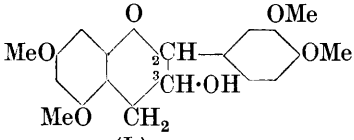
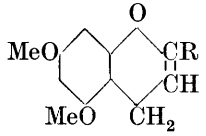
CCIX.—*Some Substances derived from the Anhydrocatechin Tetramethyl Ethers.*

By WILSON BAKER.

THE work of Freudenberg and his collaborators (*Ber.*, 1920, **53**, 1416; 1921, **54**, 1204; 1922, **55**, 1734; 1923, **56**, 1185, 2127; *Annalen*, 1924, **437**, 274, 286; 1925, **441**, 157; 1925, **442**, 309; 1925, **444**, 135; 1926, **446**, 87; 1927, **451**, 209, 213) has established the existence of six optically isomeric catechins, corresponding in structure to the tetramethyl ethers (I). Epicatechin tetramethyl ether [OH and H(in 2) in *cis*-positions] is dehydrated normally to give the anhydro-derivative (II) (R = 3 : 4-dimethoxyphenyl in this and succeeding formulæ), but in the catechin series (*trans*) dehydration is difficult, and is accompanied by migration of the 3 : 4-dimethoxyphenyl group, to give the anhydro-derivative (III) (*Annalen*, 1925, **441**, 157; 1926, **446**, 87). This compound has also been obtained by Drumm (*Proc. Roy. Irish Acad.*, 1923, **36**, 41).



(I.)



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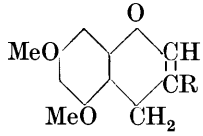
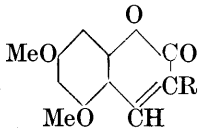


(III.)

Anhydrocatechin tetramethyl ether (III) contains the same carbon skeleton as the natural *iso*flavones (genistein, prunetin and irigenin; Baker and Robinson, J., 1925, **127**, 1981; 1926, 2713; 1928, 3115; Baker, J., 1928, 1022) and from the point of view of genetic relationships it was of importance to attempt to oxidise the methylene group in this compound to a carbonyl group with the object of producing 5 : 7 : 3′ : 4′-tetramethoxy*iso*flavone. It was considered doubtful whether such a relationship between the catechins and the *iso*flavones really exists in nature, since the *iso*flavone corresponding to the catechins (5 : 7 : 3′ : 4′-tetrahydroxy-*iso*flavone) is unknown and no catechins are known to occur which correspond to any of the known *iso*flavones.

The methylene group in anhydrocatechin tetramethyl ether (III) does not react with aromatic aldehydes or nitroso-compounds.

The actions of a number of oxidising agents were investigated, but definite results were obtained only with potassium permanganate and chromic acid. Oxidation in acetone solution with potassium permanganate gave a mixture of 5 : 7 : 3′ : 4′-*tetramethoxy*-3-*phenylcoumarin* (IV) (yield, about 12%) and a basic substance which when boiled with hydrochloric acid was converted into 5 : 7 : 3′ : 4′-tetramethoxy*iso*flavylium chloride (V) (yield, about 8%). The constitution assigned to (IV) was established by synthesis. Phloro-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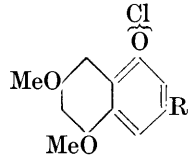
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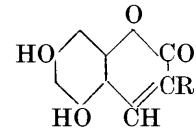
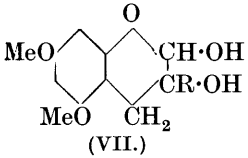

(VI.)

