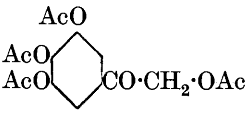
CVII.—*A Synthesis of Pyrylium Salts of Anthocyanidin Type. Part XIX. A Synthesis of Delphinidin Chloride not involving a Demethylation Process, and Syntheses of Hirsutidin Chloride and of Delphinidin Chloride 3′-Methyl Ether, possibly identical with Petunidin Chloride.*

By WILLIAM BRADLEY, ROBERT ROBINSON, and GEROLD SCHWARZENBACH.

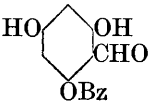
THE recognition that the purest specimens of cyanidin chloride can most readily be obtained if demethylation of methyl ethers is entirely avoided (Robertson and Robinson, Part XV, J., 1928, 1526; Willstätter and Robinson, *Ber.*, 1928, **61**, 2504) made it desirable that the improved synthetical method already applied to the cases of pelargonidin chloride (Robertson, Robinson, and Sugiura, Part XVI, J., 1928, 1533) and cyanidin chloride (Part XV, *loc. cit.*) should be extended to include the preparation of delphinidin chloride.

This has now been carried out, and the resulting hexahydroxyflavylium chloride compared with a specimen of delphinidin chloride from a natural source, no divergences of behaviour of the specimens being detected.

O-Triacetylgalloyl chloride and diazomethane furnished *ω-diazo-3 : 4 : 5-triacetoxyacetophenone*, $(AcO)_3C_6H_2{\cdot}CO{\cdot}CHN_2$ (I), and *ω : 3 : 4 : 5-tetra-acetoxyacetophenone* (II) was readily obtained from the diazo-derivative by the action of acetic acid.



(II.)



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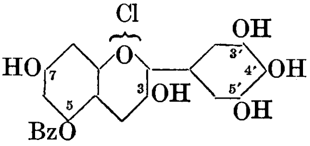


(IV.)

The tetra-acetate (II) condensed with 2-*O*-benzoylphloroglucinaldehyde (III) (Robertson and Robinson, J., 1927, 1710) in alcohol-ethyl acetate solution under the influence of hydrogen chloride, with production of *5-O-benzoyldelphinidin chloride* (IV), the acetyl groups being all removed in the course of the reaction. The final stage, namely, the elimination of the benzoyl group, gave trouble owing to the oxidisability of the substance in alkaline solution, but this difficulty was not insuperable. The debenzoylated product of the action of aqueous-alcoholic sodium hydroxide on (IV) was changed to delphinidin chloride by treatment with hydrochloric acid under special conditions which it was found necessary to observe closely.

Synthesis of Hirsutidin Chloride.—In 1927, Karrer and Widmer (*Helv. Chim. Acta*, 1927, **10**, 758) isolated a new anthocyanin, hirsutin chloride, from the *Primula hirsuta*, and found that, on hydrolysis in the usual manner, *hirsutidin chloride*, $C_{18}H_{17}O_7Cl$, was obtained.

This anthocyanidin contained three methoxyl groups, gave syringic acid on oxidation and delphinidin salts on demethylation, and was therefore recognised as a methyl ether of syringidin chloride (*O*-methylmalvidin chloride). The methyl groups might be in the 3 : 3′ : 5′-, 5 : 3′ : 5′-, or 7 : 3′ : 5′-positions, and, of these, Karrer and his collaborators preferred the last two. The synthesis of *O*-3 : 3′ : 5′-trimethyldelphinidin chloride has already been effected (Bradley and Robinson, J., 1928, 1541), and, since the properties of this salt were different from those of hirsutidin chloride, concurrence with Karrer's view was expressed.

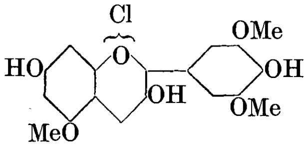
5 : 3′ : 5′-*O*-Trimethyldelphinidin chloride (V) was obtained by condensing 2-*O*-methylphloroglucinaldehyde with ω-acetoxy-4-benzyloxy-3 : 5-dimethoxyacetophenone,

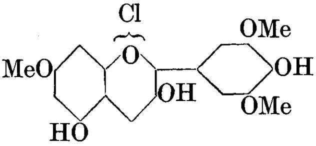
$$AcO{\cdot}CH_2{\cdot}CO{\cdot}C_6H_2(OMe)_2{\cdot}O{\cdot}C_7H_7$$

(Bradley and Robinson, *loc. cit.*), in formic acid solution in presence of hydrogen chloride. As in the synthesis of malvidin chloride, the benzyl group is eliminated.

7 : 3′ : 5′-*O*-Trimethyldelphinidin chloride (VI) was obtained by hydrolysing its 5-O-*benzoyl* derivative derived from the use of 2-*O*-benzoyl-4-*O*-methylphloroglucinaldehyde (VII) in a similar process. This salt proved to be identical with hirsutidin chloride. The aldehyde (VII) was obtained on methylating 2-*O*-benzoylphloroglucinaldehyde by means of silver oxide and methyl iodide; its constitution follows from the occurrence of the flavylium salt synthesis and from relations represented in the subjoined scheme.

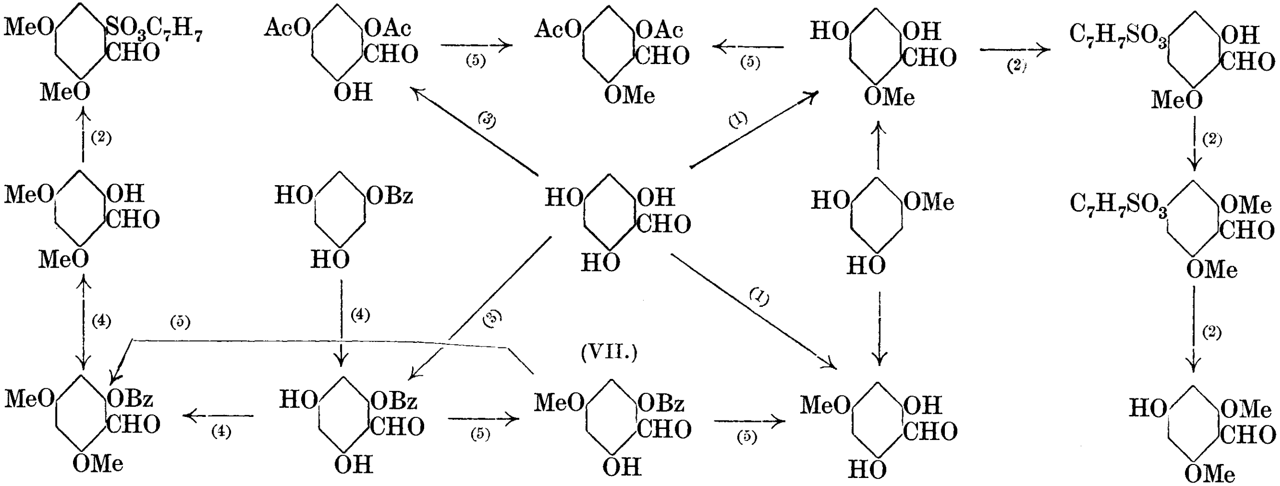
(V.)





(VI.)

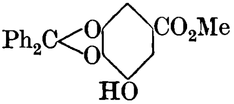
Synthesis of Delphinidin Chloride 3′-Methyl Ether.—This substance, which may be identical with petunidin chloride (Willstätter and Burdick, *Annalen*, 1916, **412**, 217), has been synthesised by an application of the *O*-benzoylphloroglucinaldehyde method; the chief difficulties were encountered in obtaining the required ketonic component.



(VII.)

(1) Karrer and Bloch, *Helv. Chim. Acta*, 1927, **10**, 374; (2) Karrer and Helfenstein, *ibid.*, p. 789; (3) Robertson and Robinson, J., 1927, 1710; (4) Robertson, Robinson, and Struthers, J., 1928, 1455; (5) this paper.

The first step was to devise a more convenient method for the preparation of 3-*O*-methylgallic acid than those recorded by Vogl (*Monatsh.*, 1899, **20**, 397) and Fischer (*Ber.*, 1913, **46**, 1123). In this, we were successful, and the new method of protection of vicinal hydroxyl groups in polyhydric phenols that was adopted is one that should find numerous applications in other directions. Methyl gallate and diphenyldichloromethane in acetone solution in presence of pyridine, with subsequent addition of sodium hydroxide, afforded *methyl* 3-*hydroxy*-4 : 5-*diphenylmethylenedioxybenzoate* (VIII). This ester was methylated by means of methyl iodide and sodium ethoxide, and, on hydrolysis by alkaline solutions, 3-*methoxy*-4 : 5-*diphenylmethylenedioxybenzoic acid* (IX) was obtained; 3-*O*-methylgallic acid (X) resulted when the methylated ester was treated with boiling concentrated hydrochloric acid.



