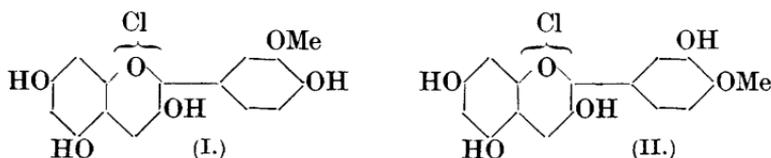


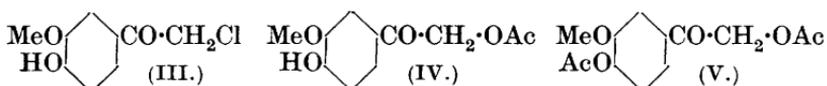
CCLXI.—*A Synthesis of Pyrylium Salts of Anthocyanidin Type. Part XI. A Synthesis of Peonidin Chloride.*

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WILLSTÄTTER and NOLAN (*Annalen*, 1915, **408**, 136) showed that peonin, the anthocyanin of the deep violet-red peony, yields, on hydrolysis with hydrochloric acid, glucose (2 mols.) and the anthocyanidin, peonidin chloride,  $C_{16}H_{13}O_6Cl$ , a monomethyl ether of cyanidin chloride. Furthermore, since the ferric chloride reaction was found to be very weak, it was suggested that the methoxy-group must be in one of the positions 3' and 4' in accordance with the expressions (I) and (II), of which the former was preferred.



A strong argument in favour of this view can now be advanced in connexion with the circumstance that peonidin dissolves in aqueous sodium carbonate to a pure blue solution. (I) is a methoxypelargonidin chloride, whilst (II) is a methoxy-derivative of the recently synthesised 3 : 5 : 7 : 3'-tetrahydroxyflavylium chloride (J., 1925, **127**, 1186); and since the alkali colour reaction of peonidin closely resembles that of pelargonidin and differs markedly from that of the *isopelargonidin*, the selection of the formula (I) is justified. An analogous constitution has been assigned to the flavonol, *isorhamnetin*, and in respect of both the anthocyanidin and the anthoxanthin the correctness of these conclusions has now been confirmed by synthesis. In an earlier paper (J., 1923, **123**, 753) it was shown that the condensation of veratrole and chloroacetyl chloride in presence of aluminium chloride under suitable conditions affords  $\omega$ -chloroacetovanillone (III), which may be reduced to acetovanillone.



The chloro-ketone yields the *acetoxy*-derivative (IV) on treatment with alcoholic potassium acetate, and the *diacetyl* derivative (V) is produced by subsequent acetylation. Both (IV) and (V) condense with 2 : 4 : 6-triacetoxybenzaldehyde in formic acid solution

in presence of hydrogen chloride, yielding products which give peonidin chloride on hydrolysis. The yield of the completely purified salt was small and in the synthesis of pelargonidin chloride by a similar method even greater difficulties were experienced.

#### EXPERIMENTAL.

*ω*-Acetoxy-4-hydroxyacetophenone,  $\text{HO}\cdot\text{C}_6\text{H}_4\cdot\text{CO}\cdot\text{CH}_2\cdot\text{OAc}$ .—A solution of *ω*-chloro-4-acetoxyacetophenone (30 g.) (Tutin, Caton, and Hann, J., 1909, **95**, 2119) and potassium acetate (20 g.) in alcohol (250 c.c.) was boiled for 4 hours, then filtered and concentrated by distillation of most of the alcohol. The oil precipitated by the addition of water to the residue was isolated by ether and solidified to a yellow mass (26 g.). The substance crystallises from benzene as a colourless crust, m. p. 127° (Found: C, 61·5; H, 5·2.  $\text{C}_{10}\text{H}_{10}\text{O}_4$  requires C, 61·8; H, 5·1%). It is soluble in aqueous sodium carbonate but not in the bicarbonate. The 4-acetoxy-group suffers hydrolysis in the above-described process.

*ω*:4-Diacetoxyacetophenone,  $\text{AcO}\cdot\text{C}_6\text{H}_4\cdot\text{CO}\cdot\text{CH}_2\cdot\text{OAc}$ .—This compound crystallised from light petroleum in colourless needles, m. p. 98° (Found: C, 61·0; H, 5·2.  $\text{C}_{12}\text{H}_{12}\text{O}_5$  requires C, 61·0; H, 5·1%), and was prepared from the foregoing phenol by the action of cold acetyl chloride during several hours. It is insoluble in aqueous sodium carbonate.