glucinaldehyde, sodium homoveratrate and acetic anhydride reacted together to give the *diacetyl* derivative of 5 : 7-*dihydroxy*-3′ : 4′-*dimethoxy*-3-*phenylcoumarin* (VI), which by hydrolysis and methylation yielded (IV) (compare Dey and Row, *J. Indian Chem. Soc.*, 1924, **1**, 121; Bargellini, *Gazzetta*, 1927, **57**, 459). The formation of (VI) from (III) affords a new proof of the structure assigned by Freudenberg to the latter product. Demethylation of (IV) yielded 5 : 7 : 3′ : 4′-*tetrahydroxy*-3-*phenylcoumarin*. The basic substance is doubtless the glycol (VII), which is converted into the *iso*-flavylium salt (V) by the action of one molecule of hydrochloric acid and elimination of two molecules of water, and into the coumarin (IV) by loss of water and oxidation of the $-CH(OH)-$ group.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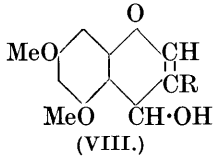
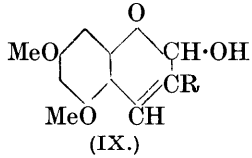

(VIII.)


(IX.)

The *iso*flavylium salt (V) was identical with the pyrylium salt obtained from (III) by the action of bromine in chloroform solution (Drumm, *loc. cit.*). This compound, considered by Drumm to possess the structure (XII), is now regarded as (V) (Freudenberg, Carrara, and Cohn, *Annalen*, 1926, **446**, 87).

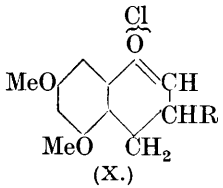
The oxidation of (III) with potassium permanganate in pyridine solution yielded the coumarin (IV) (yield, about 25%) and only a trace of the salt (V), whilst by oxidation with chromic acid in pyridine solution very poor yields (about 4%) of (IV) and (V) were obtained.

Attention was next directed to the pseudo-base of the pyrylium

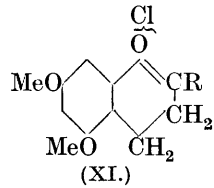
salt (V), probably (VIII), which might yield an *iso*flavone by oxidation of the $-CH(OH)-$ group. This pseudo-base, when treated under the conditions employed for the oxidation of (III), was almost unattacked, yielding a trace of the coumarin (IV), detectable only by its fluorescence, and a minute amount of an acid, probably 2-hydroxy-4 : 6-dimethoxybenzoic acid. The stability of this pseudo-base towards oxidation excludes the possibility of its being regarded as an intermediate in the oxidation of (III) to (IV). Its constitution is therefore regarded as (VIII) and not the alternative (IX), since this is a dehydration product of the glycol (VII) and should be readily oxidised to (IV).

As a result of these experiments the author is of the opinion that the *iso*flavones are not derived from catechin-like substances. This view receives support from a consideration of the number of natural compounds (those with different numbers or distribution of hydroxyl or methoxyl groups) in the progressively reduced series flavonol, flavone and anthocyanidin, flavanone and chalkone, catechin. The number of compounds in the four groups, 9, 8, 3, 1, diminishes as the degree of reduction increases. Further work is not likely to alter the relative values of these numbers to any large extent, and since there are *two* fundamental *iso*flavones it is improbable that they are derived from substances of the catechin type. It is possible that they may arise by dehydration of 2 : 3-dihydroflavonols.

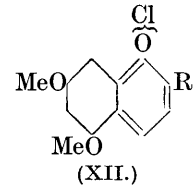
During the course of this work a matter of general interest was encountered in some experiments with anhydrocatechin tetramethyl ether (III). Freudenberg, Carrara, and Cohn (*loc. cit.*) have described a reddish-violet " hydrochloride " of this substance, prepared by treating its solution in chloroform with ethereal hydrogen chloride, and have formulated it as the dihydro*iso*flavylium salt (X). This compound is, however, identical with the true *iso*flavylium chloride (V), prepared either by Drumm's method or by oxidation of (III).



(X.)



(XI.)



(XII.)

