CCCCII.—*The Colouring Matters of Carajura.*

By Ernest Chapman, Arthur George Perkin, and Robert Robinson.

Carajura (Crajura, Chica red) (Crookes, "Handbook of Dyeing and Calico Printing," 1874, p. 388; Schützberger, "Traité des Matières Colorantes," 1867, p. 412) is a rare red pigment, prepared by the Indians of the Rio Meta and the Orinoco from *Bignonia Chica* for use as a flesh paint (compare Humboldt's "Travels," Edinburgh, 1836, p. 229). It is stated that the leaves, which on drying acquire a red colour, are extracted with water and that the extract is treated with a ground bark called *aryane*, which effects the precipitation of the colouring matter. This process is strongly suggestive of the enzymic hydrolysis of a glucoside. The yield is small and the preparation tedious, and for this reason the material appears to be of a costly character. Erdmann (Crookes, *op. cit.*) recognised the pigment nature of chica and stated that, after treatment with acid, it dyes mordanted cotton in shades similar to those derived from lac dye. He considered that the colouring matter was an isomeride of anisic acid and assigned to it the formula $C_8H_8O_3$.

The material employed in this investigation, obtained through the kindness of Messrs. Wright, Layman, and Umney, consisted of dull red fragments enclosed in crudely woven oblong bags, evidently of native production. It possessed a peculiar camphoraceous odour, was insoluble in water, alcohol, and dilute aqueous alkalis, and thus differed from that described by Crookes (*op. cit.*) as soluble in 36% alcohol and dilute aqueous alkalis. Examination of this sample of carajura showed that it was a very crude product containing approximately 4% of colouring matter as calcium or magnesium lake, peaty organic matter, perhaps " aryane " (23%), in addition to a wax and a coloured resin in small relative amount. The mineral matter as ash (38%) consisted mainly of lime, magnesia, and silica together with some potassium carbonate. Some part of the calcium appears to be present as oxalate. A preliminary account of the isolation and properties of carajurin, the main crystallisable colouring matter of carajura, has already been published (Perkin, P., 1914, **30**, 212), but as the results of later work the empirical formula of carajurin is considered to be $C_{17}H_{14}O_5$ instead of $C_{18}H_{16}O_5$, as then suggested.

Carajurin, of which only 10 g. have been available for this investigation, crystallises from benzene in garnet-coloured, prismatic needles; it has phenolic properties and contains two methoxyl groups, so the formula may be expanded to $C_{15}H_7O_2(OH)(OMe)_2$. The most characteristic property of the substance is the ease with which it combines with acids, yielding well-defined, crystalline, orange-red oxonium salts from which the base may be easily recovered. For example, the sulphate, $C_{17}H_{14}O_5,H_2SO_4$, crystallises from dilute sulphuric acid in orange needles but is decomposed on boiling with water, and the hydrochloride loses hydrogen chloride at 100°. The analogy existing between carajurin and the hydroxybenzopyranol bases prepared by Bülow and his collaborators has already been commented upon (" The Natural Organic Colouring Matters," Perkin and Everest, 1918, p. 343) and is indeed striking; physically, carajurin closely resembles anhydro-7-hydroxy-2 : 4-diphenylbenzopyranol (1 : 4) (I) (Bülow and Sicherer, *Ber.*, 1901, **34**, 2380), which crystallises from benzene. A third crystalline member of the group has been recently obtained by Hirst (this vol., p. 2490) and this (II) exhibits a still closer resemblance to carajurin.