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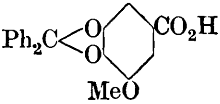

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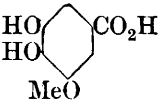
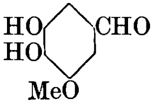


(X.)

3-*O*-Methylgallic acid had m. p. 220° (diacetyl derivative, m. p. 170—171°) in agreement with the description of Fischer (*loc. cit.*) (Vogl, *loc. cit.*, gives the m. p. 199—200°).

Shriner and McCutchan, however, in a recent paper (*J. Amer. Chem. Soc.*, 1929, **51**, 2193), have stated that the acid has m. p. 132° (diacetyl derivative, m. p. 102—103°), and it was therefore necessary to explain this discrepancy. We find that the action of 8% aqueous sodium hydroxide at 200° on bromovanillin in the presence of copper actually yields 3-*O*-methylgallaldehyde (XI) and not the corresponding acid, as Shriner and McCutchan supposed.

Starting with the diphenylmethylene ether or the diacetyl derivative of 3-*O*-methylgallic acid and passing through the stages $R\cdot CO_2H$, $R\cdot COCl$ and $R\cdot CO\cdot CHN_2$ to $R\cdot CO\cdot CH_2\cdot OAc$, we obtained the ω-acetoxygallacetophenone derivatives (XII) and (XIII), respectively, and either of these, on condensation with 2-*O*-benzoyl-



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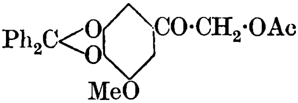

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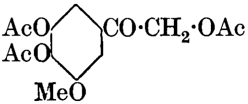

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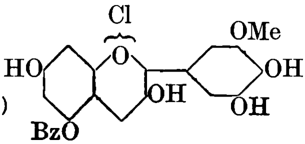

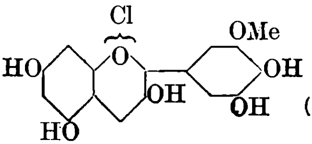

(XV.)

phloroglucinaldehyde in the usual way, gave rise to 5-*O*-benzoyl-3′-*O*-methyldelphinidin chloride (XIV). The 3′-*O*-methyldelphinidin chloride (XV) obtained on hydrolysis very closely resembles petunidin chloride, but we are unable to express any opinion at this stage on the question of its identity with that anthocyanidin.

EXPERIMENTAL.

ω-*Diazo*-3 : 4 : 5-*triacetoxyacetophenone* (I).—Triacetylgalloyl chloride was prepared by the method of Fischer, Bergmann, and Lipschitz (*Ber.*, 1918, **51**, 55). A solution of the chloride (18 g.) in chloroform (50 c.c.) was added during 10 minutes to ethereal diazomethane (140 c.c., from 25 c.c. of nitrosomethylurethane) cooled to −10°. Evolution of nitrogen accompanied the rapid separation of pale yellow crystals of the diazo-ketone, and these were collected after 30 minutes and washed with ether (yield, 17·6 g.; m. p. 120—122°). For analysis, the diazo-ketone was crystallised twice from benzene; it was obtained in stout lemon-yellow plates or tables, m. p. 125—126° with evolution of nitrogen (Found: C, 52·7; H, 3·7; N, 8·7, 8·8. $C_{14}H_{12}O_7N_2$ requires C, 52·5; H, 3·8; N, 8·7%).

ω-*Diazo*-3 : 4 : 5-*triacetoxyacetophenone* is easily soluble in alcohol and benzene, more sparingly soluble in ether, and almost insoluble in light petroleum. It possesses the usual properties of diazomethylketones. Nitrogen is eliminated by heating, by the addition of iodine or aqueous mineral acids to an alcoholic solution, or by warming with glacial acetic acid. A drop of aqueous sodium hydroxide added to the cold dilute alcoholic solution causes the development of a yellow colour; from more concentrated solutions, a green amorphous solid, soluble in water, is precipitated, and, when gently heated, these solutions become reddish-brown.

ω : 3 : 4 : 5-*Tetra-acetoxyacetophenone* (II).—A solution of the diazo-ketone (12 g.) in pure glacial acetic acid (25 c.c.) was warmed at 60—80° until the vigorous evolution of nitrogen had ceased (about 30 mins.). The cooled solution was diluted with ether (300 c.c.), and the crystalline precipitate of ω : 3 : 4 : 5-*tetra-acetoxyacetophenone* collected (yield, 9·3 g.; m. p. 118—121°). The ethereal mother-liquor was washed with potassium bicarbonate solution, filtered, dried, and evaporated; an oil (2 g.) remained which gave a bluish-green coloration with ferric chloride, and from which only a small amount of the crystalline ketone could be isolated. The proportion of the oily fraction was greater when less pure acetic acid was employed and was increased, also, by more prolonged heating during the decomposition of the diazo-ketone. When the ketone was isolated by pouring the cooled acetic acid solution into water, the oily product could not be employed directly, and, after recrystallisation, the yield was considerably smaller than that obtained by the above procedure. The ketone crystallised from ethyl alcohol (charcoal) in tables or colourless thick plates having a characteristic spearhead form, m. p. 122—123° (Found : C, 54·9 ; H, 4·8. $C_{16}H_{16}O_9$ requires C, 54·6 ; H, 4·6%).

ω : 3 : 4 : 5-Tetra-acetoxyacetophenone is readily soluble in alcohol, benzene and acetic acid, but more sparingly soluble in ether. It is insoluble in aqueous sodium carbonate, although rapidly dissolved by cold dilute sodium hydroxide solution. An alcoholic solution gives no reaction with ferric chloride, and the ketone reduces Fehling's solution in the cold.

Benzoyldelphinidin Chloride (IV) (First preparation).—Finely powdered ω : 3 : 4 : 5-tetra-acetoxyacetophenone (5·2 g.) and benzoylphloroglucinaldehyde (4·0 g.) were added to a mixture of ethyl alcohol (80 c.c.) and ethyl acetate (80 c.c.), and the solution cooled to 0°. Dry hydrogen chloride was admitted and, saturation having been attained, the mixture was allowed to reach the room temperature. At first, a portion of the aldehyde was precipitated, but later redissolved completely. After being kept over-night, the dark green flavylium salt was collected and washed with ether (yield, 2 g.). The use of ethyl alcohol alone gave an amorphous product; ethyl acetate alone furnished a crystalline substance which gave no coloration with ferric chloride in alcoholic solution. The product was obtained in short prisms, having in mass a dark olive-green appearance. It was recrystallised from hot methyl alcohol (20 vols.) containing concentrated hydrochloric acid (1 vol.), in which it was only very sparingly soluble. The recrystallised material was dull greyish-violet in appearance and consisted of slender, dark red prisms.

Benzoyldelphinidin chloride is easily soluble in alcohol to a violet-red solution; the violet shade increases on keeping or on dilution with more alcohol; the very dilute solution in methyl alcohol is pure blue. When an equal volume of water is added to the violet-red methyl-alcoholic solution, the colour fades instantly to pale blue, and the red colour is immediately restored on the addition of acid. Heated with 0·5% hydrochloric acid, the salt dissolves to a pale red solution which rapidly fades even while in contact with the undissolved substance. A pale blue colour results when a drop of aqueous sodium carbonate is added to a freshly prepared alcoholic solution of the salt; on dilution with water, the solution becomes green and then rapidly fades to yellow. A drop of 5% aqueous potassium hydroxide added to the alcoholic solution gives a bluish-green colour which fades slowly to green; on the other hand, a drop of 0·5% potassium hydroxide gives a fairly stable, pure blue colour which is still weakly blue after one hour. Similarly, solid sodium acetate added to the freshly prepared methyl-alcoholic solution gives a fairly stable, pure blue colour. The salt dissolves in aqueous sodium carbonate, but the blue colour initially produced fades almost immediately to violet.