The synthesis of (V) has been recorded by Freudenberg, Carrara, and Cohn (*loc. cit.*). The production of (V) from (III) is accompanied by the removal of two atoms of hydrogen, and this appears to be brought about by aerial oxidation, since in an atmosphere of hydrogen the formation of (V) was slow and the yield poor.

These results led to the investigation of the analogous " hydro-

chloride" of anhydroepicatechin tetramethyl ether (II) (Freudenberg, Fikentscher, and Wenner, *Annalen*, 1925, **442**, 317), which was regarded as a dihydropyrylium salt (XI). This compound was also obtained from 3 : 4-dimethoxyphenyl β-2-hydroxy-4 : 6-dimethoxyphenylethyl ketone. This "hydrochloride" is now found to be identical in all respects with tetramethyl-luteolinidin chloride (XII), a substance previously prepared, although not fully described, by Pratt, Robinson, and Williams (J., 1924, **125**, 207). A fresh proof is thus provided of the structure assigned to anhydroepicatechin tetramethyl ether.

Other cases are recorded in the literature where a true pyrylium salt is unexpectedly formed owing to oxidation. For instance, deoxytrimethylbrazilone (Perkin, Ray, and Robinson, J., 1927, 2100; 1928, 1504) is readily converted into *iso*brazilein hydrochloride trimethyl ether by the action of hydrogen chloride in chloroform. Again, the reduction of naringenin with sodium amalgam and subsequent acidification (Asahina and Inubuse, *Ber.*, 1928, **61**, 1646) gave apigeninidin chloride. It is thus evident that in substances of this type there is a great tendency to form pyrylium salts with the full aromatic structure, and there seems no evidence of the intermediate formation of partly reduced pyrylium salts.

After the manuscript of this paper had been completed in May, the author wrote to Professor Freudenberg informing him of the conclusions reached with regard to the constitutions of these two "hydrochlorides" of the anhydrocatechin tetramethyl ethers. A letter, dated June 12th, was received in reply, part of which is quoted: "—ich habe bereits vor einem Jahre in der Dissertation G. Steinbrunn" (Heidelberg, May 15th, 1928) "die Möglichkeit diskutiert, dass die beiden Oxoniumsalze Pyrylium-verbindungen sind; die Zersetzungspunkte der Oxoniumsalze haben mir jedoch für die Identifizierung nicht genügt, deshalb wurde versucht, zu gut schmelzenden Derivaten zu gelangen, aber es wurde bisher kein deutliches Ergebnis erzielt. Trotzdem halte ich die Identität für möglich und im Falle des Tetramethyl-luteolinidin für höchst wahrscheinlich."

EXPERIMENTAL.

Anhydrocatechin Tetramethyl Ether (III).—For the preparation of the somewhat large quantities of this substance which were required, the following method, based on that of Drumm (*loc. cit.*), was finally adopted and standardised.

d-Catechin tetramethyl ether (35 g., m. p. 143°), suspended in carbon disulphide (250 c.c.), was gently shaken with phosphorus pentachloride (25 g.). Hydrogen chloride was evolved and the

reactants slowly dissolved; when the reaction ceased (about ½ hour), the pink solution was poured into 10% aqueous sodium carbonate (1 l.) and well shaken. The carbon disulphide layer was separated, again shaken with dilute sodium carbonate solution, dried by potassium carbonate, and filtered, and the solvent removed under diminished pressure at about 20°. The viscous pink residue was boiled under reflux for ½ hour with pyridine (140 c.c.; oil-bath at 130°) and then stirred into water (2 l.). The white viscous product rapidly solidified and was then filtered off and washed; it crystallised from hot alcohol in colourless, highly refracting prisms, m. p. 133—134° (yield, about 24 g.).