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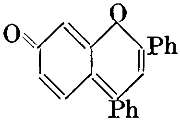

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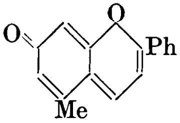
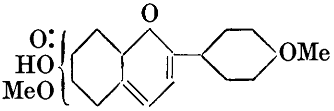


The composition of carajurin suggested that the connexion might be very close, because the colouring matter could be the anhydro-derivative of a dihydroxydimethoxyflavenol and thus be related to the large group of plant products that includes the flavones, flavonols, catechins, and anthocyanins. The coloured anhydrohydroxybenzopyranols have frequently been found to yield colourless derivatives of the hydroxybenzopyranols, and by the action of acetic anhydride and pyridine on carajurin a colourless *triacetyl* derivative, $C_{15}H_7O(OMe)_2(OAc)_3$, of hydrated carajurin was obtained. Further confirmation of this view was found in the fact that fusion of carajurin with caustic alkali at 200° afforded *p*-hydroxybenzoic acid, whilst on boiling with concentrated aqueous potassium hydroxide, *p*-acetylanisole was obtained.

Bromination of carajurin in hot acetic acid solution gives, with remarkable ease, a compound, $C_{17}H_{12}O_5Br_4$ or $C_{17}H_{14}O_5Br_4$, which crystallises in orange needles and is apparently both a hydrobromide and a perbromide. On treatment with boiling acetone it is changed into *dibromocarajurin*, $C_{17}H_{12}O_5Br_2$, crystallising in bright red needles, bromoacetone being simultaneously produced.

Carajurin is completely demethylated on boiling with hydriodic acid and yields *carajuretin hydriodide*, $C_{15}H_{11}O_5I$, which has the composition and properties of a tetrahydroxyflavylium iodide. The action of cold pyridine on this salt leads to the formation of carajuretin, $C_{15}H_{10}O_5$, which occurs in scarlet needles and forms a colourless *penta-acetyl* derivative of hydrated carajuretin, $C_{15}H_7O(OAc)_5$.

On the supposition that the carajurin and carajuretin salts are flavylium derivatives it becomes of importance to note that these substances exhibit no tendency whatever to pass into pseudo-bases. Since the effect of a hydroxyl or methoxyl group in position 3 in the pyrylium nucleus in facilitating pseudo-base formation is well established, we concluded that carajurin is related to the flavone rather than to the flavonol group, that is, bearing in mind the formation of *p*-acetylanisole (above), that carajurin has the formula (III). Such a constitution, representing the substance as a tetrahydroxybenzene derivative, served to explain the absence of phloroglucinol or other recognisable phenols from the alkali-fission products. Carajuretin hydrochloride, on this assumption, would conform to the type (IV), and in view of our strictly limited supply of the natural product we determined to synthesise flavylium salts of this nature in order to compare them with the carajuretin salts. The successful outcome of these synthetical investigations, which are described below, supplied the final proof of the correctness of the C_{17} formula for carajurin, and the fact that some of the salts which we prepared contain nuclear methyl groups is due to the uncertainty attached in the earlier stages to this question of the



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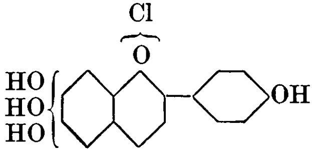
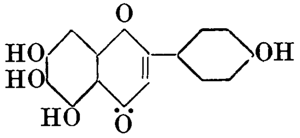


(IV.)