Delphinidin Chloride (First preparation).—Finely powdered, crude benzoyldelphinidin chloride (2 g.) was added to 10% aqueous sodium hydroxide (16 c.c.) from which air had been displaced by a stream of hydrogen, and the solution kept 4 hours after the salt had dissolved completely. The deep blue solution formed initially changed through green to orange. Ethyl alcohol (10 c.c.) and concentrated hydrochloric acid (10 c.c.) were then added, and the deep red solution was kept in the cold during 3—4 days until a portion dissolved in aqueous sodium carbonate with a pure blue colour. Attempts to hasten the re-synthesis of the flavylium salt by warming the solution or by increasing the concentration of acid gave oily products from which crystalline material could not be obtained. Concentrated hydrochloric acid (30 c.c.) was then added in several small portions, and, next day, almost the whole of the product had separated in a microcrystalline condition. Washed with hydrochloric acid and dried in the air, it formed a dense, dark brownish-red powder, having a greenish lustre.

Preliminary purification was effected by solution in a small volume of ethyl alcohol and precipitation of the salt from the filtered solution by means of concentrated hydrochloric acid. The flocculent material was collected, dried, and washed with ether (Specimen A). The product was obtained in an oily condition when precipitation was effected from an alcoholic hydrogen chloride solution by the addition of ether.

Specimen A separated completely from solution in 15% hydrochloric acid, but several repetitions of this treatment failed to give definitely crystalline material. When dry hydrogen chloride was admitted above the surface of a concentrated alcoholic solution of Specimen A cooled in ice-water, crystalline material was readily obtained in small yield as an olive-green lustrous substance. The mother-liquor could be almost completely precipitated by dilution with aqueous hydrochloric acid, but the material (an ethyl ether ?) obtained in this way was much more sparingly soluble than delphinidin chloride. Attempts to obtain delphinidin chloride tetrahydrate from the crystalline portion under the conditions of Willstätter and Weil (*Annalen*, 1916, **412**, 190) were unsuccessful.

When, however, Specimen A was heated with hydriodic acid under Zeisel conditions, as described by Willstätter and Weil (*loc. cit.*), delphinidin iodide separated in a well-crystallised condition, although in small yield. The crystal form, pointed plates, was identical with that of the specimen from material of natural origin. Willstätter and Weil remark that the crude anthocyanidin obtained from the glucoside could not be crystallised from methyl-alcoholic hydrogen chloride, but the crystalline iodide was readily obtained and from this the crystalline chloride. The iodide was obtained in better yield by dissolving Specimen A (1·15 g.) in cold 0·5% hydrochloric acid (30 c.c.) and adding freshly distilled hydriodic acid (15 c.c., b. p. 127°) to the filtered solution. A small amount of crystalline material was precipitated rapidly, but the crystallisation was complete only after several days, during which the containing flask was filled with carbon dioxide and kept in the dark. The crystals were collected, washed with a little dilute hydriodic acid, dried in the air, and washed with ether (yield, 0·45 g.). Only a very small additional amount was obtained when the mother-liquor was concentrated. The iodide was obtained in this manner in stout prisms or tables, green in mass and having a bright yellow lustre. This salt crystallises from its solution in hot dilute hydriodic acid on the addition of concentrated hydriodic acid in well-shaped, elongated rhombic plates, often connected by their acute-angled corners so as to form rosettes. The crystals are deep red by transmitted light and exhibit a marked yellow glitter. The same crystal shape and appearance have been noted in material of natural origin (demethylation of natural malvidin).

The crude crystalline iodide (0·95 g.) was dissolved in 0·5% hydrochloric acid (30 c.c.), and the chloride precipitated by adding concentrated hydrochloric acid (30 c.c.) to the filtered solution. The amorphous chloride, which separated at once and completely, was crystallised by dissolving 0·13 g. in 5% hydrochloric acid (9 c.c.) and adding hot concentrated hydrochloric acid (18 c.c.) to the hot solution. The chloride separated on cooling in long, dark red prisms or in crystalline granules. The former were green by reflected light and had a bright yellow lustre. Two recrystallisations were effected under the same conditions (Specimen B) (Found : C, 48·3; H, 4·0; Cl, 9·2; loss at 110° in a high vacuum, 9·3. Found in anhydrous material: C, 53·4; H, 3·2; Cl, 10·1. $C_{15}H_{11}O_7Cl,2H_2O$ requires C, 48·1; H, 4·0; Cl, 9·5; H_2O, 9·6%. $C_{15}H_{11}O_7Cl$ requires C, 53·2; H, 3·3; Cl, 10·5%).

Benzoyldelphinidin Chloride (Second preparation).—Numerous further experiments on the conditions for the preparation of this salt were carried out. The product obtained by condensation of the components in ether–alcohol was not homogeneous and the yield was inferior; a very considerable improvement followed on the adoption of the following method.

2-*O*-Benzoylphloroglucinaldehyde (7·4 g.) and ω : 3 : 4 : 5-tetra-acetoxyacetophenone (9·6 g.), along with ethyl alcohol (150 c.c.), were mixed in a flask provided with an efficient stirrer, a tap funnel, inlet and outlet (calcium-chloride tube) tubes, and cooled in melting ice. The mixture was saturated with hydrogen chloride and, after 2 hours, was warmed at 30° for 1½ hours; it was then again cooled to near 0°, and acetyl chloride (167 c.c.) gradually introduced. The process was interrupted for 3 hours when about half of the acetyl chloride had been added. The product was collected (8·2 g.) after about 12 hours. Altogether, 22·6 g. of the salt were obtained from six experiments in which the conditions were slightly modified; cooling at 0° during the whole period greatly diminished the yield, but substituting the room temperature for the 30° mentioned above gave good results (1·9 g. from 2 g. of the aldehyde and 6·4 g. from 6 g.). It was now found that *benzoyldelphinidin chloride* could be crystallised, by adding concentrated hydrochloric acid to its solution in ethyl alcohol, in prisms forming a glistening green mass (Found in material dried over sulphuric acid: C, 57·6; H, 3·7. $C_{22}H_{15}O_8Cl,H_2O$ requires C, 57·4; H, 3·7%).

Delphinidin Chloride (Second preparation).—After a preliminary test, 20 g. of the crude benzoyl compound prepared by the acetyl chloride method were hydrolysed in five similar experiments as follows:—

The finely powdered benzoyl compound (4·0 g.) was added to 10% aqueous sodium hydroxide (30 c.c.), cooled in ice and frequently shaken until dissolution was complete (15 mins.). Air was previously displaced from the apparatus by hydrogen, and a current of the latter was passed through the alkaline solution during the hydrolysis. After 15 minutes, the solution was allowed to reach the room temperature, and, after 3½ hours, an ice-cold mixture of ethyl alcohol (20 c.c.) and concentrated hydrochloric acid (20 c.c.) was added. The clear, deep red solution was kept 10—12 days until a portion gave a pure blue coloration with a little sodium carbonate solution; the time required for the completion of this stage was considerably longer than the corresponding period for the earlier preparation. Concentrated hydrochloric acid (120 c.c.) was then added in several portions, the solution kept over-night, and the precipitated mixture of salts and benzoic acid collected, washed with 20% hydrochloric acid, and dried (Y).

The united filtrates gave, on keeping, a further crop of the flavylium salt (Z; yield, 3·15 g.), which was almost free from benzoic acid and inorganic salts and for this reason was conveniently worked up separately.

The united first fractions Y were dried in the air, finely powdered, and washed with ether; when wet with the solvent, the material became pasty, but friable again immediately the solvent had evaporated. After being powdered again, the product was extracted with cold ethyl alcohol–concentrated hydrochloric acid (in all, EtOH, 120 c.c.; 30% HCl, 30 c.c.): there was a considerable residue (R) (see below). The filtered extracts were mixed with an equal volume of water and with concentrated hydrochloric acid (250 c.c.). The amorphous product was collected and extracted with cold 0·5% hydrochloric acid (about 500 c.c. in several portions and with mechanical stirring). Almost the whole of the substance dissolved, and it was recovered by the addition of concentrated hydrochloric acid (1300 c.c.) to the filtered solution so as to make the final hydrogen chloride concentration about 25%. When the precipitate was collected, dissolved in hot 0·5% hydrochloric acid, and freshly distilled hydriodic acid (80 c.c., *d* 1·7) added to the filtered solution, the iodide slowly separated during several days in a beautifully crystalline condition. The usual precautions—protection from light and replacement of the air of the containing flask by carbon dioxide—were observed.

The fraction Z of the crude chloride was treated in a very similar fashion, the iodides from Y and Z were united and dissolved in hot 5% hydrochloric acid (400 c.c.), and the chloride was precipitated by the addition of concentrated hydrochloric acid (600 c.c.). This product was amorphous, but crystallised by repetition of the solution in 5% hydrochloric acid and increase of the acid concentration to 25% (Specimen C) (Found in air-dried material: C, 48·5; H, 3·9; loss at 110° in a high vacuum, 9·0. Found in anhydrous material: C, 53·3; H, 3·1%).

