CXCII.—*Experiments on the Synthesis of Anthocyanins. Part IV. The Constitution of O-Benzoylphloroglucinaldehyde.*

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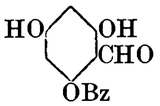
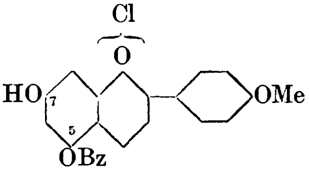
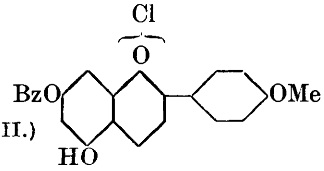
THE *O*-benzoylphloroglucinaldehyde that is obtained by the monobenzoylation of phloroglucinaldehyde by the Schotten–Baumann method (Robertson and Robinson, J., 1927, 1710) has been found to be a very convenient starting point in syntheses of anthocyanidins and even of certain anthocyanins; it therefore became necessary to determine its constitution. The first indication that the hydroxyl in the *o*-position to the aldehydo-group is the one that is benzoylated and that the derivative has the formula (I) was afforded by the properties of benzoylacacetinidin chloride (II), obtained by condensation of *O*-benzoylphloroglucinaldehyde and *p*-acetylanisole.

(I.)

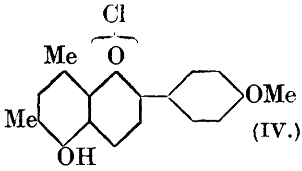




(II.)



(III.)



(IV.)

This flavylium salt yielded an alkali-insoluble (therefore not debenzoylated), red anhydro-base quite similar to those derived from authentic 7-hydroxyflavylium salts, and consequently the formula (III), which is the alternative, seemed improbable. Flavylium salts with one free hydroxyl and that in position 5 give violet or blue anhydro-bases (compare Collie and White, J., 1915, **107**, 369; and see below).

Confirmation of the formulæ (I) and (II) as valid representations of *O*-benzoylphloroglucinaldehyde and benzoylacacetinidin chloride was found in the observations that these substances could be obtained by the condensation of *O*-benzoylphloroglucinol (Fischer, *Annalen*, 1910, **371**, 303) with hydrogen cyanide and anisoylacetaldehyde, respectively, in presence of hydrogen chloride. The yield of the aldehyde was poor, but on the other hand isomerides could not be isolated.

The use of diazomethane and of methyl sulphate and sodium hydroxide having proved unsuccessful, we found it possible to methylate *O*-benzoylphloroglucinaldehyde by means of potassium carbonate and methyl iodide in boiling acetone solution. The product was characterised as 2-*benzoyloxy*-4 : 6-*dimethoxybenzaldehyde*, $BzO\cdot C_6H_2(OMe)_2\cdot CHO$, since on hydrolysis it yielded benzoic acid and the known 2-hydroxy-4 : 6-dimethoxybenzaldehyde. The method is very suitable for the preparation of this substance.

The benzoylation of phloroglucinaldehyde may be contrasted with that of phloroglucinolcarboxylic acid (Fischer, *loc. cit.*), in which it is the hydroxyl group in the *p*-position to carboxyl that is first attacked. These results can be explained on the assumptions that a carbonyl group cannot inactivate more than one *o*-situated hydroxyl group and that apart from this well-known influence the *o*-hydroxyl is more acidic than the *p*-hydroxyl. Furthermore, the reaction of phloroglucinolcarboxylic acid with benzoyl chloride depends on the formation of a dipotassium derivative, and the application of recognised principles makes it clear that the charge on the bivalent anion will be concentrated first on the carboxyl ion and then on the most remote phenolic oxygen atom; the kationoid carbon atom of benzoyl chloride, therefore, finds electrons available for new co-valency formation most easily at the oxygen atom in the *p*-position to the carboxyl group. Benzoylation of the carboxyl group may also occur, but under the conditions of the reaction the product cannot survive.