empirical formula. Guided by the assumed constitution of the flavone, scutellarein (V) (compare Bargellini, *Gazzetta*, 1915, **45**, i, 69; 1919, **49**, ii, 47), we prepared *scutellareinidin chloride* (VI) and found that this salt was identical with carajuretin hydrochloride. This solved the major problem and left four possibilities for carajurin (VII, VIII, IX, X) differing only in the arrangement of substituents in the tetrahydroxybenzene nucleus; (VIII) and (IX) are tautomeric and would yield identical hydrochlorides (XI). This 5 : 7-dihydroxy-6 : 4′-dimethoxyflavylium chloride has been synthesised (see below) and it is not identical with carajurin hydrochloride. Moreover, the latter gives a ferric chloride colour reaction indicating the existence of vicinal hydroxyl groups in the salt; (XI) exhibits no such reaction. The choice between (VII) and (X) cannot yet be made definitely, but (VII) is preferable on account of the colour and stability of carajurin. The analogies already quoted support the formula (VII), whereas (X) should be a violet or blue substance. In making this statement we are taking cognisance of unpublished observations on the anhydro-bases from 5-hydroxyflavylium salts, which are violet or blue and characterised by instability. The only recorded work bearing on this point is that of Collie and White (J., 1915, **107**, 369), who condensed orcinol with acetylacetone in presence of hydrogen chloride and isolated two structurally different hydroxytrimethylbenzopyrylium chlorides, of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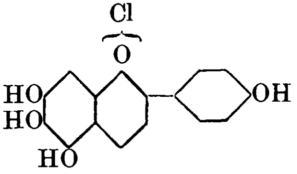
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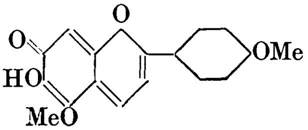
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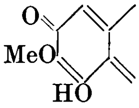
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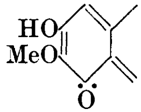
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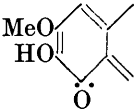
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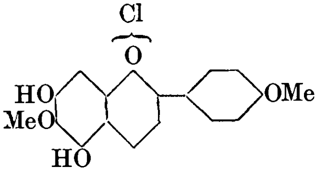
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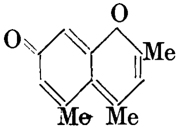
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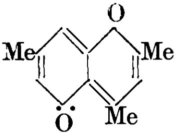

(XIII.)

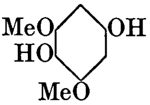
which one had a yellow and the other, obtained in smaller relative amount, an orange colour. The yellow salt gave a red quinonoid base (XII) and the orange salt gave a deep violet base (XIII). Provisionally, therefore, we suggest that carajurin has the formula (VII), and attempts to synthesise the colouring matter are in progress.

In addition to carajurin, carajura contains a second colouring matter, *carajurone*, $C_{15}H_9O_5{\cdot}OMe$, which has been isolated in a micro-crystalline condition. This substance resembles carajurin in many of its properties, but is insoluble in benzene. It is probably a carajuretin monomethyl ether, but a clear proof of this is not available. Carajurin and carajurone dye mordanted fabrics in almost identical shades (see p. 3027), whereas those given by carajuretin are somewhat yellower. The red resin contained in carajura was not closely examined.

Derivatives of 1 : 2 : 3 : 5-*Tetrahydroxybenzene.*

The work involved in the synthesis of carajuretin necessitated the preparation of a number of partly methylated derivatives of 1 : 2 : 3 : 5-tetrahydroxybenzene and we have investigated more particularly those which may be used as the starting points of syntheses that can only proceed in one direction at each stage. We have had in mind not merely our immediate purpose but also the possibility of the synthesis, ultimately, of quercetagetin and gossypetin by such unambiguous methods.

The readily accessible 2 : 6-dimethoxyquinol (XIV) was the starting point in many of our experiments; it could, for example, be directly condensed with anisoylacetone to a flavylium salt. On the other hand the introduction of the formyl group by Gattermann's method gave so poor a yield of the aldehyde (XV) that the process was useless for practical purposes. This was certainly due in part to the sparing solubility of dimethoxyquinol in ether, but also in all probability to its intrinsically small nuclear reactivity.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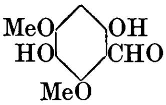
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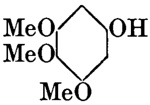
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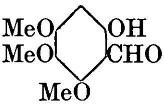
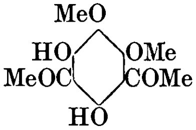

(XVII.)

The methylation of dimethoxyquinol yields only antiarol (XVI) and tetramethoxybenzene, and we have confirmed the orientation of antiarol and worked out satisfactory conditions for its preparation. Antiarolaldehyde (XVII) could be obtained by an application of Gattermann's synthesis, but all attempts to prepare ketones such as acetylantiarol and ω-methoxyacetylantiarol by the Hoesch method failed.