The crystals of this specimen were deep red prisms by transmitted light and olive-green in mass; under some conditions, which it is not possible to define precisely, the material separated in ill-defined granules, and occasionally as opaque aggregates, from which well-shaped crystals appeared to protrude.

The residue R (above) crystallised directly from methyl alcohol–hydrochloric acid (9 vols. CH_4O and 1 vol. 30% hydrochloric acid) (Specimen D), and the material recovered from the mother-liquor was crystallised in the usual way from 25% hydrochloric acid (Specimen E). Subsequent to these experiments, it was found that less difficulty was experienced in crystallising the delphinidin chloride, made substantially as described, if the hydrogen used to displace air from the apparatus during the hydrolysis was freed from traces of oxygen by passage through an alkaline pyrogallol solution.

The specimens B, C, D and E exhibited identical colour reactions, and these were, further, identical with those of specimens of delphinidin chloride prepared by demethylation of malvidin (syringidin) chloride and by the hydrolysis of vicin picrate with hydrochloric acid. We are greatly indebted to Professor P. Karrer for kindly supplying the delphinidin chloride (*ex* malvidin) and the vicin picrate. Vicin is an anthocyanin of the sweet pea (Karrer and Widmer, *Helv. Chim. Acta*, 1927, **10**, 67) and is a delphinidin glucoside.

The colours observed in a range of buffered solutions of definite p_H under the conditions prescribed by Robertson and Robinson (*Biochem. J.*, 1929, **23**, 35) were the following, the observations in parentheses referring to 5-*O*-benzoyldelphinidin chloride.

1% Hydrochloric acid, red with blue tinge (rose red, bluer than delphinidin and partly precipitated on standing), unchanged after 15 minutes; 10% hydrochloric acid, the same (similar, but all the salt was precipitated, leaving a colourless solution); (1) permanganate (purplish-red, fading to violet); (2) similar, but shade bluer [similar to (1)]; (3) similar to (2) (no change); (4) not much change, violet-red (deeper violet); (5) deeper violet-red (deeper violet); (6) similar reddish-violet (bluer violet); (7) reddish-violet (violet-blue); (8) reddish-violet, bluer in thin layers (blue); (9) blue in thin layers, violet in thick layers (blue); (10) blue (blue with no violet tinge); (11) rather dull greenish-blue (blue); (12), (13) and (14), no change [(14) and (15) are greener and duller]; (15) similar colour, quickly becoming slate blue and then very pale brown.

After 15—20 minutes, the colours observed were: (1) faded rose pink (very weak violet); (2) and (3) weak violet [(2), (3) and (4) form a series in which a reddish-violet colour increased]; (4) a little more intense reddish-violet; (5) and (6) more intense reddish-violet; (7) bluer violet; (8) weaker blue-violet; (9)—(13) inclusive, greenish-blue [(5), (6), (7), (8) and (9) form a series in which the violet colour becomes bluer; (10), (11) and (12) blue; (13) bluish-green]; (14) weak, faded green (pale green); (15) yellowish-brown (pale brownish-yellow).

After 1½ hours, the colours were: (1), (2) and (3), weak violet, increasing in (4), (5) and (6), bluer in (7) and violet-blue in (8); (9), (10), and (11) were green, tinged with blue; (12), (13), (14) and (15), yellowish-brown [all faded; (1), (2), (3) and (4), increasing weak violet; (5), (6), (7) and (8), bluer; (9), (10) and (11), blue; (12), bluish-green; (13), pale green; (14) and (15), pale brownish-yellow].

After 24 hours, (1), (2), (3), (4) and (5), practically colourless, with a small, flocculent, violet precipitate; (6) very faint violet, no flocks; (7) and (8), almost colourless; (9) very faint yellow; (10), (11), (12), (13) and (14), yellow, increasing in intensity to weak golden-yellow; (15), weaker yellow [(1), very faintly blue, a trace of violet flocculent precipitate; (2) and (3), faintly blue, a little more precipitate; (4) and (5) weak blue, maximum precipitation; (6) and (7), weak blue; (8), very pale blue, no precipitate; (9) and (10), almost colourless; (11), (12), (13), (14), (15), (16) and (17), weak lemon-yellow].

The comparisons of the different specimens of delphinidin chloride, natural and synthetic, disclosed no divergences whatever, either in regard to the shades of colour observed, the relative amounts of precipitates or the rate of change of the colours of the solutions. The specimens (B), (C), (D) and (E) had all the ordinary properties of delphinidin chloride as recorded by Willstätter and his collaborators, and specimen (D) was used for the preparation of the characteristic monohydrate under the conditions prescribed by Willstätter and Weil (*Annalen*, 1916, **412**, 192). The experiment succeeded, and well-shaped, dark brownish-violet, rhombic plates, all of them elongated, as shown in some cases in Willstätter and Weil's figure, were obtained (Found: loss at 110° in a vacuum, 6·0. $C_{15}H_{11}O_7Cl,H_2O$ requires H_2O, 4·9%). The somewhat high value for the loss in weight may be due to loss of hydrogen chloride or to admixture with one of the other hydrates, but it is interesting to note that Willstätter and Weil (*loc. cit.*) found the loss in a vacuum desiccator to be 5·88% and 5·57% in two experiments.

The crystals of the monohydrate exhibited the behaviour towards 5% hydrochloric acid which was described by Willstätter and Weil in the case of the specimen of natural origin.

6-*Hydroxy*-2-*benzoyloxy*-4-*methoxybenzaldehyde* (VII).—The preparation of a monomethyl ether of *O*-benzoylphloroglucinaldehyde was unsuccessfully attempted in several different ways, using methyl iodide and alkali-metal salts of the hydroxy-aldehyde, but the following process gave moderately satisfactory results.

A mixture of *O*-benzoylphloroglucinaldehyde (2·5 g.), methyl iodide (4·1 g.), finely divided silver oxide (3·3 g.), and acetone (25 c.c.) was mechanically shaken for 12 hours, filtered, and the precipitate washed with acetone. The pale yellow filtrates were united and the solvent was removed under reduced pressure. The orange-yellow viscous residue was dissolved in ether (50 c.c.), filtered from a trace of insoluble flocculent material, and washed with 10% aqueous sodium carbonate. Acidified, this fraction gave only a negligible amount of a colourless crystalline substance, although *O*-benzoylphloroglucinaldehyde is readily removed from its solution in ether by this means. The ethereal solution was then twice shaken with 5% aqueous potassium hydroxide (10 c.c., 5 c.c.) and the alkaline solutions were separated and acidified with dilute acetic acid, without delay. This product was a pink crystalline precipitate and a colourless emulsion, which became resolved into a mass of fine needles in the course of 4—5 hours; yield, 1·9 g., m. p. 95—102°. The ethereal solution was again washed with 5% potassium hydroxide solution, dilute sulphuric acid, and water; dried and evaporated, it gave an oily solid (0·23 g.) which consisted essentially of benzoyldimethylphloroglucinaldehyde (Robertson, Robinson, and Struthers, J., 1928, 1455).

In a second experiment, *O*-benzoylphloroglucinaldehyde (5·2 g.) and methyl iodide (4·6 g.) in acetone (40 c.c.) were shaken with silver oxide (3·5 g.) during 5 hours, after which methyl iodide (4·6 g.) in acetone (10 c.c.) and silver oxide (3·5 g.) were added and the shaking was continued over-night. Benzoyldimethylphloroglucinaldehyde (2·2 g., m. p. 143—145°) and benzoylmethylphloroglucinaldehyde (1·5 g.) were isolated.

6-*Hydroxy*-2-*benzoyloxy*-4-*methoxybenzaldehyde* crystallised from ethyl alcohol in colourless plates, m. p. 109° (Found: C, 66·0; H, 4·5. $C_{15}H_{12}O_5$ requires C, 66·2; H, 4·4%), easily soluble in benzene and chloroform, very sparingly soluble in light petroleum and insoluble in water. The alcoholic solution gives a brownish-red coloration with ferric chloride. A solution of the aldehyde (1·8 g.) in cold 10% aqueous sodium hydroxide (10 c.c.) was kept in an atmosphere of hydrogen (probably unnecessary) during 4 hours. The acidified solution was extracted with ether, and the extract was washed with aqueous potassium bicarbonate, in order to remove benzoic acid, then with water, dried, and evaporated. The colourless residue crystallised from benzene in slender needles, m. p. 141—142°, unchanged by further recrystallisation from water.

