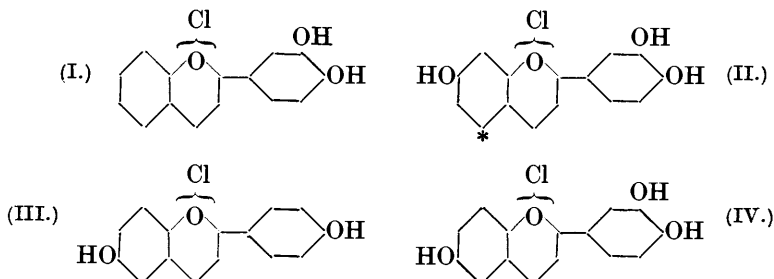


CCLIX.—*A Synthesis of Pyrylium Salts of Anthocyanidin Type. Part IX. Some Hydroxyflavylium Salts.*

By ALEXANDER ROBERTSON and ROBERT ROBINSON.

A KNOWLEDGE of the behaviour of various hydroxylated flavylium salts is of great importance as an accessory in the determination of the constitution of the anthocyanins and we have prepared new members of the group in order to confirm conclusions already drawn and to ascertain whether fresh features of interest would emerge. An intense ferric chloride reaction in this series is regarded by Willstätter as diagnostic of a free catechol grouping, the hydroxyl groups being usually in positions 3' and 4'. We now find that the simplest conceivable flavylium salt (I) satisfying the condition

exhibits the reaction and therefore there can be no auxiliary requirements. Other 3' : 4'-dihydroxyflavylium salts described in



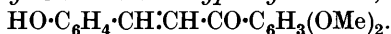
this communication develop an intense coloration with ferric chloride, whilst those not containing *o*-situated hydroxyl groups do not. Butinidin chloride (II) exhibits practically the same reactions with alkalis as luteolinidin chloride, which contains a further hydroxyl group in the asterisked position 5. This confirms the view, previously arrived at from a comparison of fisetinidin and cyanidin, that position 5 is of little value in the alkali reaction provided that position 7 is hydroxylated.

The effect of a hydroxyl group in position 6 on the alkali colour reaction of flavylium salts is remarkable. 6 : 4'-Dihydroxyflavylium chloride (III) and 6 : 3' : 4'-trihydroxyflavylium chloride (IV) dissolve in aqueous sodium carbonate to stable crimson and purplish-blue solutions, respectively.

All the salts described in this communication are completely extracted from an aqueous acid solution by *iso*amyl alcohol.

#### EXPERIMENTAL.

##### 2-Hydroxystyryl 3 : 4-Dimethoxyphenyl Ketone,



—A mixture of salicylaldehyde (2.4 g.), acetoveratrone (3.6 g.), potassium hydroxide (4 g.) dissolved in a little water, and methyl alcohol (200 c.c.) was boiled under reflux for 8 hours, then cooled, and acidified with dilute acetic acid. The dark orange oil precipitated by the addition of water solidified on standing; it (4.5 g.) then crystallised from methyl alcohol in glistening, orange-yellow, elongated prisms, melting at 150—151° to a dark green liquid (Found: C, 71.5; H, 5.6.  $\text{C}_{17}\text{H}_{14}\text{O}_4$  requires C, 71.8; H, 5.6%).

3' : 4'-Dimethoxyflavylium Ferrichloride.—The unsaturated ketone (4 g.) just described was converted by the action of hydrogen chloride in cold absolute formic acid solution into a pyrylium chloride, which was isolated (3.9 g.) by the addition of ether and crystallised from 2% hydrochloric acid in fine red needles. The

*ferrichloride* was precipitated in the usual manner as a red, amorphous mass and crystallised from acetic acid in red plates with jagged saw-like edges, exhibiting a brilliant green reflex. The salt, m. p. 196—196·5°, is moderately readily soluble in hot acetic acid (Found: C, 44·2; H, 3·4.  $C_{17}H_{15}O_3Cl_4Fe$  requires C, 43·9; H, 3·2%).