Anhydrocatechin tetramethyl ether gives a bright orange solution in concentrated sulphuric acid. Its solution in acetic acid treated with a few drops of concentrated nitric acid gives an orange-yellow colour which rapidly develops a greenish tint, and then more slowly becomes a dull slaty-blue [*d*-catechin tetramethyl ether and the supposed tetramethyl ether of cyanomaclurin (J., 1905, **87**, 720), which has a constitution similar to that of anhydrocatechin tetramethyl ether, both give a bluish-green colour, which rapidly assumes an intense, pure blue tint]. When the ether is boiled with acetic acid and hydriodic acid (*d* 1·7), demethylation occurs, and addition of water to the resulting red solution precipitates a flocculent, amorphous, reddish-brown substance. This closely resembles the product obtained in a similar manner from *d*-catechin tetramethyl ether, or from *d*-catechin itself by heating with hydrochloric acid in acetic acid, and is undoubtedly of the type of the so-called "catechin anhydrides" or "phlobaphenes," which can also be obtained from cyanomaclurin. This failure to obtain a demethylation product is paralleled by the impossibility of obtaining *d*-catechin by demethylation of its tetramethyl ether (in this connexion see Nierenstein, J., 1921, **119**, 169; *Ber.*, 1922, **55**, 3833; Freudenberg, *Ber.*, 1922, **55**, 1940). Anhydrocatechin tetramethyl ether yielded no recognisable products either by fusion with potassium hydroxide, towards which it is remarkably stable, or by oxidation with chromic acid in acetic acid solution.

Oxidation of Anhydrocatechin Tetramethyl Ether with Potassium Permanganate.—A solution of the ether (4·0 g.) in acetone (240 c.c.) at 12° was treated with a solution of potassium permanganate (5·0 g.) in a mixture of acetone (150 c.c.) and water (15 c.c.), also at 12°, in two portions, the second portion being added 5 minutes after the first. The temperature rose 10°, and when the permanganate was completely reduced (about ¾ hour) the filtered yellow solution, which exhibited a marked greenish-blue fluorescence, was poured into much water. The pale yellow precipitate was collected, washed

with dilute aqueous sodium hydroxide and with water, and the pyrylium base was removed by boiling with a mixture of equal volumes of concentrated hydrochloric acid and water (100 c.c.). The bright red filtrate on cooling deposited the *iso*flavylium salt (V) (0·35 g.), and the remaining solid was washed with hot dilute hydrochloric acid and with water and crystallised from alcohol (50 c.c.; charcoal). Compact spherical bunches of needles separated, m. p. 175° (0·48 g.). A further crystallisation from alcohol gave a felted mass of exceedingly pale yellow needles, m. p. 177°, whose melting point was not raised by further crystallisation (Found : C, 66·3; H, 5·3. $C_{19}H_{18}O_6$ requires C, 66·7; H, 5·3%).

5 : 7 : 3′ : 4′-*Tetramethoxy*-3-*phenylcoumarin* (IV) is sparingly soluble in ethyl and methyl alcohols and acetic acid, fairly readily soluble in benzene and acetone, and very readily soluble in chloroform. The solutions are all very pale yellow; the alcoholic solutions exhibit a bluish-green, those in benzene and acetone a fine blue, and the solution in chloroform a strong greenish-blue fluorescence. The coumarin gives a yellow solution in concentrated sulphuric acid which is almost devoid of fluorescence, and, unlike methylated members of the *iso*flavone group, does not give an oxonium salt on warming with concentrated hydrochloric acid.

