

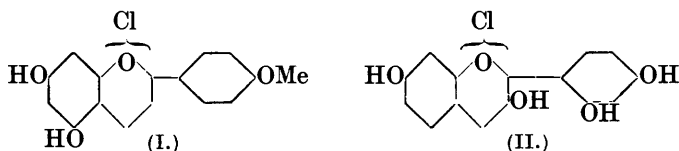
CCLVIII.—*A Synthesis of Pyrylium Salts of Anthocyanidin Type. Part XII.*

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WHEN acacetinidin chloride (I) (Part IV, Pratt, Robinson, and Williams, J., 1924, 125, 200) was demethylated, it yielded a very well-characterised trihydroxyflavylium chloride which had the reactions but not the crystalline form of apigeninidin chloride prepared by demethylation of its trimethyl ether (Part VI, J., 1925, 127, 1133). The properties of the two specimens were closely similar, but not identical in every respect, and for this reason there was a doubt in regard to the course of the condensation of benzoyl-acetaldehyde and its derivatives with phloroglucinol in the presence of hydrogen chloride. Hitherto no unmethylated phloroglucin-aldehyde derivative could be condensed with ketones of the form  $\text{CH}_3\cdot\text{CO}\cdot\text{R}$  to flavylium salts, but we have now found that *O*-benzoylphloroglucinaldehyde (this vol., p. 1713) can be utilised for this purpose. With *p*-methoxyacetophenone, it gives a benzoylacacetinidin chloride, and, after hydrolysis with methyl-alcoholic ammonia and subsequent treatment with hydrochloric acid, acacetinidin chloride, identical with the salt already described, was obtained. There is, therefore, no doubt that the condensation of anisoylac-

aldehyde and phloroglucinol proceeds normally and does not, as was at one time suspected, give rise to an *epiflavylum* derivative. The specimen of apigeninidin chloride, prepared as described in this communication, is unquestionably more pure than that which was obtained previously by demethylation of the trimethyl ether. These results have been confirmed in the chrysinidin series and one and the same chrysinidin has been obtained on the one hand by the condensation of benzoylacetaldehyde and phloroglucinol, and on the other by hydrolysis of the benzoylchrysinidin chloride derived from *O*-benzoylphloroglucinaldehyde and acetophenone.

The condensation of benzoylacetaldehyde with acetophenone by means of hydrogen chloride in acetic acid solution was first described by Bülow and Sicherer (*Ber.*, 1901, **34**, 3896). The quantity of acetic acid employed was not stated, but the red product,  $C_{15}H_{13}O_4Cl$ , was very sparingly soluble in organic solvents and soon separated from the reaction mixture. These authors do not mention the necessity for any special precautions in carrying out the process, and in the first attempts which we made to repeat it the product was invariably an ochre-red, very sparingly soluble substance which separated quickly in almost quantitative amount. This substance can be easily prepared by adding phloroglucinol and benzoylacetaldehyde in molecular proportion to formic acid or by adding a few drops of hydrochloric acid to an acetic acid solution of the components. It appears to have the composition  $C_{30}H_{22}O_7$  and, on treatment with a boiling mixture of acetic and hydrochloric acids, it slowly passes into chrysinidin chloride. Later it was found that the Bülow condensation could be effected in ethereal solution, and also in acetic acid solution if the materials were free from water and access of moisture to the reaction mixture was prevented. In the latter case, the dark reddish-brown product had the composition  $C_{15}H_{11}O_3Cl$  and only began to separate after some hours. An account of the preparation of resomorinidin chloride (II) is included in this communication.



#### EXPERIMENTAL.

*Trianhydrobisbenzoylacetalddehydphloroglucinol*. — Cold filtered solutions of benzoylacetaldehyde (2.9 g.) in formic acid (5 c.c.) and of phloroglucinol (2.5 g.) in formic acid (40 c.c.) were mixed; an orange-red product soon began to separate. After 2 hours,

water was added and the substance was collected, washed, and dried at 100° (Found: C, 72.9, 73.2; H, 4.5, 4.6.  $C_{30}H_{22}O_7$  requires C, 72.8; H, 4.5%). The yield was 5.1 g., and only when relatively more phloroglucinol was employed could the phenol be detected in the filtrate. The substance can also be obtained by addition of a few drops of hydrochloric acid to a solution of the components in equimolecular proportion in acetic acid or by passing hydrogen chloride into an acetic acid solution of benzoylacetaldehyde and phloroglucinol without precautions aimed at the exclusion of water. Attempts to crystallise this very sparingly soluble compound were unsuccessful. On heating, the substance darkens slightly from 210—280° and above this temperature gradually chars without melting.

