was prepared essentially as described by Chapman, Perkin, and Robinson (J., 1927, 3015); the ketimine was best precipitated by the addition of 100 c.c. of a mixture of equal volumes of ether and ligroin, and was hydrolysed by heating with water (20 c.c.) and concentrated hydrochloric acid (2 c.c.) on the steam-bath for 2 hours. After treatment with charcoal and filtration, the ketone separated on cooling.

5-*Hydroxy*-3 : 6 : 7 : 3′ : 4′-*pentamethoxyflavone* (O-*Pentamethylquercetagetin*) (XI).—A mixture of the above ketone (1·0 g.), veratric anhydride (15 g.), and sodium veratrate (6 g.) was heated at 180—190° for 8 hours. The resulting resin was warmed with much dilute sodium carbonate solution, and the collected product was dissolved in hot alcohol (100 c.c.) and hydrolysed by boiling for 15 minutes with potassium hydroxide (6 g.) dissolved in a little water. The solution, when diluted with water (100 c.c.) and saturated with

carbon dioxide, deposited yellow crystals; the separation was completed by the further addition of water (400 c.c.). Crystallisation from alcohol (charcoal) gave thin, lustrous, pale yellow needles (1 g.), m. p. 158—159°. Further crystallisation from methyl alcohol raised the melting point to 159—160° (Found : C, 62·0; H, 5·3. $C_{20}H_{20}O_8$ requires C, 61·9; H, 5·2%). This O-*pentamethylquercetagetin* is almost insoluble in cold, aqueous alkaline solutions, but dissolves on warming or on the addition of a little alcohol. Its solution in alcohol develops a brownish colour with a trace of ferric chloride and an intense, dull olive-green with an excess. In concentrated sulphuric acid it gives an intensely yellow solution, which becomes cherry-red on addition of a trace of nitric acid.

O-*Hexamethylquercetagetin.*—*O*-Pentamethylquercetagetin (0·3 g.) was methylated in acetone solution at about 60° by shaking with aqueous sodium hydroxide and methyl sulphate. The initial bright yellow colour faded, and the alkaline solution was then heated for a short time on the steam-bath. Addition of water caused the separation of colourless needles, which were washed and crystallised from 50% alcohol. The lustrous prismatic needles (0·3 g.) obtained consisted of the α-form, m. p. 141—143°. On crystallisation from acetone, larger, somewhat irregular prisms of the pure α-form were deposited, m. p. 143—144° (Found : C, 62·7; H, 5·5. Calc. for $C_{21}H_{22}O_8$: C, 62·7; H, 5·5%). This specimen again crystallised from acetone in the α form. A different specimen, however, separated at once from acetone in tiny, thick, rhomboidal prisms (hexagonal in outline when crystallised very slowly) of the β-form, m. p. 157°. The molten α-form at about 145°, when seeded with the solid β-form, at once solidified to a mass of the β-form, m. p. 157°. The melting point of an intimate mixture of the two forms was also 157°. *O*-Hexamethylquercetagetin dissolves in concentrated hydrochloric acid with production of an intensely yellow colour, which fades on dilution and disappears on neutralisation.

Dimorphic forms of *O*-hexamethylquercetagetin of the same melting points have been described by A. G. Perkin (*loc. cit.*) in the case of the ether prepared from natural quercetagetin, and the recurrence of these observations in the case of our synthetic specimens affords very strong evidence that the natural and the synthetic product are indeed identical.

There is a theoretical possibility that some gossypetin derivative might accompany the synthetic quercetagetin methyl ethers. The following observation suggests that this may be so.

The methylation of a specimen of *O*-pentamethylquercetagetin obtained by working up its alcoholic mother-liquors gave the hexamethyl ether as very fine needles from acetone. After slight sinter-

ing, these gave a turbid, incompletely fluid melt at 157°, which cleared suddenly and became perfectly fluid at 170° (gossypetin hexamethyl ether has m. p. 170—172°). The small amount of material at our disposal did not allow us to follow up this interesting point.

3 : 5 : 6 : 7 : 3′ : 4′-*Hexahydroxyflavone* (*Quereetagetin*) (III).—When *O*-pentamethylquercetagetin (0·5 g.) was treated with freshly distilled hydriodic acid (5 c.c.; *d* 1·7), solution first took place and then orange crystals of a hydriodide separated. The mixture was heated for 1 hour at 140° (bright orange-red crystals of a hydriodide separating), water (100 c.c.) added, and the whole heated on the steam-bath for 15 minutes. The light yellow product was crystallised twice from 50% acetic acid (charcoal) and obtained in tiny, pale yellow, prismatic needles which melted when rapidly heated at about 316° with much decomposition and darkening (Found in material dried at 160°: C, 56·4; H, 3·2. Calc. for $C_{15}H_{10}O_8$: C, 56·6; H, 3·2%). When crystallised from 50% acetic acid, the substance contains water of crystallisation (Found: H_2O, 9·9. $C_{15}H_{10}O_8,2H_2O$ requires H_2O, 10·2%).