5 : 7 : 3′ : 4′-*Tetrahydroxy*-3-*phenylcoumarin*. — 5 : 7 : 3′ : 4′-Tetramethoxy-3-phenylcoumarin (0·2 g.) was demethylated with hydriodic acid (*d* 1·7; 10 c.c.) at 140° for ½ hour. The yellow crystals were collected after the addition of water, dissolved in boiling 50% acetic acid, and the filtered solution brought to a small volume by boiling. The substance separated in yellow, branching clusters of tiny prisms, m. p. 337° (decomp.) when rapidly heated. The melting point is difficult to determine accurately owing to much darkening, and to the fact that it varies considerably with the rate of heating (Found in material dried at 150° : C, 62·7; H, 3·8. $C_{15}H_{10}O_6$ requires C, 62·9; H, 3·5%). 5 : 7 : 3′ : 4′-*Tetrahydroxy*-3-*phenylcoumarin* is very sparingly soluble in most solvents; it dissolves slightly in boiling water to a pale yellow solution. The solution in concentrated sulphuric acid is yellow and exhibits a very weak green fluorescence. A suspension in air-free water, treated with a drop of 1% sodium hydroxide, yields a bright yellow solution which when shaken rapidly darkens and becomes dull reddish-brown. Addition of ferric chloride to an alcoholic solution gives at first a greenish-yellow colour, changing with excess of the reagent through dull yellowish-brown to red-brown. The aqueous solution under similar conditions gives a weak reddish-violet colour, changing to a weak reddish-pink. On mordanted woollen cloth the following dyeings were obtained : tin, yellow; iron, dull olive-

green. Methylation with methyl sulphate and aqueous potassium hydroxide readily gave the tetramethyl ether, m. p. 176—177°.

5 : 7-*Dihydroxy*-3′ : 4′-*dimethoxy*-3-*phenylcoumarin* (VI).—The *diacetyl* derivative was prepared by boiling phloroglucinaldehyde (2·2 g.) and sodium homoveratrate (4 g.) with acetic anhydride (20 c.c.) for 24 hours. By shaking with water and a few drops of hydrochloric acid a solid separated, which after crystallisation from alcohol (charcoal), in which it was sparingly soluble, was obtained in pale yellow, prismatic needles, m. p. 151° (2·4 g.) (Found : C, 63·2; H, 4·6. $C_{21}H_{18}O_8$ requires C, 63·3; H, 4·5%). Its alcoholic solution is devoid of fluorescence, but that in chloroform has a marked bluish-green fluorescence. It was hydrolysed with hot aqueous-alcoholic sodium hydroxide for 5 minutes, and the substance precipitated from the diluted solution by addition of hydrochloric acid was dissolved in much boiling alcohol (charcoal) and separated after concentration in small, yellow, thin prisms, m. p. about 327° (decomp.) when rapidly heated (Found in material dried at 140° : C, 64·9; H, 4·7. $C_{17}H_{14}O_6$ requires C, 64·9; H, 4·5%). 5 : 7-*Dihydroxy*-3′ : 4′-*dimethoxy*-3-*phenylcoumarin* is soluble in alkalis and concentrated sulphuric acid to bright yellow solutions devoid of fluorescence. The alcoholic solution is yellow and has an intense greenish-blue fluorescence, and gives no colour on the addition of ferric chloride. The coumarin is very sparingly soluble in methyl alcohol and acetone and insoluble in benzene, toluene and chloroform.

Methylation by means of methyl sulphate and dilute alkali at about 40° readily gave an alkali-insoluble solid, which after twice crystallising from alcohol (charcoal) formed pale yellow, hair-like needles, m. p. 176°. A mixed melting-point determination with the material, m. p. 177°, obtained by the oxidation of anhydrocatechin tetramethyl ether gave m. p. 176—177° and the melt immediately solidified on removal from the bath. The solubilities, fluorescences, etc., of the two specimens were identical.

5 : 7 : 3′ : 4′-*Tetramethoxy*iso*flavylium Chloride* (V).—The *iso*-flavylium chloride obtained as previously described (p. 1598) crystallised from a mixture of equal volumes of concentrated hydrochloric acid and water in small, bright red, prismatic needles which, when placed in a melting-point bath at 115° while the temperature was rising 5° a minute, melted at 128—129° with darkening and subsequent evolution of gas. As the melting point of this substance varies somewhat with the rate and manner of heating, the conditions just described were used in taking the melting points of the different specimens which are recorded in this paper.