*Chrysinidin Chloride* (5 : 7-Dihydroxyflavylium Chloride).—(A) The product of condensation of benzoylacetaldehyde and an equivalent amount of anhydrous phloroglucinol in ethereal solution by means of hydrogen chloride in the cold during 4 hours was collected and extracted with boiling dilute hydrochloric acid. The salt crystallised from the hot filtrates (poor yields) in reddish-brown prismatic needles, which were dried over sulphuric acid (Found: C, 58.7; H, 4.7.  $C_{15}H_{11}O_3Cl \cdot 2H_2O$  requires C, 58.1; H, 4.8%). This salt darkens at 250° but does not melt at 300°. Its yellow solution in concentrated sulphuric acid does not fluoresce, nor do the orange-red alcoholic solutions exhibit this property. The salt is sparingly soluble in aqueous hydrochloric acid (even 0.05%) and dissolves in aqueous sodium carbonate to a deep brownish-red solution which is orange in thin layers. Sodium hydroxide gives the same colour, but the solutions soon become orange, especially on heating.

(B) A solution of the salt was obtained by boiling the orange-red compound,  $C_{30}H_{22}O_7$ , for 6 hours with an excess of a mixture of acetic acid (2 vols.) and concentrated hydrochloric acid (1 vol.). Water was added, and the perchlorate precipitated from the filtered solution.

(C) A solution of anhydrous phloroglucinol (5 g.) and benzoylacetaldehyde (8 g.) in pure glacial acetic acid (35 c.c.) was saturated with hydrogen chloride in an apparatus designed to exclude moist air, and then kept for 12 hours. The deep reddish-brown crystals which slowly separated were collected, washed with acetic acid, and dried over sodium hydroxide in a vacuum (Found: C, 65.6, 65.4; H, 4.4, 4.1.  $C_{15}H_{11}O_3Cl$  requires C, 65.6; H, 4.0%). The yield was 2 g. By adding ether to the filtrate a solid was precipitated which was extracted by boiling 0.5% hydrochloric acid; this gave a further 2.2 g. of chrysinidin chloride and left 5.5 g. of a dark red, insoluble material.

(D) A cold solution of *O*-benzoylphloroglucinaldehyde (1.6 g.) and acetophenone (3 g.) in dry ethyl acetate (30 c.c.) was saturated with hydrogen chloride and kept for 3 days. The orange-red liquid acquired a greenish-yellow fluorescence and gradually deposited crystals (2 g.). The orange *O*-benzoylchrysinidin chloride (1.9 g.) was dissolved in methyl alcohol (100 c.c.) and the solution was saturated with ammonia at 0° and kept at this temperature for 24 hours. The ammonia and methyl alcohol having been removed under diminished pressure at room temperature, the residue was dissolved in warm methyl alcohol (20 c.c.), and hot hydrochloric acid (40 c.c.) added. The amorphous precipitate was collected and extracted with boiling 0.5% hydrochloric acid, and the salt again precipitated from the filtered solution by the addition of concentrated hydrochloric acid. It was now partly crystalline and was converted into the perchlorate, which was fully purified.

*Chrysinidin perchlorate.* The various specimens of chrysinidin chloride have been identified with each other by conversion into this characteristic derivative, which crystallises from acetic acid in glistening, deep red, rectangular, prismatic needles (Found in material from B above: C, 53.3; H, 3.4.  $C_{15}H_{11}O_7Cl$  requires C, 53.2; H, 3.3%). The substance darkens at 208° and melts with decomposition at 244°. It is very readily soluble in alcohol and on the addition of aqueous perchloric acid the substance crystallises in slender, glistening, orange-red needles. Careful comparison showed that all the specimens were identical; on the other hand, the chrysinidin obtained by demethylation of the dimethyl ether (Part VI, *loc. cit.*) must have been contaminated with methoxy-containing salts, since the perchlorate decomposed at 185°.

*O-Benzoylacacetinidin Chloride.*—A solution of *O*-benzoylphloroglucinaldehyde (0.6 g.) and *p*-methoxyacetophenone (2 g.) in dry ethyl acetate (30 c.c.) was saturated in the cold with hydrogen chloride; in the course of an hour it became deep orange and exhibited a striking greenish-yellow fluorescence. The mixture was kept for 3 days and the salt which had separated was then collected (2 g.); a further quantity (0.5 g.) was obtained by addition of ether to the filtrate. Concentrated hydrochloric acid was added to a solution of the salt in a hot mixture of equal volumes of alcohol and 0.5% hydrochloric acid until a faint turbidity appeared; on cooling, the substance crystallised in bright, orange-red sheaves of slender, prismatic needles (Found in material dried over sulphuric acid: C, 64.6; H, 4.7.  $C_{23}H_{17}O_5Cl \cdot H_2O$  requires C, 64.7; H, 4.5%). The alcoholic solutions of this benzoylacacetinidin chloride are orange to orange-red and exhibit strong green fluorescence.