This aldehyde is identical with phloroglucinaldehyde 4-methyl ether, isolated by Karrer and Bloch (*Helv. Chim. Acta*, 1927, **10**, 374) from the product of methylation of phloroglucinaldehyde by diazomethane, and from the mixture of aldehydes obtained from *O*-monomethylphloroglucinol by the Gattermann reaction. We were able to confirm this by direct comparison with a specimen of the substance kindly sent to us by Professor Karrer; the m. p. of a mixture of the specimens was not depressed.

6-*Hydroxy*-2-*benzoyloxy*-4-*benzyloxybenzaldehyde*.—A solution of *O*-benzoylphloroglucinaldehyde (5·4 g.) and benzyl chloride (7·5 g.) in acetone (40 c.c.) was shaken during 14 hours with silver oxide (7·0 g.). The silver compounds were separated, washed with acetone, and the united solutions evaporated in a vacuum. The residue was dissolved in ether and the solution washed first with aqueous sodium carbonate and then with 5% aqueous potassium hydroxide. The latter fraction was acidified without delay and the precipitated oil, which solidified in the course of a few hours, was taken up in benzene and the dried solution concentrated to 5—6 c.c. Crystals of the benzylated aldehyde separated, and these were collected (yield, 1·5 g.; m. p. 198°) and recrystallised first from benzene containing ethyl alcohol (m. p. raised to 201—203°) and finally from light petroleum, forming thin, colourless, rhomboidal plates, m. p. 202—203° (Found: C, 72·6; H, 4·4. $C_{21}H_{16}O_5$ requires C, 72·4; H, 4·6%). The aldehyde is easily soluble in ethyl alcohol, more sparingly soluble in benzene and very sparingly soluble in light petroleum. In alcoholic solution, it gives with ferric chloride a reddish-brown coloration which suggests that the substance is 6-*hydroxy*-2-*benzoyloxy*-4-*benzyloxybenzaldehyde.*

4 : 6-*Diacetoxy*-2-*methoxybenzaldehyde.*—2-*O*-Methylphloroglucinaldehyde (Herzig and Wenzel, *Monatsh.*, 1903, **24**, 860; Karrer and Glattfelder, *Helv. Chim. Acta*, 1921, **4**, 724) was prepared from phloroglucinol monomethyl ether (Herzig and Aigner, *Monatsh.*, 1900, **21**, 435) by the Gattermann reaction. In the final stage, it was found advisable to wash the aldimine hydrochloride with fresh ether, to dry it in a vacuum, and to hydrolyse it at 80° with about 10 times its weight of water for 25—30 minutes. The aldehyde crystallised during the process in yellow needles, which were almost pure, m. p. 200—202°, after a single recrystallisation from dilute alcohol. When hydrolysis is effected in the presence of mineral acid, the product is brown (Herzig and Wenzel, *loc. cit.*) and dissolves in aqueous sodium carbonate with a greenish fluorescence which renders it valueless for our purpose.

The aldehyde was only incompletely acetylated by ice-cold aqueous sodium hydroxide (4 mols.) and ethereal acetic anhydride (3 mols.), but readily under the conditions of Pratt and Robinson (J., 1925, 1184). Anhydrous potassium carbonate (2 g.) was added in small amounts to a mixture of acetic anhydride (5 c.c.) and finely powdered 2-*O*-methylphloroglucinaldehyde (1 g.) so as to maintain a vigorous evolution of carbon dioxide. The pasty mass was kept for 1 hour, water added, and the product stirred with potassium bicarbonate until the excess of acetic anhydride had been decomposed; it was then collected, washed with water, and dried.. Recrystallised from benzene–light petroleum, light petroleum, and finally ligroin, the 4 : 6-*diacetoxy*-2-*methoxybenzaldehyde* formed colourless plates, m. p. 107° (Found: C, 56·8; H, 4·6. $C_{12}H_{12}O_6$ requires C, 57·1; H, 4·8%). This derivative was very easily soluble in alcohol or benzene, more sparingly so in ligroin, light petroleum or ether. An alcoholic solution gave no reaction with ferric chloride, but when an aqueous-alcoholic solution was heated hydrolysis occurred and a reddish-brown ferric chloride reaction was observed.

The substance was also obtained by the methylation of *O*-diacetylphloroglucinaldehyde (Robertson and Robinson, J., 1927, 1712), in the preparation of which the following quantities were employed : phloroglucinaldehyde 5 g., acetic anhydride 14 c.c., *N*-sodium hydroxide 100 c.c. The yield was about 6 g., m. p. 102—103°, from 20 g. of phloroglucinaldehyde. *O*-Diacetylphloroglucinaldehyde (1·05 g.) and methyl iodide (2·1 g.) in acetone (5 c.c.) were shaken with silver oxide (1·8 g.) during 6 hours. Isolated in the usual manner, only 0·1—0·2 g. of material, insoluble in sodium hydroxide, was obtained. *O*-Diacetylphloroglucinaldehyde (2·4 g.) and methyl iodide (4·5 g.) in acetone (15 c.c.) were shaken with silver carbonate (6 g.) during 16 hours; evolution of carbon dioxide then appeared to have ceased. The silver compounds were separated and washed with acetone, and the filtrates evaporated in a vacuum. The residue crystallised in contact with ether in colourless elongated plates (0·9 g., m. p. 106—107°). The mother-liquor furnished a small additional amount (0·5 g.) of crystalline material. Recrystallised from ligroin, the main fraction was obtained in colourless elongated plates, m. p. 107—108° alone or mixed with the acetylated 2-methylphloroglucinaldehyde.

5-O-*Benzoyl*-7 : 3′ : 5′-O-*trimethyldelphinidin Chloride*.—In the presence of dry hydrogen chloride, a solution of 4-*O*-methylphloroglucinaldehyde in ethyl acetate or ether rapidly becomes brownish-red and deposits a brownish or reddish-brown amorphous substance (xanthylium salt ?). For this reason, the benzoylated aldehyde was employed for the condensations to flavylium salts. A solution of 4-*O*-methyl-2-*O*-benzoylphloroglucinaldehyde (1·35 g.) and ω-acetoxy-4-benzyloxy-3 : 5-dimethoxyacetophenone (1·72 g.) (Bradley and Robinson, J., 1928, 1560) in ethyl acetate (30 c.c.) was cooled in ice while being saturated with dry hydrogen chloride, and then kept at room temperature over-night. An intense reddish-purple solution was very rapidly formed, and the flavylium salt crystallised in fine needles, which were collected, washed with ethyl acetate, ether, and dried, forming a green spongy mass (yield, 1·98 g.). An additional amount of equally pure material (0·15 g.) separated from the mother-liquor during 48 hours. The salt was recrystallised by cooling a hot solution in methyl alcohol containing concentrated hydrochloric acid (about 7 vols. %); the fine needles obtained appeared purple by transmitted and lustrous green by reflected light (Found : C, 59·5; H, 4·6; Cl, 6·8. $C_{25}H_{21}O_8Cl,H_2O$ requires C, 59·8; H, 4·6; Cl, 7·1%).

This salt is practically insoluble in hydrochloric acid; hot 1% hydrochloric acid dissolves it to a pink solution which, when cold, gives with aqueous sodium carbonate only a yellow coloration. The violet-red alcoholic solution is readily decolorised on dilution, and the colour is restored by the addition of acid. A freshly prepared solution of the salt in methyl alcohol gives, with solid sodium acetate, only a lilac coloration. Aqueous sodium carbonate, added to an acidified methyl-alcoholic solution, gives a pale blue coloration, which fades almost completely. Under the same conditions, 5% sodium hydroxide solution gives a bluish-green solution which rapidly becomes pale green and finally yellow. The solution of the salt in concentrated sulphuric acid is violet-red and not fluorescent.

7 : 3′ : 5′-O-*Trimethyldelphinidin Chloride* (*Hirsutidin Chloride*) (VI).—Hydrolysis of the benzoyl derivative could not be conveniently effected by aqueous sodium hydroxide, since complete solution was not attained even after several hours. After several trials, the following procedure was adopted. The crude crystalline benzoyl derivative (0·7 g.) was finely powdered and suspended in methyl alcohol (7 c.c.) through which a current of hydrogen was passed. Potassium hydroxide (0·9 g.) in water (3 c.c.) was then added. Dissolution was effected in 10—15 minutes, and the blue solution initially produced changed slowly through green to deep orange. After 4 hours, concentrated hydrochloric acid (3·4 c.c.) was added, and this precipitated a voluminous colourless solid which filled the liquid. Gently warmed at 50—60° during 25—30 minutes, this dissolved to a clear, deep red solution, from which the debenzoylated flavylium salt separated during the process in a well-crystallised condition (yield, 0·26 g.), leaving the mother-liquor almost colourless.