3' : 4'-*Dihydroxyflavylium Chloride* (I).—A mixture of 3' : 4'-dimethoxyflavylium chloride (3 g.), phenol (8 g.) and hydriodic acid (60 c.c.;  $d$  1·7) was gently boiled for 30 minutes in an atmosphere of carbon dioxide and on cooling, the demethylated iodide partly separated in red, prismatic needles. After the addition of water (50 c.c.) and ether (100 c.c.), the salt was collected, washed with ether, and dried (2·5 g.). The iodide was dissolved in methyl alcohol (150 c.c.) containing a trace of hydrogen chloride and converted into the *chloride* by treatment with an excess of silver chloride at the b. p. of the solvent for 15 minutes. The filtered solution, after being concentrated to half its volume, was mixed with 50 c.c. of 10% hydrochloric acid; on cooling, dark red, prismatic needles were deposited (Found in material dried in a high vacuum over sulphuric acid for 48 hours: C, 63·4; H, 4·5.  $C_{15}H_{11}O_3Cl, 0\cdot5H_2O$  requires C, 63·5; H, 4·2%). The analysed specimen was hygroscopic; its alcoholic ferric chloride reaction was intense purplish-violet and its solution in aqueous sodium carbonate was violet and stable for 15 minutes. The violet coloration did not become blue on the addition of sodium hydroxide.

7-Hydroxy-3' : 4'-*dimethoxyflavylium Ferrichloride*.—A slow stream of dry hydrogen chloride was led through a solution of  $\beta$ -resorcyaldehyde (3·45 g.) and acetoveratrone (4·25 g.) in acetic acid (20 c.c.) for 3 hours and next day the pyrylium salt was precipitated by the addition of ether (400 c.c.). It crystallised from 2% hydrochloric acid in characteristically twinning, stellate aggregates of slender, red needles (yield, 3·5 g.). The corresponding *ferrichloride* crystallised from acetic acid in dull, brick red, slender, prismatic needles, m. p. 182—183° (Found: C, 42·4; H, 3·4.  $C_{17}H_{15}O_4Cl_4Fe$  requires C, 42·3; H, 3·1%).

7 : 3' : 4'-*Trihydroxyflavylium Chloride* (*Butinidin Chloride*) (II).—7-Hydroxy-3' : 4'-dimethoxyflavylium chloride (2·5 g.) was subjected to a demethylation process similar to that described above and, on cooling, the iodide separated in red prisms (2 g.). After this had been converted into the *chloride*, the volume of the hot methyl-alcoholic solution was reduced to 50 c.c. and 50 c.c. of 10% hydrochloric acid were added. Dark red, prismatic needles with a purple lustre separated, and these were washed and dried in a high vacuum over sulphuric acid for 48 hours (Found: C, 60·4;

H, 4.2.  $C_{15}H_{11}O_4Cl \cdot 0.5H_2O$  requires C, 60.1; H, 4.0%). The orange-red solution in alcohol becomes pink on dilution and gives a bluish-violet coloration on the addition of ferric chloride. The alkali reactions in alcoholic solution resemble those of mecocyanin in aqueous solution, that is, with sodium carbonate a fine reddish-blue is obtained and this becomes greenish-blue on the addition of sodium hydroxide. In aqueous solution, the colours, especially with sodium hydroxide, are much redder.