*Acacetinidin Chloride (I).*—The debenzoylation of benzoylacacetin-

idin chloride (3 g.) was accomplished in much the same way as described above in the case of benzoylchrysinidin chloride and the crude acacetinidin chloride (1.5 g.) was crystallised by solution in hot 0.5% hydrochloric acid and addition of concentrated hydrochloric acid until turbidity appeared. After three such processes, the salt was obtained in microscopic, reddish-brown balls. It was then crystallised by addition of concentrated hydrochloric acid to an alcoholic solution and obtained in prismatic needles, and on repetition in diamond-shaped and rhombic plates with a brilliant green reflex but exhibiting much twinning. A third crystallisation in this way gave clear-cut, individual crystals having a form identical with that of crystals of acacetinidin chloride (Part IV, *loc. cit.*). The reactions of the two specimens were also identical and in addition the perchlorates and picrates were examined and compared, with the result that no difference could be detected between the specimens of the respective derivatives obtained from benzoylacacetinidin chloride from acacetinidin chloride.

*Acacetinidin perchlorate* crystallised from hot aqueous perchloric acid in red, glistening, slender, prismatic needles and from acetic acid in red, elongated, pointed prisms having a bluish-green reflex. The substance darkens at 260° and melts at 278—280° (decomp.). A mixture of the two specimens behaved in the same way.

*Acacetinidin picrate* crystallised from 40% alcohol, containing picric acid, in long, red, prismatic needles which darkened at 220—225° and melted to a black liquid at 231—233° (mixed—the same).

*Apigeninidin Chloride* (5 : 7 : 4'-Trihydroxyflavylium Chloride).—Acacetinidin chloride (2.1 g.) was demethylated by gently boiling with hydriodic acid (60 c.c.; *d* 1.7) and phenol (9 g.) in a stream of carbon dioxide. Methyl iodide was rapidly evolved and after 15 minutes the acacetinidin iodide had passed into solution. The reaction was continued for a further 10 minutes; a test then proved that only traces of methyl iodide were being produced. On cooling, the apigeninidin iodide quickly crystallised in scarlet, prismatic needles and these were collected on asbestos, washed with ether, and dried at 100° (2.2 g.). The substance is readily soluble in hot alcohol and on the addition of hydrochloric acid the chloride crystallises from the solution, but in order to ensure complete conversion the following method was adopted. The iodide (2.2 g.) and silver chloride (about 10 g.) were added to ethyl alcohol (400 c.c.) and concentrated hydrochloric acid (5 c.c.), and the solution was boiled during 10 minutes, filtered and mixed with concentrated hydrochloric acid (50 c.c.). On cooling, apigeninidin chloride separated in very well-shaped, glistening, rhombic prisms. Individual crystals are seen under the microscope to be light orange-yellow by transmitted

light and the mass is bright salmon-red. The substance was washed with alcohol and dried in a vacuum (Found: C, 58.5; H, 4.4.  $C_{15}H_{11}O_4Cl \cdot H_2O$  requires C, 58.4; H, 4.2%). This hydrate is very stable and when quickly heated appears to suffer no change below 200°. At about 230° it darkens and turns green. The anhydrous substance chars above 350° but does not melt. Prolonged heating at 100° does not effect dehydration, but at 140° in a vacuum the substance loses weight and becomes hæmatite-red.