EXPERIMENTAL.

4 : 6-*Dihydroxy-2-benzoyloxybenzaldehyde* (I).—In the preparation of *O*-benzoylphloroglucinaldehyde (Robertson and Robinson, *loc. cit.*) the weight of benzoyl chloride employed should be 4·2 g. and not 2·35 g. as previously stated.

A mixture of *O*-benzoylphloroglucinol (E. Fischer, *loc. cit.*) (5·5 g.), anhydrous hydrogen cyanide (5 c.c.), and absolute ether (100 c.c.) was saturated with hydrogen chloride at room temperature. A thick syrup separated in about an hour and after 48 hours the ether was decanted from the semi-crystalline mass that had collected. This was washed with ether, dried in a vacuum, and dissolved in water (100 c.c.) and the solution was heated at 80° for 15 minutes. The red solid that separated appeared to contain benzoic acid; it was dissolved in alcohol (50 c.c.; charcoal), and the solution then added to aqueous sodium bicarbonate (200 c.c.). The crude product was collected and crystallised from chloroform (charcoal) with much loss; only 0·08 g. of the pure substance was obtained. The yield was doubled when the hydrolysis was effected by means of 5% aqueous sodium acetate for 5 minutes at 80°. The aldehyde was obtained in colourless, elongated prisms which darkened at 185°, turned red at 195°, and melted at 198—200° (Found : C, 65·0; H, 4·1. Calc. for $C_{14}H_{10}O_5$: C, 65·1; H, 3·9%). The behaviour on heating was unaltered by admixture with *O*-benzoylphloroglucinaldehyde from phloroglucinaldehyde, and a comparison of crystal form under the microscope and of the ferric chloride reaction (wine-red in alcohol) showed that the specimens were identical. No other product of this reaction could be isolated from the mother-liquors in a homogeneous condition.

2-*Benzoyloxy*-4 : 6-*dimethoxybenzaldehyde*.—A mixture of *O*-benzoylphloroglucinaldehyde (3 g.), acetone (30 c.c.), and methyl iodide (20 c.c.) was boiled, and finely powdered potassium carbonate (15 g.) introduced; the solution was then refluxed for 40 minutes and most of the solvent removed by distillation. Ether and water were added and the ethereal layer was thoroughly washed with fresh water, dried with sodium sulphate, and evaporated. The residue crystallised from ethyl alcohol in long, well-shaped prisms and then from ethyl acetate in colourless, pointed, prismatic needles, m. p. 148° (Found in air-dried material: C, 65·5; H, 5·0. $C_{16}H_{14}O_5,0{\cdot}5H_2O$ requires C, 65·1; H, 5·1%. Found in material dried at 105° in a high vacuum: C, 67·3; H, 4·4. $C_{16}H_{14}O_5$ requires C, 67·1; H, 4·9%). The substance is sparingly soluble in alcohol and is unaffected in a short time by boiling aqueous sodium hydroxide. It was also obtained by the action of benzoyl chloride and warm aqueous sodium hydroxide on 2-hydroxy-4 : 6-dimethoxybenzaldehyde.

Hydrolysis. The benzoate was readily attacked by hot aqueous-alcoholic sodium hydroxide. The product, isolated by acidification and extraction with ether and separated by means of sodium bicarbonate, was 2-hydroxy-4 : 6-dimethoxybenzaldehyde, which crystallised from aqueous methyl alcohol in colourless needles, m. p. 70° (alone or mixed with an authentic specimen). It condensed with ω-methoxyacetoveratrone in presence of hydrogen chloride to a flavylium salt having the properties of *O*-pentamethylcyanidin chloride. The *ferrichloride* had m. p. 210° with previous softening. Acidification of the sodium bicarbonate solution gave benzoic acid.