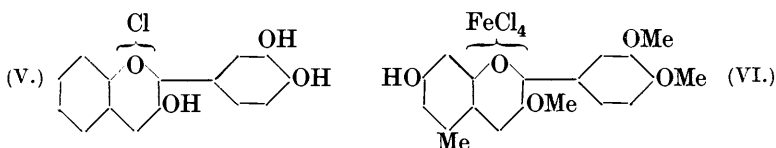
*3 : 3' : 4'-Trimethoxyflavylium Ferrichloride*.—The condensation of salicylaldehyde and  $\omega$ -methoxyacetoveratrone\* (J., 1925, 127, 170) in methyl-alcoholic solution in presence of potassium hydroxide did not proceed in a satisfactory manner, but the direct process was found to be feasible in this case.† A solution of salicylaldehyde (1.4 g.) and  $\omega$ -methoxyacetoveratrone (2 g.) in acetic acid (10 c.c.) was saturated with hydrogen chloride for  $\frac{1}{2}$  hour, and the pyrylium salt then precipitated as a red mass by the addition of ether. The chloride is readily soluble in dilute hydrochloric acid and crystallises from 10% hydrochloric acid in very slender, long, red needles with a golden-green reflex. The *ferrichloride*, prepared in the usual way, crystallised from acetic acid in long, glistening, dark reddish-crimson prisms, m. p. 173° (Found : C, 43.7; H, 3.4.  $C_{18}H_{17}O_4Cl_4Fe$  requires C, 43.6; H, 3.4%).

*3 : 3' : 4'-Trihydroxyflavylium Chloride* (V).—A mixture of 3 : 3' : 4'-trimethoxyflavylium chloride (4.5 g.), phenol (12 g.), and hydriodic acid (100 c.c.; *d* 1.7) was gently boiled (oil-bath at 130—132°) in a stream of carbon dioxide for 30 minutes. After the introduction of water (50 c.c.) the phenolic layer was separated, added to an excess of ether, and the red precipitate of the iodide collected and dried (2.5 g.). Following conversion of the iodide into the *chloride* in the usual manner in methyl-alcoholic solution, the volume of the liquid was reduced to 20 c.c. and warm concentrated hydrochloric acid (5 c.c.) and ether (100 c.c.) were successively added, the mixture being then kept in a stoppered vessel. Slender, dark brown, prismatic needles gradually separated and these were collected and dried in a high vacuum over phosphoric anhydride for 48 hours. The substance acquired a dull green reflex and was very hygroscopic (Found : C, 56.9; H, 4.8.  $C_{15}H_{11}O_4Cl \cdot 1.5H_2O$  requires C, 56.7; H, 4.4%). This salt is very readily soluble in dilute hydrochloric acid. A purplish-violet coloration is developed

\* Employing ethyl methoxyacetate (150 g.) and sodium (18 g.), we obtained 90—92 g. of ethyl  $\alpha$ -dimethoxyacetoacetate, b. p. 128—130°/15 mm.; and from 38 g. of the latter ester and 40 g. of veratroyl chloride, 23 g. of  $\omega$ -methoxyacetoveratrone, m. p. 62°, could be isolated.

† Exceptional when salicylaldehyde is one of the components.

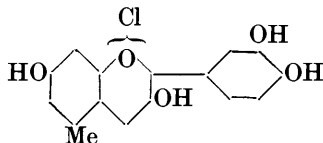
with ferric chloride in alcoholic solution, whilst sodium carbonate gives a reddish-purple coloration which quickly fades, especially in aqueous solution. The addition of sodium hydroxide to an acid aqueous solution gives almost at once a yellow liquid. The behaviour recalls that of galanginidin chloride and therefore stability to alkalis appears to be associated with the simultaneous occurrence of hydroxyl groups in both benzene nuclei of the flavylum system.