Apigeninidin chloride is sparingly soluble in hot dilute hydrochloric acid and in most organic solvents. On boiling with not too much water, it dissolves and at once separates again as a flocculent precipitate consisting of orange, microscopic needles. This substance is a basic chloride and on the addition of a drop of hydrochloric acid is converted into the normal salt, recognised by its characteristic mode of crystallisation in rhombic prisms. *n*-Butyl or *iso*amyl alcohol extracts most of the salt from aqueous solution, giving an orange-red solution, but the aqueous layer always retains a canary-yellow colour. This behaviour differs from that of pelargonidin chloride, which is completely extracted from aqueous solution by *iso*amyl alcohol. The bright yellow solution in concentrated sulphuric acid exhibits an intense green fluorescence. The colour base, obtained by the action of sodium acetate on the chloride in aqueous solution, is a brownish-red precipitate, sparingly soluble in butyl alcohol to an eosin-red solution. On great dilution, the yellow solutions of apigeninidin salts become red, but under no conditions is a colourless pseudo-base formed. The chloride or the colour base dissolves in aqueous sodium carbonate or ammonia to a rich crimson solution, the colour of which is much bluer, brighter and more persistent on dilution than that of an alkaline solution of acetinidin chloride. The orange-red solution in alcohol becomes intense yellowish-brown on the addition of ferric chloride. The ferrichloride could not be obtained because it is more soluble than the chloride. For example, a suspension of the chloride in boiling acetic acid gives a clear solution on the addition of a little ferric chloride dissolved in concentrated hydrochloric acid, but on cooling the chloride separates. The *mercurichloride* is extremely sparingly soluble in dilute hydrochloric acid containing mercuric chloride and crystallises in hair-like, orange, microscopic needles. The chloride dissolves somewhat readily in hot dilute perchloric acid and on quickly cooling the *perchlorate* separates in very slender, long, irregular fibres which, on standing in contact with the solvent, change into very dense clusters of microscopic needles. The *periodide* behaves similarly, being precipitated as a stringy, dark brown mass which is resolved into slender needles. Numerous attempts to

oxidise apigeninidin to apigenin were fruitless. The alkaline solution retains its colour when air is aspirated through it during 12 hours.

*Hydroxymethyleneacetoveratrone*.—Methyl alcohol (1.6 g.) was added to a suspension of granular sodium (1.1 g.) in dry ether (50 c.c.) and when the formation of alkyloxide was complete a mixture of ethyl formate (5.2 g.) and acetoveratrone (9.7 g.) was slowly introduced with frequent shaking; a white, pasty mass was formed. Next day, ice, acetic acid, and ether were added and the separated ethereal solution was shaken with a concentrated solution of copper acetate. The *copper* derivative (7.0 g.) crystallised from toluene in pale green needles which softened at 180° and decomposed at 188° (Found: Cu, 13.0.  $C_{22}H_{22}O_8Cu$  requires Cu, 13.3%). Similarly, the *copper* derivative of hydroxymethylene-2:4-dimethoxyacetophenone was obtained from resacetophenone dimethyl ether (yield, 13 g. from 14 g. of the ketone). It crystallised from toluene in pale green prisms, m. p. 190° (Found: Cu, 13.4%).

5:7-*Dihydroxy-3'*:4'-*dimethoxyflavylium Chloride*.—An ethereal solution of hydroxymethyleneacetoveratrone (itself an oil exhibiting the usual properties of its class) was obtained by shaking the copper derivative (5.5 g.) with dilute sulphuric acid and ether; the separated ethereal layer was dried with sodium sulphate. This solution was added to one of anhydrous phloroglucinol (3 g.) in ether, and a stream of hydrogen chloride led through the mixture for 4 hours. After 12 hours, the bright red condensation product was collected, washed with ether, and dried (5 g.). This product was boiled under reflux with alcohol (1500 c.c.) and concentrated hydrochloric acid (12 c.c.) for an hour, and the solution distilled until separation of the salt commenced. After keeping for 24 hours, the solid was collected and further purification was effected by solution in and separation from 2% hydrochloric acid. After several such processes, the substance crystallised in a homogeneous form in opaque, microscopic, spherical masses. Further slow crystallisation from hot dilute solutions gave reddish-brown, prismatic needles which decomposed at 272° (Found in material dried in a vacuum over sulphuric acid: C, 56.4; H, 4.8.  $C_{17}H_{15}O_5Cl \cdot 1.5H_2O$  requires C, 56.5; H, 4.9%). This salt dissolves in aqueous sodium carbonate to an intense blood-red solution.

*Demethylation*. A mixture of this luteolinidin dimethyl ether (1.4 g.) with phenol (4 g.) and concentrated hydriodic acid (30 c.c.) was boiled in an atmosphere of carbon dioxide for 30 minutes. A bright red iodide crystallised from the solution and this was collected and converted in the usual manner into the corresponding *chloride*. The latter crystallised from alcohol in small, orange-red needles,