This crude product was dried, washed with ether, and a portion (0·4 g.) added to boiling methyl alcohol (60 c.c.). After 4—5 minutes, the solution was filtered (undissolved residue, 0·06 g.) and concentrated hydrochloric acid (2 c.c.) was added to the filtrate, which was kept at 50—55° while concentrated hydrochloric acid (8 c.c.) was added in portions of 1 c.c. : each addition was accompanied by the precipitation of a quantity of the flavylium salt. After 12 hours, the crystals were collected and dried in air (yield, 0·15 g.). The salt was obtained in short, dark red, pointed prisms, which were frequently arranged in rosettes (Found : C, 56·5; H, 4·6; Cl, 9·1. $C_{18}H_{17}O_7Cl$ requires C, 56·8; H, 4·5; Cl, 9·3%).

Heated with water, the salt dissolves to a weak red solution with a slight violet tinge, but this fades rapidly at the boiling point and becomes colourless; the red colour is restored by the addition of acid. In hot 0·5% hydrochloric acid, the salt is already sparingly soluble; it dissolves to a reddish solution, whereas a cold saturated solution in 4% hydrochloric acid is only pink. The cooled solution in hot 0·25% hydrochloric acid presumably contains much pseudo-base, since excess of aqueous sodium carbonate gives a brownish-green solution which changes to olive-green. The fresh dilute solution in methyl alcohol is violet-red and gives with sodium carbonate solution or solid sodium acetate a pure blue coloration. On the other hand, when the solution is kept for some time previous to the test, a greenish-blue coloration is obtained. The salt dissolves in aqueous *N*/10-sodium hydroxide to a purple-blue solution which rapidly becomes crimson-blue (dichroic) and then fades to emerald-green.

5 : 3′ : 5′-O-*Trimethyldelphinidin Chloride* (V).—2-*O*-Methylphloroglucinaldehyde resembles its isomeride in yielding in ethereal ethyl acetate or formic acid solution, in the presence of dry hydrogen chloride, an amorphous brownish-red substance, which is soluble in water and alcohol but insoluble in ether or benzene and dissolves in aqueous alkalis to red solutions exhibiting green fluorescence.

In many of our preliminary experiments on the aldehyde-ketone condensations, a fluorescent by-product was obtained, and the intensity of the fluorescence was apparently greater than that resulting by self-condensation of the aldehyde alone. The proportion of this by-product appeared to be smaller in formic acid than in ethyl acetate solution, and it was completely eliminated by the following procedure.

A solution of ω-acetoxy-4-benzyloxy-3 : 5-dimethoxyacetophenone (2·0 g.) in formic acid (10 c.c.) was saturated with dry hydrogen chloride at room temperature, and 2-*O*-methylphloroglucinaldehyde (0·8 g.) was then added in several small portions during 5 hours. A deep crimson solution was rapidly formed (in previous experiments the medium became brownish-red) and a well-crystallised substance separated. After 12 hours this was collected, washed with formic acid and then with ethyl alcohol (8 c.c.) containing concentrated hydrochloric acid (2 c.c.), and dried in the air (0·35 g.). An additional amount of material separated during 2 days, but the solution was too viscous to permit of filtration and the salt was more conveniently isolated by diluting the product with alcohol (50 c.c.) containing concentrated hydrochloric acid (20 c.c.) and collecting the precipitate which slowly formed. This fraction was not completely crystalline (yield, 0·9 g.).

The crystalline material was recrystallised by solution in methyl alcohol containing 2·5% by volume of concentrated hydrochloric acid and addition of concentrated hydrochloric acid to the filtered solution (Found : C, 56·1 ; H, 4·5 ; Cl, 9·1%). This specimen was recrystallised by dissolving 0·1 g. of the salt in methyl alcohol (350 c.c.) containing concentrated hydrochloric acid (9 c.c.), and adding concentrated hydrochloric acid (40 c.c.) to the filtered solution. Collected and dried in air, this material was a green crystalline powder having a bright yellow lustre (Found : C, 56·1 ; H, 4·5 ;

Cl, 9·2. $C_{18}H_{17}O_7Cl,0·25H_2O$ requires C, 56·1; H, 4·5; Cl, 9·2%). It was seen under the microscope to consist of dark red, hexagonal tables and short slender prisms, and it may have contained two hydrates, as the analyses suggested, one having been precipitated immediately on the addition of acid to the warm solution and the other having crystallised more slowly on cooling. The salt dissolves in sodium carbonate solution with a pure blue colour, and the same colour is obtained by adding sodium acetate to a freshly prepared solution in methyl alcohol.

To test the possibility of the presence of benzylated material, a portion of the specimen first analysed (0·1 g.) was finely powdered, suspended in glacial acetic acid (100 c.c.), and heated at 80° in a stream of dry hydrogen chloride during 3 hours. Only a very small portion of the salt dissolved, but complete debenzylation was assured under these conditions. The product was collected, washed, and dried: it gave the same qualitative reactions as the original specimen.

Comparison of the Colour Reactions of Hirsutidin Chloride (H) *with those of* 7 : 3′ : 5′-O-*Trimethyldelphinidin Chloride* (S) *and of* 5 : 3′ : 5′-O-*Trimethyldelphinidin Chloride* (A).—All the reactions of H were found on direct comparison to be identical with those of S and to differ from those of A. When ammonia was added to an alcoholic solution, a greenish-blue solution resulted; when derived from H or S, this was blood-red by transmitted artificial light, but under these conditions the A solution was violet or bluish-violet. By transmitted sunlight, H and S solutions were blue and violet in thick layers; A was greenish-blue. Alcoholic solutions of H and S were magenta; that of A was violet.

Under the standard procedure of Robertson and Robinson (*loc. cit.*), the colours in a range of buffered solutions from p_H 3·2 to p_H 11·6 were the following :—

H and S : (1) bluish-red, rapidly changing to brownish-red; (2) the same; (3) reddish-brown; (4) weak brownish-red; (5) violet tinged brownish-red; (6) fading violet; (7) bluish-violet, blue in thin layers; (8)—(15) inclusive, blue, red in shade by comparison with (A) solutions.

After ½ hour : (1), (2), (3) and (4), almost colourless but more coloured than (A) solutions; (5) very weak brownish-red; (6), (7) and (8), increasing violet; (9)—(12), blue, violet by transmitted artificial light; (13), (14) and (15), blue, redder violet by transmitted artificial light.

After 24 hours : (1)—(5), colourless; (6)—(8), increasing pale violet; (9)—(12), bluish-green; (13)—(15), greenish-blue.

(A) gave colours in marked contrast, on direct comparison : (1)

bluish-red; (2) same; (3) same, but fading; (4) bluer red, fading quickly; (5) reddish-violet, fading; (6) violet, fading; (7) and (8) no change; (9)—(15) inclusive, blue with green shade.

After ½ hour: (1)—(8), almost colourless; (9) very pale violet-blue; (10) blue, very different from (9); (11)—(15), greenish-blue.

After 24 hours: (1) and (2), colourless; (3), (4) and (5), colourless, minute flocculent precipitate (none in H and S); (6), (7), (8) and (9), very feeble yellowish-green; (11) and (12), very pale greenish-yellow; (13) weak orange-yellow; (14) and (15), pale orange.

Throughout, blue solutions of H and S were much redder by artificial light, but A gave blue solutions even when examined by artificial light.

4 : 5-*Dihydroxy*-3-*methoxybenzaldehyde* (XI).—A mixture of 5-bromovanillin (31 g.), copper bronze (12 g.), and 8% sodium hydroxide solution (600 c.c.) was heated in a rotating autoclave at 200—210° during 1 hour. The cooled product was acidified with a slight excess of dilute sulphuric acid and filtered from a small tarry precipitate; after 12 hours, crystalline material (0·98 g.) had separated and this also was removed. The dark filtrate (1400 c.c.) was concentrated under diminished pressure. The distillate (800 c.c.) gave only 0·24 g. of a red insoluble precipitate when mixed with an excess of 2 : 4-dinitrophenylhydrazine hydrochloride in 2*N*-hydrochloric acid. The residual solution was extracted with ether and the dark product so isolated was extracted with benzene, yielding almost pure 3-O-*methylgallaldehyde* (19·4 g.), m. p. 129—131° with slight previous softening. The aldehyde crystallised from water, benzene or light petroleum in almost colourless needles, m. p. 132—134° (Found in material dried at 100° in a vacuum: C, 57·3; H, 4·8. $C_8H_8O_4$ requires C, 57·1; H, 4·8%).