*7-Hydroxy-3:3':4'-trimethoxy-5-methylflavylum Ferrichloride (VI).*

—A stream of hydrogen chloride was passed through a solution of orcyaldehyde (2 g.) and  $\omega$ -methoxyacetoveratrone (2.5 g.) in absolute formic acid (15 c.c.) for 2 hours. The chloride partly separated in fine, dark red, elongated prisms with a striking golden glance and a further quantity was precipitated by the addition of ether (yield, 3.5 g.). The salt is moderately readily soluble in hot 1% hydrochloric acid and crystallises, on cooling, in deep crimson needles which are bronze in mass; it is sparingly soluble in hot 10% hydrochloric acid. The rhodamine-pink solution in alcohol becomes crimson on the addition of sodium acetate and the aqueous solution is completely decolorised on great dilution, the colour being fully restored by the addition of hydrochloric acid. The *ferrichloride* crystallised from acetic acid in long, reddish-brown prisms, melting at 182–183° to a green liquid after softening at 178° (Found: C, 43.6; H, 4.0.  $C_{19}H_{19}O_5Cl_4Fe$  requires C, 43.5; H, 3.6%). This derivative is more readily soluble in cold acetic acid than most flavylum ferrichlorides; it exhibits a golden-green streak when rubbed on a glass surface.

*3:7:3':4'-Tetrahydroxy-5-methylflavylum Chloride,*



—In the demethylation of the chloride (2 g.) described in the last section, the usual method was employed, but the amount of phenol had to be increased (to 26 g.) in order to avoid premature separation of iodides. The bright red, prismatic needles (1.8 g.) of the iodide were collected and converted into the *chloride*, by means of silver

chloride, in ethyl-alcoholic solution (500 c.c.) containing concentrated hydrochloric acid (10 c.c.). The liquid was concentrated by distillation to about half its volume; on cooling, the chloride was deposited as a mass of slender, crimson needles with a brilliant green reflex (Found in material dried in a vacuum over sulphuric acid for 24 hours: C, 58.9; H, 4.4; and in material dried in a vacuum over phosphoric anhydride for 24 hours and then at 105° in a high vacuum for 20 minutes: C, 60.1; H, 4.4.  $C_{16}H_{13}O_5Cl \cdot 0.25H_2O$  requires C, 59.1; H, 4.2%.  $C_{16}H_{13}O_5Cl$  requires C, 60.0; H, 4.1%). This salt is sparingly soluble in cold 1% hydrochloric acid and in hot 10% hydrochloric acid. It is also sparingly soluble in alcohol, giving a bluish-pink solution. Its ferric chloride reaction is similar to that of fisetinidin and cyanidin. In aqueous solution it gives a pure blue coloration with sodium carbonate or sodium hydroxide and in alcoholic solution the reaction closely resembles that of cyanidin.

6 : 4'-*Dihydroxyflavylium Chloride* (III).—6 : 4'-Dimethoxyflavylium chloride (Ridgway and Robinson, J., 1924, **125**, 221) (3 g.) was demethylated in the usual manner in presence of phenol (18 g.), and the iodide (2.8 g.) was precipitated by the addition of ether to the separated phenolic layer. Conversion into the *chloride* was accomplished in boiling 2% hydrochloric acid solution by means of silver chloride; the salt separated from the filtered solution in long, glistening, orange-red needles which were recrystallised from 2% hydrochloric acid and then dried in a high vacuum over sulphuric acid for 24 hours (Found: C, 61.8; H, 4.4.  $C_{15}H_{11}O_3Cl \cdot H_2O$  requires C, 61.5; H, 4.4%). Sodium carbonate or hydroxide added to an aqueous acid solution gives a stable, bright crimson solution. The shade is a little bluer in alcoholic solution.

6 : 3' : 4'-*Trimethoxyflavylium Ferrichloride*.—Hydrogen chloride was passed into a mixture of 2-hydroxy-5-methoxybenzaldehyde (3.0 g.), acetoveratrone (3.6 g.), and acetic acid (20 c.c.) for 1 hour and, next day, ether (400 c.c.) was added, causing the separation of the pyrylium salt in an amorphous condition. The substance was collected, dissolved in hot 5% hydrochloric acid, and sufficient hot concentrated hydrochloric acid added to the filtered liquid to produce a 15% acid solution. On cooling, the salt crystallised in stellate aggregates of slender, red needles (6 g.). The *ferrichloride*, prepared in the usual manner, crystallised from a rapidly cooled solution in acetic acid in dull, red needles, but, by slow cooling, it could be obtained in red plates, m. p. 186°, exhibiting a bright green reflex (Found: C, 43.5; H, 3.5.  $C_{18}H_{17}O_4Cl_4Fe$  requires C, 43.6; H, 3.4%).