*Pelargonidin Chloride*,  $(\text{HO})_2\text{C}_6\text{H}_2\cdot\text{C}_3\text{HO}(\text{OH})\cdot\text{C}_6\text{H}_4\cdot\text{OH}\cdot\text{Cl}$ .—A solution of *ω*:4-diacetoxyacetophenone (6·0 g.) and 2:4:6-triacetoxybenzaldehyde (7·2 g.) in absolute formic acid (30 c.c.) was saturated with hydrogen chloride during 6 hours and then kept for 2 days. The solid precipitated by the addition of much ether was collected, dissolved in alcohol (200 c.c.), and after the addition of concentrated hydrochloric acid (20 c.c.) the solution was boiled for an hour, concentrated in a vacuum to a small bulk, and the precipitate collected. The flavylium salt was purified by repeated solution in boiling 0·5% hydrochloric acid and precipitation with concentrated acid and then by crystallisation from 1% hydrochloric acid and by evaporation of an alcoholic solution to which some 10% hydrochloric acid had been added. The substance was then crystallised as iodide from a mixture of phenol and hydriodic acid, reconverted in the usual manner into chloride, and finally crystallised from aqueous alcoholic hydrochloric acid. The products from two experiments were combined and ultimately about 0·05 g. of pure pelargonidin chloride exhibiting the correct crystalline form and reactions was isolated (Found: C, 55·9; H, 4·2; Cl, 10·7. Calc. for  $\text{C}_{15}\text{H}_{11}\text{O}_5\text{Cl}\cdot\text{H}_2\text{O}$ : C, 55·6; H, 4·0; Cl, 10·9%). Improvements in this direct synthesis of pelargonidin are still being sought.

*ω*-Acetoxy-3-methoxy-4-hydroxyacetophenone (IV).—*ω*-Chloroaceto-vanillone (20 g.), potassium acetate (15 g.), and alcohol (200 c.c.) were employed in the preparation of this substance under conditions identical with those described above. A solution of the crude product (15 g.) in a mixture of benzene and light petroleum very slowly deposited large, colourless prisms, m. p. 110° (Found: C, 59.1; H, 5.3. C<sub>11</sub>H<sub>12</sub>O<sub>5</sub> requires C, 58.9; H, 5.3%). The substance is readily soluble in aqueous sodium carbonate and in most organic solvents.

*ω*: 4-Diacetoxy-3-methoxyacetophenone (V).—The phenol last described was acetylated by means of acetyl chloride; the product crystallised from light petroleum in clusters of colourless needles, m. p. 73° (Found: C, 58.5; H, 5.4. C<sub>13</sub>H<sub>14</sub>O<sub>6</sub> requires C, 58.6; H, 5.3%). The substance is insoluble in aqueous sodium carbonate.

*Peonidin Chloride* (I).—(A) A solution of *ω*-acetoxy-3-methoxy-4-hydroxyacetophenone (5 g.) and 2:4:6-triacetoxybenzaldehyde (8.0 g.) in absolute formic acid (35 c.c.) was saturated with hydrogen chloride for 3 hours, being meanwhile cooled in running water. On the following day ether was added and the hygroscopic, crimson precipitate collected and boiled with a mixture of alcohol (150 c.c.) and concentrated hydrochloric acid (30 c.c.) for 10 minutes. Most of the alcohol was then evaporated, water (250 c.c.) added to the residue, and the mixture boiled and filtered. The deep bluish-red solution now became dichroic (bluish-red) on the addition of sodium carbonate, whereas peonidin develops a pure blue coloration. Attempts to induce the direct crystallisation of the anthocyanidin chloride were fruitless. The liquid was gently heated and picric acid (5 g.) introduced with stirring. The picrate, at first amorphous, soon crystallised in brownish-crimson leaflets and after cooling and standing for 12 hours was collected along with some picric acid.

(B) *ω*: 4-Diacetoxy-3-methoxyacetophenone (7 g.) was condensed with 2:4:6-triacetoxybenzaldehyde (7.5 g.) in a similar manner, except that the crude product was collected after the hydrolysis, extracted with boiling 0.5% hydrochloric acid (150 c.c.), and 10% hydrochloric acid (30 c.c.) added to the filtered solution. The whole was kept for 3 days in the ice-chest, and the brown, semi-crystalline material was then collected and dissolved in 0.5% hydrochloric acid (35 c.c.). No crystallisation occurred on keeping, but an amorphous film separated and was removed. Aqueous picric acid was added until the solution was almost decolorised, and the picrate was collected.

The picrates from (A) and (B) exhibited the same properties and

the subsequent procedure was identical in each case, the resulting peonidin chlorides being ultimately combined. The picrate separated from methyl alcohol in dark brownish-crimson, glistening, microscopic needles. The crystallised material was dissolved in methyl alcohol containing hydrogen chloride, and the chloride precipitated by ether in a flocculent condition. This process was repeated and the salt was then crystallised several times from dilute hydrochloric acid (at first 2% and later 1%), separating in chocolate needles which, air-dried, lost 4.9% in a vacuum over phosphoric anhydride (Found: C, 57.2; H, 3.9; MeO, 8.9.  $C_{16}H_{13}O_6Cl \cdot H_2O$  requires  $H_2O$ , 5.1%.  $C_{16}H_{13}O_6Cl$  requires C, 57.1; H, 3.9; MeO, 9.2%). Willstätter and Nolan (*loc. cit.*) showed that peonidin chloride crystallises with  $1H_2O$  which is lost in a vacuum. A small specimen of peonidin chloride was available for direct comparison and the synthetical material showed all the properties of the material of natural origin. The appearance and shape of the crystals under the microscope, the solubility relations and colour (visual comparison of absorption spectra) of the solutions in aqueous acid and alcohol, the speed of pseudo-base formation, and the extent of recovery of colour on acidification, as well as the behaviour with potassium acetate and sodium carbonate, were all observed with identical results in the case of the two specimens. The synthetical specimen gave a weaker reaction than the natural specimen with ferric chloride, no doubt because the latter contained a trace of cyanidin.

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