The 2 : 4-*dinitrophenylhydrazone* was precipitated when a cold solution of the aldehyde (0·44 g.) in water was added to an excess of 2 : 4-dinitrophenylhydrazine in 2*N*-hydrochloric acid. The solid was collected and dried at 100° (yield, 0·83 g. Calc., 0·88 g.). The hydrazone crystallised from ethyl alcohol, in which it was sparingly soluble, in dark red, pointed prisms, which began to decompose at 230° (Found in material dried over sulphuric acid: C, 48·2; H, 3·7; N, 15·5, 15·9. $C_{14}H_{12}O_7N_4$ requires C, 48·3; H, 3·5; N, 16·1%).

Methylation. Methyl sulphate (2·5 g.) and aqueous sodium hydroxide (10 c.c. of 10%) were added gradually and alternately to a suspension of the aldehyde (0·5 g.) in water (5 c.c.). The whole was mechanically shaken during 1 hour and then sodium hydroxide solution (10 c.c. of 20%) was added and the shaking continued.

During this process, the methylated aldehyde separated from the strongly alkaline solution in colourless needles (0·33 g.), m. p. 73—75°, and, after recrystallisation, m. p. 74—75° (Heffter and Capellmann give m. p. 77°, and Semmler and Mauthner, respectively, record the m. p.'s 75° and 74—75° for 3 : 4 : 5-trimethoxybenzaldehyde).

Acetylation. The aldehyde (1·7 g.) was acetylated by dissolving it in ether containing acetic anhydride (6 g.) and shaking the solution with water to which 5% aqueous potassium hydroxide (68 c.c.) was added in small successive amounts, the whole being cooled to 0°. The separated ethereal solution was washed with 5% aqueous potassium hydroxide, then with dilute sulphuric acid and water. The product crystallised from benzene–light petroleum in needles, m. p. 98—99° (Shriner and McCutchan record the m. p. 102—103° for the acetylation product, prepared by another method, and, on analysis, obtained data in agreement with the formula $C_{12}H_{12}O_7$, which indicates that the substance crystallises with $1H_2O$).

Methyl 5-*Hydroxy*-3 : 4-*diphenylmethylenedioxybenzoate* (VIII).—In the course of preliminary experiments on the condensation of diphenyldichloromethane with methyl gallate, considerable quantities of a sparingly soluble, oily by-product, probably $CPh_2[O{\cdot}C_6H_2(OH)_2{\cdot}CO_2Me]_2$, were obtained. A two-stage process under the following conditions gave the best results.

A solution of methyl gallate (84 g.) and pyridine (36·5 c.c.) in acetone (200 c.c.) was added to one of diphenyldichloromethane (108 g.) in acetone (100 c.c.) and kept for 12 hours. A solution of sodium hydroxide (37 g.) in water (100 c.c.) was then slowly added; the temperature rose and reached the boiling point of the mixture; after 2 hours, the whole was added to water (2000 c.c.). The brown oily material was separated and dissolved in ether, and the extract washed with aqueous sodium carbonate and then with aqueous sodium hydroxide (20 g. in 400 c.c.). The *methyl* ester precipitated from the latter extract on acidification was collected; it crystallised from benzene (yield, 60 g.; m. p. 163° after two crystallisations) in colourless needles, m. p. 165° (Found : C, 73·6; H, 5·0; loss at 110° in a vacuum, 10·1. $C_{21}H_{16}O_5,0{\cdot}5C_6H_6$ requires C, 73·7; H, 5·1; C_6H_6, 10·1%).

The presence of benzene in this material was confirmed by means of a test devised by Professor W. Ramsden. This can be used for the detection of traces of aromatic hydrocarbons, and depends on the insoluble film (often pink) obtained by condensation with formaldehyde in the presence of concentrated sulphuric acid. It may be demonstrated by shaking one drop of benzene with half a test-tube full of water, pouring away the liquid, and adding a few c.c. of sulphuric acid and two or three drops of 40% aqueous formaldehyde.

Methyl 3-Methoxy-4 : 5-diphenylmethylenedioxybenzoate (Methyl ester of IX).—Methyl hydroxydiphenylmethylenedioxybenzoate (68 g.) was dissolved in hot methyl alcohol (300 c.c.), the solution cooled and forthwith mixed with an alcoholic solution of sodium ethoxide (4·5 g. of sodium in 50 c.c.) and methyl iodide (20 c.c.). The mixture was gently boiled for ½ hour and, on cooling, short colourless prisms (61 g.), m. p. 134·5°, separated; the m. p. was not raised by recrystallisation (Found: C, 72·8; H, 5·2. $C_{22}H_{18}O_5$ requires C, 72·9; H, 5·0%). The *ester* (20 g.) was refluxed for 2 hours with water (100 c.c.) and potassium hydroxide (6 g.); the precipitate obtained on acidification of the cooled solution crystallised from aqueous acetone in thick polyhedral plates (16 g.), m. p. 217° (Found: C, 72·3; H, 4·7. $C_{21}H_{16}O_5$ requires C, 72·4; H, 4·6%).

This *3-methoxy-4 : 5-diphenylmethylenedioxybenzoic acid* (8 g.) was mixed with carbon tetrachloride (12 c.c.) and phosphorus pentachloride (8 g.), and the whole gently boiled until the evolution of hydrogen chloride slackened. The *chloride* crystallised, on the addition of light petroleum to the cooled clear liquid, in large compact prisms (1·5 g.), m. p. 109° (Found: Cl, 9·9. $C_{21}H_{15}O_4Cl$ requires Cl, 9·7%).

ω-*Diazo-3-methoxy-4 : 5-diphenylmethylenedioxyacetophenone*, $CPh_2O_2{:}C_6H_2(OMe){\cdot}CO{\cdot}CHN_2$.—A solution of methoxydiphenylmethylenedioxybenzoyl chloride (8·5 g.) in chloroform (20 c.c.) was slowly added to an ethereal solution of diazomethane (from 13 c.c. of nitrosomethylurethane and 75 c.c. of ether) cooled in a freezing mixture. A brisk evolution of nitrogen occurred and pale yellow needles separated (7·5 g.). The *substance* crystallised from benzene–light petroleum in yellow needles, which became darker at 135° and decomposed from 160—170°: these temperatures, however, are not characteristic and depend on a particular rate of heating (Found: C, 70·7; H, 4·6; N, 7·2. $C_{22}H_{16}O_4N_2$ requires C, 70·9; H, 4·4; N, 7·5%).

ω-*Acetoxy-3-methoxy-4 : 5-diphenylmethylenedioxyacetophenone* (XII).—The foregoing diazo-ketone (7·5 g.) was cautiously heated with acetic acid (20 c.c.) on the steam-bath for 15 minutes; the acetic acid was then distilled in a good vacuum. The residue crystallised from benzene–light petroleum in stout prisms (6·3 g.), m.p. 126—127° (Found: C, 71·6; H, 5·2. $C_{24}H_{20}O_6$ requires C, 71·3; H, 5·0%).

3-O-*Methylgallic Acid* (X).—A mixture of methyl 3-methoxy-4 : 5-diphenylmethylenedioxybenzoate (40 g.) and concentrated hydrochloric acid (150 c.c.) was refluxed for 2 hours, cooled, and neutralised with potassium bicarbonate. The undissolved benzophenone was pulverised, and the filtered solution acidified with hydrochloric acid, giving 16 g. of grey needles. The acid crystallised from water (charcoal) in elongated colourless prisms, m. p. 220°, in agreement with Fischer's statement (*loc. cit.*). The air-dried product was found to contain $\frac{1}{2}H_2O$ (Found : C, 49·6; H, 4·8; loss at 110° in a vacuum, 4·8. Calc. for $C_8H_8O_5,\frac{1}{2}H_2O$: C, 49·7; H, 4·7; H_2O, 4·7%). The *diacetyl* derivative was obtained by heating the acid (16 g.) with acetic anhydride (60 g.) and zinc chloride (1·5 g.) on the steam-bath for 2 hours. The product was purified by solution in aqueous potassium bicarbonate and recovery; it finally crystallised from aqueous alcohol in colourless prisms (17 g.), m. p. 170—171° (Found : C, 53·8; H, 4·7. $C_{12}H_{12}O_7$ requires C, 53·7; H, 4·5%).