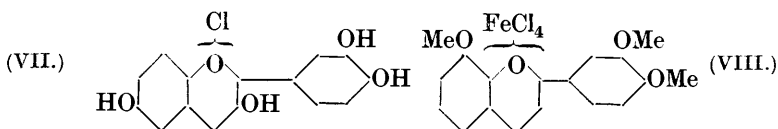
6 : 3' : 4'-*Trihydroxyflavylium Chloride* (IV).—The chloride (2.5 g.)

last described was demethylated in the usual way in presence of phenol (2 g.), and the resulting iodide (1.5 g.) was deposited from the cooled hydriodic acid solution in stellate aggregates of bright red needles. The double decomposition with silver chloride was carried out in presence of hot 5% hydrochloric acid and after the reaction the concentration of acid in the filtered solution was doubled. Almost complete separation of the salt ensued on cooling and the substance was recrystallised in a similar manner and obtained in long, dark crimson, prismatic needles with a bluish-purple lustre (Found in material dried in a high vacuum over sulphuric acid for 24 hours: C, 58.1; H, 4.2.  $C_{15}H_{11}O_4Cl \cdot H_2O$  requires C, 58.3; H, 4.2%). Ferric chloride added to the deep red, alcoholic solution produces a purplish-violet coloration, whilst the colour of the solution in aqueous sodium carbonate is purplish-blue and stable. In presence of sodium hydroxide the blue colour is similar, but gradually becomes green and fades.

3 : 6 : 3' : 4'-*Tetramethoxyflavylium Ferrichloride*.—The condensation of 2-hydroxy-5-methoxybenzaldehyde (2.3 g.) and  $\omega$ -methoxyacetoveratrone (3 g.) was carried out like the analogous process last described; the salt precipitated by ether crystallised from 5% hydrochloric acid in very long, slender, bright red needles (5.4 g.). The *ferrichloride* is readily soluble in formic acid and sparingly soluble in acetic acid; it crystallises from a mixture of equal volumes of the two in long, shining, dark red, prismatic needles, m. p. 198—199° (Found: C, 43.6; H, 3.7.  $C_{19}H_{19}O_5Cl_4Fe$  requires C, 43.5; H, 3.6%).

3 : 6 : 3' : 4'-*Tetrahydroxyflavylium Chloride* (VII).—4.5 Grams of 3 : 6 : 3' : 4'-tetramethoxyflavylium chloride were demethylated by hydriodic acid (150 c.c.;  $d$  1.7) in presence of phenol (24 g.) as usual, and water (100 c.c.) was added to the cooled solution. The phenolic layer was separated and added to ether (500 c.c.), which caused the deposition of a mass of microscopic, red needles (2.3 g.). Conversion into the *chloride* and crystallisation of the resulting salt were accomplished in 2% and from 10% hydrochloric acid solutions, respectively, and on recrystallisation from 10% hydrochloric acid (2% increased to 10% by the addition of concentrated acid) the chloride was obtained in dark red plates exhibiting a brilliant green glance (Found in material dried in a high vacuum over phosphoric anhydride for 48 hours; C, 58.9; H, 4.0.  $C_{15}H_{11}O_5Cl$  requires C, 58.7; H, 3.6%). The eosin-red, alcoholic solution gives a violet-blue coloration with ferric chloride. The solution in aqueous sodium carbonate is reddish-blue, whilst in alcoholic sodium carbonate only a permanganate-coloured solution is obtained—a quite unusual reversal of the changes commonly

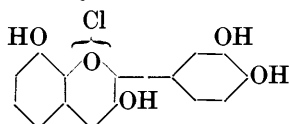
observed. Sodium hydroxide produces unstable colorations, but in alcoholic solution the reaction is pure blue.