The corresponding *iso*flavylium bromide was obtained from

anhydrocatechin tetramethyl ether by Drumm's method (*loc. cit.*), and was converted into the chloride by twice crystallising it from a mixture of equal volumes of concentrated hydrochloric acid and water. The chloride melted at 128—129° either alone or mixed with the specimen described above.

As noted by Pratt and Robinson (J., 1925, **127**, 1132), who examined the bromide, this pyrylium salt is derived from a very weak base. It passes with great readiness into the colourless pseudo-base, as may be seen by diluting a solution in fairly concentrated hydrochloric acid, the colour rapidly fading. The pseudo-base is completely extracted from this solution by shaking with benzene, and addition of concentrated hydrochloric acid regenerates the *iso*flavylium salt in the upper layer as microscopic red crystals, which, on shaking, dissolve in the aqueous layer to a red solution, the benzene becoming colourless. These changes may be repeated *ad libitum* by the addition of water and then acid. A suspension of the *iso*flavylium chloride in water immediately gives the white solid pseudo-base when shaken with dilute aqueous ammonia. The attempted demethylation of the salt gave a black, tarry, phenolic product.

Oxidation of Anhydrocatechin Tetramethyl Ether in Pyridine with Potassium Permanganate.—This experiment yielded a negligible amount of the *iso*flavylium salt (V), and the yield of 5 : 7 : 3′ : 4′-tetramethoxy-3-phenyl-coumarin (IV) was rather more than twice that obtained when the oxidation was carried out in acetone solution.

Anhydrocatechin tetramethyl ether (2 g.) in pyridine (50 c.c.) at 12° was treated in portions during 10 minutes with a solution of potassium permanganate (2·5 g.) in pyridine (100 c.c.) and water (5 c.c.). A rise in temperature of 10° occurred. After ½ hour the product was poured into water (1·5 l.), sulphur dioxide passed until the manganese dioxide dissolved, and then concentrated hydrochloric acid was added until the solution was on the point of becoming pink. After 2 hours the light flocculent precipitate was collected, washed, and boiled with a mixture of equal volumes of concentrated hydrochloric acid and water (50 c.c.). The faintly pink filtrate deposited no *iso*flavylium salt, nor were any phenolic or acidic substances obtained by washing the residue with dilute aqueous sodium hydroxide. The residue crystallised from alcohol in fine needles, m. p. 176°, consisting of pure 5 : 7 : 3′ : 4′-tetramethoxy-3-phenylcoumarin (0·5 g.).

Oxidation of the iso*Flavylium Pseudo-base* (VIII).—The pseudo-base (the ethyl ether of which has been described by Drumm as colourless needles, m. p. 133—134°) was obtained (*a*) by shaking the chloride in water with benzene, drying the benzene layer with

sodium sulphate and distilling it, the base being left as a colourless viscous oil, and (*b*) as a solid by shaking the chloride with dilute aqueous ammonia and filtering the liquid. Both specimens regenerated the pyrylium salt with hydrochloric acid, and behaved identically on oxidation.

The pseudo-base (2 g.) in acetone (120 c.c.) was oxidised at 12° by the addition in two portions of potassium permanganate (1·25 g.; half the amount used in the analogous oxidation of the anhydro-derivative III) in acetone (40 c.c.) and water (4 c.c.). The reduction of the permanganate was slow. After 18 hours the liquid was filtered, and the filtrate, which was pale yellow with a scarcely visible greenish fluorescence, was poured into water. After the acetone had been expelled by boiling, the white suspension dissolved completely to a bright red solution on warming with quarter its volume of concentrated hydrochloric acid; the *iso*flavylium chloride crystallised on cooling. The coumarin derivative (IV) is therefore only present in an amount detectable by its fluorescence, and no *iso*flavone is produced, since, although feebly basic, all *iso*flavones are insoluble in the strength of hydrochloric acid used above, even at the boiling point. By using twice the weight of potassium permanganate, exactly the same result was obtained, and an experiment similar to the first with 4 g. of the pseudo-base gave back 2·3 g. of the initial material.