4 : 5-*Diacetoxy*-3-*methoxybenzoyl chloride* was obtained by heating a mixture of the acid (15 g.), phosphorus pentachloride (12 g.), and chloroform (17 c.c.) until solution occurred and the reaction was completed. On addition of light petroleum and cooling in a freezing mixture, the derivative separated; it crystallised from carbon tetrachloride in stout prisms, m. p. 109° (Found : Cl, 12·6. $C_{12}H_{11}O_6Cl$ requires Cl, 12·4%).

ω-*Diazo*-4 : 5-*diacetoxy*-3-*methoxyacetophenone*,

$$(AcO)_2C_6H_2(OMe)\cdot CO\cdot CHN_2,$$

was obtained by the usual method and precipitated from the reaction mixture on the addition of light petroleum as a quickly crystallising oil (7 g. from 9·5 g. of the chloride). It crystallised from benzene–light petroleum at a low temperature in pale yellow, short prisms, m. p. 90—91° (Found : C, 53·4; H, 4·4; N, 9·2. $C_{13}H_{12}O_6N_2$ requires C, 53·4; H, 4·1; N, 9·6%).

ω : 4 : 5-*Triacetoxy*-3-*methoxyacetophenone* (XIII).—The foregoing diazo-ketone (5 g.) gave in the usual way 4·8 g. of pale yellow prisms. The *substance* crystallised from benzene–light petroleum in elongated prisms, m. p. 138·5°, softening at 136° (Found : C, 55·4; H, 5·0. $C_{15}H_{16}O_8$ requires C, 55·5; H, 5·0%).

5-O-*Benzoyl*-3′-O-*methyldelphinidin Chloride* (XIV).—(A) This is much the better of the two methods for the preparation of the salt; the condensation occurs with greater facility and the yield is higher than in (B).

A solution of ω-acetoxy-3-methoxy-4 : 5-diphenylmethylenedioxyacetophenone (1·6 g.) and 2-*O*-benzoylphloroglucinaldehyde (1 g.) in ethyl acetate (60 c.c.) was cooled in melting ice, saturated with hydrogen chloride, and kept for 12 hours under the pressure of the hydrogen chloride generator. The dark violet deposit of prisms, brown by transmitted light under the microscope, was collected (1 g.) and crystallised (0·9 g.) by solution in hot ethyl alcohol (200 c.c.) containing a few drops of concentrated hydrochloric acid and addition of 7% hydrochloric acid (200 c.c.) to the filtered solution. The glistening needles (0·5 g.) that separated had a fine bronze lustre (Found: C, 55·9; H, 4·4; MeO, 6·0; Cl, 7·1. $C_{23}H_{17}O_8Cl,2H_2O$ requires C, 56·1; H, 4·3; 1MeO, 6·3; Cl, 7·2%).

The substance is insoluble in water and acetone and very sparingly soluble in hot dilute hydrochloric acid. It gives a crimson alcoholic solution, becoming blue on the addition of ferric chloride. The alkali-colour reactions resemble those of *O*-benzoylcyanidin and *O*-benzoyldelphinidin chlorides.

(B) A mixture of ω : 4 : 5-triacetoxy-3-methoxyacetophenone (1·2 g.), 2-*O*-benzoylphloroglucinaldehyde (1 g.), and alcohol (25 c.c.) was cooled in melting ice and saturated with hydrogen chloride whilst being vigorously mechanically stirred. The temperature was then maintained at 35° for 2 hours, after which the dark red, homogeneous liquid was cooled in ice, and acetyl chloride (25 c.c.) slowly added during 1 hour. Next day, the violet deposit was collected (0·5 g.) and crystallised as described under (A). The colour reactions and other properties of this specimen were identical with those of the product obtained by the method A. It was apparent that the presence of the acetoxy-groups attached to the aromatic nucleus retarded the condensation, and flavylium salt was only obtained under conditions favouring the removal of the acetyl residues by hydrolysis. Herein lies the explanation of the necessity for the period of heating at 35° and the selection of a hydroxylic solvent.

3′-O-*Methyldelphinidin Chloride* (XV).—The benzoyl derivative (0·5 g.) was added to alcohol (5 c.c.) and 10% aqueous sodium hydroxide (5 c.c.), and the mixture kept for 2 hours and occasionally shaken; air was excluded by hydrogen, washed by permanganate and alkaline pyrogallol. After the addition of concentrated hydrochloric acid (3 c.c.), the whole was heated on the steam-bath for 1 hour, cooled, and more hydrochloric acid (10 c.c.) added. The dark precipitate was washed with acetone and ether and dried. The crude product was dissolved in ethyl alcohol (125 c.c.), containing a few drops of concentrated hydrochloric acid, and the filtered solution mixed with an equal volume of 7% hydrochloric acid. The chloride crystallised in yellowish-green, elongated, rhombohedral plates, yellowish-brown by transmitted light under the microscope (Found: C, 51·6; H, 4·0; Cl, 9·6; loss at 110° in a vacuum, 3·4. Found in material dried at 110°: C, 53·4; H, 3·9; Cl, 9·8. $C_{16}H_{13}O_7Cl,H_2O$ requires C, 51·9; H, 4·1; Cl, 9·6; $\frac{1}{2}H_2O$, 2·4%. $C_{16}H_{13}O_7Cl,\frac{1}{2}H_2O$ requires C, 53·2; H, 3·9; Cl, 9·8%). Apparently the salt loses rather more than $\frac{1}{2}H_2O$ at 110°, but, being then very hygroscopic, regains the composition $C_{16}H_{13}O_7Cl,\frac{1}{2}H_2O$ during the brief period of exposure preceding the analysis of the dried material by combustion.

3′-O-*Methyldelphinidin chloride* closely resembles cyanidin chloride in its general properties; the alcoholic acid solutions are a little bluer, and the precipitation of colour-base on the addition of water, so characteristic of cyanidin, does not take place to the same extent. The colour reactions in a range of buffered solutions (Robertson and Robinson, *loc. cit.*) were the following :—

(1) Deep cherry-red; (2) very slightly bluer; (3) the same; (4) a little bluer; (5) a little bluer, still cherry-red; (6) reddish-violet; (7) bluer reddish-violet; (8) bluer violet; (9) violet-blue in thin layers; (10) blue; (11), (12) and (13), greener blue; (14) greenish-blue, fading very rapidly; (15) greenish-blue, quickly changing to pale green. (3), (4) and (5) faded rapidly to brownish-red, and the presence of colour-base was confirmed by centrifuging the solution in a high-speed apparatus, a solid deposit and a colourless solution then being obtained.

After 3½ hours, the colours were : (1) and (2), colourless; (3), (4) and (5), colourless, brownish-red precipitate; (6) reddish-violet, a little precipitate; (7), (8) and (9), violet; (10), (11), (12) and (13), a series from greenish-blue to bluish-green; (14) and (15), orange.

After 24 hours : (1)—(8), colourless, with precipitate in (4), (5) and (6); (9)—(13), very weak orange to weak orange; (14) and (15), a little deeper orange.

These appearances (denoted as caused by S) were directly compared with those produced under the same conditions by natural petunidin chloride (P) (Willstätter and Burdick, *loc. cit.*), natural myrtillidin chloride (M) (Willstätter and Zollinger, *Annalen*, 1915, **408**, 83; 1916, **412**, 205), for specimens of which we are deeply indebted to Professor R. Willstätter, and with mixtures (DM) of malvidin chloride and delphinidin chloride. There was a very close resemblance between all these series when the anthocyanidin and buffered solutions were first mixed, especially between S and P, the only divergence being that P did not separate colour-base in (3), (4) and (5). S and P remained similar and, after 24 hours, were identical, but S and M diverged at several points after 10 minutes, and this divergence reached a maximum after 1 hour; after 24 hours, there were still marked differences, but, on long keeping, both S and M exhibited the deepest orange colour at (9) and (10). DM gave colours undoubtedly closer to M than to P, but there were differences between M and DM at certain points. Colorimetric observations of the blue ferric chloride and copper sulphate reactions in alcoholic solution showed that the order (stronger to weaker) was: S, P, M, DM; the ratio of intensity S/P was about 7/5.

The only conclusion which can be legitimately drawn from these observations at the present stage is that petunidin is not perfectly pure 3′-*O*-methyldelphinidin, but it is still possible that the anthocyanidin has essentially this constitution. Small percentages of impurities would suffice to change the crystal form and alter the composition of the hydrate.

Further work on this unsolved problem is in progress.

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