8 : 3' : 4'-*Trimethoxyflavylium Ferrichloride* (VIII).—Hydrogen chloride was led for 2 hours into a cold solution of *o*-vanillin (1.7 g.) and acetoveratrone (2 g.) in formic acid (8 c.c.) and, after a few hours, the pyrylium salt was precipitated by ether and collected (3 g.). The chloride crystallised very slowly from a solution in 5% hydrochloric acid in red, prismatic needles (1.5 g.). This salt is readily soluble even in moderately concentrated hydrochloric acid, and it does not appear to be so stable as the majority of analogous substances. The *ferrichloride* crystallises from acetic acid in short, pointed, flat prisms, m. p. 193—194° (Found : C, 43.6; H, 3.4.  $C_{18}H_{17}O_4Cl_4Fe$  requires C, 43.6; H, 3.4%). The derivative has a dark red colour in suspension in acetic acid, but in mass appears green on account of the brilliant reflex. All attempts to demethylate the salts of this series were fruitless, and complete decomposition occurred under the usual conditions.

3 : 8 : 3' : 4'-*Tetramethoxyflavylium Ferrichloride*.—The condensation of *o*-vanillin and  $\omega$ -methoxyacetoveratrone with the aid of hydrogen chloride was carried out in acetic acid solution, and the crude product precipitated by ether was dissolved in 2% hydrochloric acid; after the concentration of the acid had been quintupled, the chloride crystallised in long, dark crimson needles with a purple lustre. A further quantity was collected after the hydrochloric acid concentration had been brought to 15%. The total yield was good. The *ferrichloride* crystallised from acetic acid in long, glistening, dark red, prismatic needles, m. p. 162—163° (Found : C, 43.7; H, 3.8.  $C_{19}H_{19}O_5Cl_4Fe$  requires C, 43.5; H, 3.6%).

3 : 8 : 3' : 4'-*Tetrahydroxyflavylium Chloride*,



—A mixture of 3 : 8 : 3' : 4'-tetramethoxyflavylium chloride (2 g.), phenol (14 g.), and hydriodic acid (75 c.c.; *d* 1.7) was gently boiled (bath at 130—132°) for 30 minutes in an atmosphere of carbon dioxide. After the addition of water (50 c.c.), the phenolic layer was separated and the iodide (1.0 g.) precipitated as a bright red, amorphous mass by the addition of ether (300 c.c.). The iodide



(2 g.) was dissolved in methyl alcohol (80 c.c.) containing a trace of hydrogen chloride, and the solution heated for 15 minutes after the introduction of an excess of precipitated silver chloride. The filtered liquid was concentrated to one-half its volume, 5 c.c. of concentrated hydrochloric acid were added, and the solution was concentrated to about 30 c.c. The salt then separated, on the gradual addition of ether, in aggregates of microscopic, prismatic needles. A solution of the salt in a little 5% hydrochloric acid was mixed with so much concentrated acid that the concentration was raised to 15% and, on standing 48 hours, dark red, prismatic needles were deposited and were then collected. The yield was poor and the material from several operations was combined and twice recrystallised in a similar manner (Found in material dried over phosphoric anhydride in a high vacuum for 36 hours: C, 55.2; H, 5.1; and in material dried similarly for 18 days: C, 59.0; H, 4.3.  $C_{15}H_{11}O_5Cl$  requires C, 58.7; H, 3.6%.  $C_{15}H_{11}O_5Cl \cdot H_2O$  requires C, 55.4; H, 4.0%).

The high values found for the hydrogen content are undoubtedly due to the extremely hygroscopic nature of this salt. The orange-red alcoholic solution becomes purplish-violet on the addition of ferric chloride. With sodium carbonate, this isomeride of fisetinidin chloride gives an unstable purplish-red coloration, and the reaction with sodium hydroxide is similar.

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