Similar results were obtained by oxidising the pseudo-base (1 g.) with potassium permanganate in pyridine solution using (*a*) the same conditions as were employed for the oxidation of the anhydro-derivative (III), and (*b*) half the weight of potassium permanganate. In both cases the pseudo-base was largely unattacked and the amount of the coumarin (IV) produced, judging by its fluorescence, was certainly less than 1 mg. Further, about 2 mg. of a carboxylic acid were obtained which crystallised from hot water in tiny, colourless, prismatic needles, m. p. 154—155°. This acid evolved gas above its melting point and gave an intense reddish-violet ferric chloride reaction, and there can be little doubt that it is 2-hydroxy-4 : 6-dimethoxybenzoic acid, which has m. p. 152—154° (Herzig and Wenzel, *Monatsh.*, 1901, **23**, 95, give m. p. 150°, decomp.). Owing to the small amount of this acid available its complete investigation was not possible.

"*Hydrochloride*" *of Anhydrocatechin Tetramethyl Ether* (5 : 7 : 3′ : 4′-*Tetramethoxy*isoflavylium *Chloride*) (V).—(A) Prepared by the method of Freudenberg, Carrara, and Cohn (*loc. cit.*), 0·5 g. of this substance was obtained after 3 days from 1 g. of anhydrocatechin tetramethyl ether. As stated by these authors, it crystallised with considerable loss from 2*N*-hydrochloric acid; but it

crystallised without loss from a mixture of equal volumes of concentrated hydrochloric acid and water in tiny, bright red, prismatic needles, m. p. 128—129° (decomp.; under the conditions given on p. 1599).

(B) This compound was more readily obtained by dissolving anhydrocatechin tetramethyl ether (1 g.) in a warm mixture of equal volumes of glacial acetic acid and acetic anhydride (30 c.c.), and saturating the solution while still warm with a moderately rapid stream of hydrogen chloride without cooling. The cherry-red solution soon deposited red crystals, separation being practically complete in about 2 hours. The deep red crystals (0·5 g.) gave m. p. 128—129° both before and after recrystallisation. An appreciable quantity of the substance remained dissolved in the original mother-liquor.

Prepared by either method, the two specimens were identical in all respects, pseudo-base formation and regeneration of salt, etc., and also identical with the *iso*flavylium chlorides prepared by Drumm's method and by oxidising the anhydro-derivative (III). Complete identity was confirmed by careful mixed melting-point determinations with all four specimens. The appearance of this compound varies slightly with the size of the crystals when it separates from a non-aqueous solvent, the larger crystals having a somewhat deeper red colour.

The anhydro-derivative, when treated by method (B) above, in an atmosphere of hydrogen gave a light red solution, but after about 6 hours this deposited only colourless prisms of the initial material and after 24 hours only a relatively small amount of the *iso*flavylium salt had separated. The small yield of (V) obtained by method (B) was not increased by bubbling air through the solution during the saturation with hydrogen chloride.

This salt may also be obtained from (III) by saturating an acetic acid solution with hydrogen chloride, although the separation is not so rapid or complete as in the presence of acetic anhydride. It is also formed by boiling (III) with equal volumes of glacial acetic acid and concentrated hydrochloric acid, though the reaction is not complete and continued boiling appears to cause partial demethylation and formation of phlobaphenes.

An attempt was made to prepare the corresponding *iso*flavylium sulphate by dissolving anhydrocatechin tetramethyl ether (1 g.) in warm glacial acetic acid (50 c.c.) and adding a mixture of concentrated sulphuric acid (1 c.c.) and glacial acetic acid (5 c.c.). The solution immediately became red and soon deposited small, scarlet, prismatic needles (0·4 g.), m. p. when rapidly heated 200° with partial decomposition and darkening from about 170°. Sulphur

estimations varied, and indicated that sulphonation had probably taken place.