7-*Hydroxy*-5-*benzoyloxy*-4'-*methoxyflavylium Chloride* (II).—When an ethereal solution of anisoylacetaldehyde (from 4·2 g. of the copper derivative) and *O*-benzoylphloroglucinol (4 g.) at 15° was saturated with hydrogen chloride, a red condensation product quickly separated. On the following day this was collected (5·0 g. or 80%) and dissolved in acetic acid and the solution was saturated with hydrogen chloride. The salt then slowly separated in a crystalline condition and it was recrystallised by solution in a hot mixture of 0·5% aqueous hydrochloric acid and an equal volume of alcohol and addition of concentrated hydrochloric acid until a faint turbidity appeared. The sheaves of orange-red, prismatic needles were dried over sulphuric acid (Found : C, 64·2; H, 4·8. Calc. for $C_{23}H_{17}O_5Cl,H_2O$: C, 64·7; H, 4·5%). The salt exhibited the characteristic properties of the benzoylacacetinidin chloride previously prepared by Pratt, Robertson, and Robinson (J., 1927, 1978) and in addition to a careful direct comparison of the specimens the *picrates* were obtained from both sources and found to be identical in all respects. This derivative separated, when picric acid was added to a boiling alcoholic solution of the chloride, as a mass of curved, hair-fine, orange needles or bundles of needles. It is almost insoluble in hot ethyl alcohol and when heated it darkens at 215° and melts at 230—231° with decomposition. A mixture of the specimens showed the same behaviour.

5-*Hydroxy*-4'-*methoxy*-6 : 8-*dimethylflavylium Chloride* (IV).—A slow stream of hydrogen chloride was passed through a solution of *m*-xylorcylaldehyde (0·8 g.) (Robertson and Robinson, J., 1927, 2202) and *p*-acetylanisole (1·2 g.) in absolute formic acid (40 c.c.) until it was saturated. After 48 hours, the product was precipitated by ether, and crystallised by addition of hot concentrated hydrochloric acid to a solution in hot 4% hydrochloric acid (final concentration 10%); it formed fine, reddish-violet needles (1·2 g.)

which appeared red by transmitted light (Found in air-dried material: C, 58·2; H, 6·2. $C_{18}H_{17}O_3Cl,3H_2O$ requires C, 58·2; H, 6·2%). The substance is dehydrated in a high vacuum over sulphuric acid and becomes deeper red in colour; the product is hygroscopic.

This salt readily forms in dilute hydrochloric acid (up to 10%) orange to deep orange-red solutions. The colour-base precipitated on the addition of sodium acetate to its aqueous solutions dissolves in benzene to a blue solution. When the benzene extract is shaken with dilute hydrochloric acid, it is decolorised and the orange flavylium salt dissolves in the aqueous layer.

Previously the only known 5-hydroxyflavylium salt, not containing hydroxyl groups in other positions, was 5-hydroxy-3 : 3′ : 4′-trimethoxy-6 : 8-dimethylflavylium chloride (Robertson and Robinson, J., 1927, 2204) and this we now find gives a bluish-violet colour-base that is soluble in benzene.

A small amount of tectochrysin (5-hydroxy-7-methoxyflavone) was boiled with acetic anhydride and a little potassium acetate for 30 seconds. An excess of zinc dust was then added and the boiling continued for 30 seconds. The orange-yellow solution was diluted with alcohol (then exhibiting a vivid green fluorescence), filtered, mixed with concentrated hydrochloric acid, and boiled until it became turbid. The deep orange solution obtained was twice extracted with much ether, separated, treated with sodium acetate, and extracted with benzene. The *violet* benzene solution was decolorised on being shaken with dilute hydrochloric acid, the aqueous layer becoming orange; and this alternation could be continued. A similar experiment with 7-hydroxy-4′-methoxyflavone gave a *red* benzene solution and yellow acid aqueous solution. Clearly this behaviour is due to the formation of 5- and 7-hydroxyflavylium salts in the two cases mentioned. The fact that the violet base gives an acid solution having a deeper orange colour than that given by the red base is in harmony with the experience of Collie and White (*loc. cit.*) in connexion with the isomeric benzopyrylium salts derived from orcinol and acetylacetone.

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