This synthetic quercetagetin was slightly soluble in boiling water, and the cooled air-free solution, treated with a drop of exceedingly dilute, air-free sodium hydroxide solution, became at first pure yellow, but, on shaking, rapidly turned bright olive-green and then deep yellowish-brown. With stronger alkali the green colour was not observed. The oxidation of quercetagetin in buffered alkaline solution is much less facile than that of gossypetin. At p_H 9·8 the yellow solution slowly becomes bright green, brown-green, and brown; at p_H 10·4 the same changes occur more rapidly; and a solution of p_H 11·0 is at first yellow, rapidly becomes green and then yellow-brown, duller brown, and brownish-red. A dilute alcoholic solution treated with ferric chloride gave an intense, dull olive-green coloration. The addition of an alcoholic solution of lead acetate threw down a bright orange-red precipitate which slowly became more yellow. A solution in alcohol treated with a drop of alcoholic potassium hydroxide gave a yellow precipitate which slowly (or quickly on the addition of more alkali) turned green and finally brownish-black, and the addition of a trace of sodium amalgam gave greenish flocks. This last reaction is characteristic of scutellarein, baicalein (Bargellini, *Gazzetta*, 1919, **49**, ii, 47) and irigenol (Baker, J., 1928, 1030), all of which contain hydroxyl groups in positions 5, 6, and 7.

The *hexa-acetyl* derivative was obtained by boiling the synthetic quercetagetin with acetic anhydride and a few drops of pyridine for 1½ hours. It slowly separated from the filtered solution after the addition of alcohol, and crystallised from acetic acid–alcohol in

bunches of colourless needles, m. p. 210° with slight previous softening (Found : C, 56·8; H, 3·8. $C_{27}H_{22}O_{14}$ requires C, 56·9; H, 3·8%).

A specimen of the derivative similarly prepared from quercetagetin of natural origin also melted at 210° with slight previous softening, and a mixture of the synthetic and the natural specimen had exactly the same softening and melting point.

Dyeing Properties of the Flavonols.—The behaviour of the synthetic and the natural specimens of gossypetin (that obtained from the acetate and also a second larger specimen of the flavonol itself, kindly supplied by Professor A. G. Perkin) and of quercetagetin towards alkaline solutions and in other respects was found to be identical by direct comparison, but, doubtless owing to a difference in the conditions employed, we thought there was some divergence between the results of our dye-trials with synthetical quercetagetin and the shades recorded by Perkin (*loc. cit.*). A direct comparison showed that no variations actually exist. The shade on tin-mordanted wool was brownish-orange and on chromium-mordanted wool dull yellowish-greenish-brown.

The colours on calico mordanted with iron and aluminium were the following, natural and synthetic specimens giving identical results :

	Weak Al.	Strong Al.	Al + Fe.	Strong Fe.	Weak Fe.
Gossypetin ...	Brownish-grey	Khaki-brown	Dull greenish-brownish-grey	Smoke-brown	Mouse-grey
Quercetagetin	Greenish-yellow	Deep brownish-yellow	Greenish-brown	Intense bluish-black	Greenish-grey

1 : 2 : 3 : 5-*Tetramethoxybenzene.*—When this work was completed it occurred to us that a valuable confirmation of the view that gossypetin and quercetagetin are derivatives of the same tetrahydroxybenzene could be obtained by equating the starting points of the syntheses. Accordingly 2 : 5-dimethoxyresorcinol and 4 : 5-dimethoxyresorcinol were separately methylated by means of methyl sulphate and sodium hydroxide in aqueous acetone solution. The products were isolated in the usual manner and vacuum-distilled from very small flasks. The ether from 2 : 5-dimethoxyresorcinol, which was prepared first, solidified when rubbed. The small quantity of the ether produced from 4 : 5-dimethoxyresorcinol remained liquid, but crystallised immediately when a crystal of the ether prepared from 2 : 5-dimethoxyresorcinol was introduced. A mixture of the two specimens and that from 2 : 5-dimethoxyresorcinol separately exhibited an identical behaviour on fusion and solidification; the m. p. was 45—46° (Will, *Ber.*, 1888, **21**, 609, gives 47°).

THE UNIVERSITIES OF OXFORD AND MANCHESTER.
UNIVERSITY COLLEGE, LONDON. [*Received, November 9th*, 1928.]