5 : 7 : 3′ : 4′-*Tetramethoxyflavylium Chloride* (XII).—(A) *Tetramethyl-luteolinidin chloride.* This compound was obtained as described by Pratt, Robinson, and Williams (*loc. cit.*) by the action of hydrochloric acid on 2-hydroxy-4 : 6-dimethoxystyryl 3 : 4-dimethoxyphenyl ketone. It was stated to separate from concentrated hydrochloric acid in glistening, red, prismatic needles, and on the addition of water to form a hydrate as orange-red clusters of microscopic needles. The characteristic ferrichloride was described and analysed. Tetramethyl-luteolinidin chloride was recrystallised by dissolving it in a hot mixture of equal volumes of concentrated hydrochloric acid and water and saturating the solution while still hot with hydrogen chloride. It separated in deep red, boat-shaped crystals, or in blunt-ended prisms having a greenish-yellow reflex, m. p. when fairly rapidly heated 161—162° (decomp.; the melting point varies somewhat with the rate of heating). It was also obtained in sheaves of orange-red pointed needles with greenish-yellow reflex, m. p. 161—162°, by dissolving it in hot 8% hydrochloric acid, cooling the solution in water, and saturating it with hydrogen chloride. This salt is not a simple compound, but is a hydrochloride of (XII) containing $2H_2O$ (Found : C, 51·8; H, 5·4; Cl, 16·0; loss at 105° in a vacuum over phosphoric oxide, 16·2. $C_{19}H_{19}O_5Cl,HCl,2H_2O$ requires C, 52·4; H, 5·6; Cl, 16·2; loss of HCl and $2H_2O$, 16·6%). Other cases of such anomalous hydrochlorides are known, *e.g.*, flavylium chloride itself and 4-methoxyflavylium chloride (Perkin, Robinson, and Turner, J., 1908, **93**, 1111). The properties of the substance are not altered by drying in a vacuum at 105° over phosphoric oxide, but the substance, whilst actually deep red, appears almost black, and has a fine green reflex; the crystals become red when powdered.

Tetramethyl-luteolinidin chloride is easily soluble in water and alcohol to stable orange-red solutions, the former being immediately decolorised by sodium bisulphite or by zinc and acetic acid. It is somewhat soluble in chloroform, but insoluble in ether. Addition of concentrated hydrochloric acid to the aqueous solution precipitates the chloride, and the addition of alkali precipitates a weakly coloured, non-crystalline base which regenerates the salt with acids. These properties agree exactly with those previously described for the " hydrochloride " of anhydroepicatechin tetramethyl ether.

(B) " *Hydrochloride* " *of anhydroepicatechin tetramethyl ether.* 3 : 4-Dimethoxyphenyl β-2-hydroxy-4 : 6-dimethoxyphenylethyl ketone (prepared by the catalytic reduction of the corresponding unsaturated ketone) was dissolved in benzene, and the solution

saturated with hydrogen chloride (Freudenberg, Fikentscher, and Wenner, *loc. cit.*). Deep red, blunt-ended prisms quickly separated. These possessed no reflex and melted, when rapidly heated, at 161—162° (decomp.). By cooling a solution of these crystals in hot 8% hydrochloric acid and saturating it with hydrogen chloride, the characteristic sheaves of pointed orange-red needles with greenish-yellow reflex, m. p. 161—162°, identical with those described under (A), were obtained. By drying in a vacuum as before, the substance became very dark and acquired a green reflex. The complete identity of the two specimens prepared under (A) and (B) was established by their identical behaviour under all the conditions previously mentioned, and was confirmed by mixed melting-point determinations, which showed no depression of the melting point.

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[*Received, June 18th,* 1929.]