which decomposed at  $282^{\circ}$  (Found in material dried in a vacuum over sulphuric acid : C, 58.6; H, 3.4; MeO, 10.5; Cl, 10.1; loss at  $105^{\circ}$  in a high vacuum, 2.7.  $C_{16}H_{12}O_5Cl \cdot 0.5H_2O$  requires C, 58.4; H, 3.7; 1MeO, 9.5; Cl, 10.7;  $H_2O$ , 2.8%). The substance is therefore a luteolinidin chloride monomethyl ether. It gives a Bordeaux-red to reddish-purple solution in aqueous sodium carbonate and its acid solutions have the same colour as those of luteolinidin chloride. The alkali colour reaction provides the only available evidence in regard to constitution and suggests that the salt is 5 : 7 : 4'-tri-hydroxy-3'-methoxyflavylium chloride rather than the possible isomeride. The purified substance must contain a trace of luteolinidin chloride, since it gives a weak ferric chloride reaction. On further demethylation with a mixture of hydriodic acid ( $d$  1.75) and phenyl acetate, during the course of which the rate of evolution of methyl iodide was observed, luteolinidin iodide was obtained. The corresponding chloride showed all the reactions and properties of the substance previously obtained from luteolinidin chloride trimethyl ether (Part VI, *loc. cit.*).

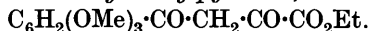
*7-Hydroxy-3 : 2' : 4'-trimethoxyflavylium Chloride.*—A solution of  $\omega$  : 2 : 4-trimethoxyacetophenone (4.4 g.) and  $\beta$ -resorcyaldehyde (2.8 g.) in dry ether (100 c.c.) was saturated with hydrogen chloride for 2 hours and kept over-night. The product separated in orange-red needles with a dark green reflex (8 g.). It crystallised from dilute hydrochloric acid in crimson, prismatic needles which darkened at  $140^{\circ}$  and decomposed at  $185^{\circ}$  (Found in material dried in a vacuum over sulphuric acid : C, 58.8; H, 5.4.  $C_{18}H_{17}O_5Cl$  requires C, 59.0; H, 5.2%). The colour base is bluish-red, a pseudo-base is readily formed, and the yellow solution in concentrated sulphuric acid exhibits bright apple-green fluorescence.

*3 : 7 : 2' : 4'-Tetrahydroxyflavylium Chloride (Resomorinidin Chloride) (II).*—A mixture of the trimethyl ether (4 g.), phenol (8 g.), and hydriodic acid (80 c.c.;  $d$  1.7) was gently boiled during 35 minutes in a stream of carbon dioxide. On cooling, glistening prismatic needles, exhibiting golden-green reflex, separated and these were collected and dried (2.8 g.). Conversion into chloride by means of silver chloride and a trace of hydrogen chloride was accomplished in alcoholic solution and, on the addition of 10% aqueous hydrochloric acid to the filtrate, the salt crystallised in small, red needles which decomposed at  $216^{\circ}$  (Found in material dried in a vacuum over sulphuric acid : C, 54.3; H, 4.2.  $C_{15}H_{11}O_5Cl \cdot 1.5H_2O$  requires C, 54.0; H, 4.2%). Resomorinidin chloride is very sparingly soluble in cold dilute hydrochloric acid and moderately easily soluble in the hot solvent to an orange-red solution. Its solution in sulphuric acid exhibits bright apple-green



fluorescence. Sodium carbonate added to an aqueous solution gives an intense reddish-violet or permanganate-like coloration. An alcoholic solution of the salt is bluish-red and on addition of sodium carbonate becomes dichroic, red in thick layers, blue in thin layers, and exhibits dark red fluorescence. A hydrochloric acid solution was decolorised on boiling with zinc dust, and the cooled mixture was then extracted with ether. Addition of very dilute sodium hydroxide to the separated ethereal layer gave a blue solution which soon became violet and then rose-coloured. On warming, the aqueous layer became greenish-yellow and developed an intense ivy-green fluorescence.

*Ethyl 2 : 4 : 6-Trimethoxybenzoylpyruvate,*



—This substance was prepared in the hope that it might prove to be a convenient source of 5 : 7-dimethoxychromone, which was required in connexion with attempts to obtain representatives of the *epiflavylium* series. Phloracetophenone trimethyl ether (5.2 g.) (Kostanecki and Tambor, *Ber.*, 1899, **32**, 2261) and ethyl oxalate (5.5 g.) were added to an absolute alcoholic solution (30 c.c.) of sodium ethoxide (1.4 g. of sodium) and next day ether was added to complete the separation of the sodium derivative. This was collected and dissolved in water and the *ester*, liberated by means of acetic acid, was isolated (5 g.); it crystallised from aqueous alcohol in long, pale yellow needles, m. p. 84° (Found : C, 58.3; H, 5.9.  $\text{C}_{15}\text{H}_{18}\text{O}_7$  requires C, 58.1; H, 5.8%). This ester exhibits the usual properties of its class and in the solid state, preferably as a well dispersed precipitate suspended in a faintly acid medium, forms a highly characteristic blue compound with iodine.

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