A series of experiments aiming at the *C*-acetylation of antiarol under varied conditions did not give the desired ketone, but two substances were isolated in small yield from the products of the action of aluminium chloride on antiarol and acetyl chloride in nitrobenzene solution. The first, m. p. 92—93°, gave analytical results agreeing with the formula (XVIII), whereas the second, m. p. 160—161°, is probably (XIX).



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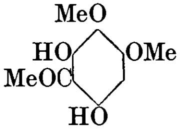

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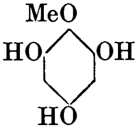

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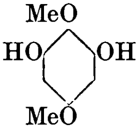
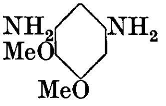


(XXI.)

Bargellini and Bini (*Atti R. Accad. Lincei*, 1910, **19**, ii, 595; compare Bargellini, *Gazzetta*, 1919, **49**, ii, 47) isolated (*a*) tetramethoxyacetophenone, m. p. 48—50°, (*b*) a substance, m. p. 106—108°, regarded as 6-hydroxy-2 : 3 : 4-trimethoxyacetophenone, and (*c*) a substance, m. p. 162—163°, to which the formula (XIX) was assigned, from the products of interaction of 1 : 2 : 3 : 5-tetramethoxybenzene and acetyl chloride in carbon disulphide solution in presence of aluminium chloride. Repetition of the experiment gave (1) cream-coloured crystals, m. p. 177—178°, (2) yellow prisms, m. p. 111—112°, (3) brownish-yellow crystals, m. p. 162—163°, (4) 2 : 3 : 4 : 6-tetramethoxyacetophenone, m. p. 53—54°. The m. p. of a mixture of the substance, m. p. 160—161°, from antiarol with either (1) or (3) showed a large depression. It is hoped that further work will elucidate the nature of these substances and a detailed description is therefore postponed. It may also be pointed out that Nierenstein (J., 1917, **111**, 4) has ascribed the constitution (XIX) to a product, m. p. 166—168°, of the incomplete methylation of 2 : 3 : 4 : 6-tetrahydroxyacetophenone.

We have utilised iretol (XX) for the preparation of certain flavylium salts, although in this case the reactions could proceed in alternative directions. Investigation of the products showed that the hydroxyl in the *p*-position to the methoxyl group is the one which is involved in the ring closure. An interesting confirmation of this is found in the proof that the monomethyl ether of iretol, obtained by de Laire and Tiemann (*Ber.*, 1893, **26**, 2015) by treatment of the phenol with methyl-alcoholic hydrogen chloride, has the constitution (XXI). This and (XXIII) are the only possibilities and we have synthesised a dimethoxyresorcinol of the formula (XXIII) from 3 : 5-dinitroveratrole. A dilute aqueous solution of the hydrochloride of the corresponding diamine (XXII), containing a little stannous chloride, was boiled for many hours. The resulting phenol (XXIII) differs from de Laire and Tiemann's iretol monomethyl ether, a direct synthesis of which is being attempted.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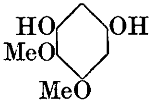
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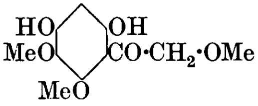
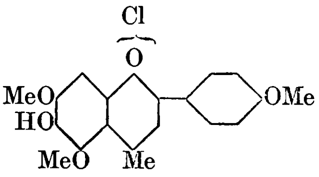

(XXIV.)

The dimethoxyresorcinols (XXIII and XXI) are the most suitable starting points in unambiguous syntheses of 3 : 5 : 6 : 7 : 3′ : 4′- and 3 : 5 : 7 : 8 : 3′ : 4′-hexahydroxyflavone, the constitutions, in all probability, of quercetagetin and gossypetin, respectively. In the former case we have demonstrated the feasibility of the scheme by the preparation of 2 : 4-dihydroxy-ω : 5 : 6-trimethoxyacetophenone (XXIV) from (XXIII) and methoxyacetonitrile in accordance with Hoesch's method (compare Slater and Stephen, J., 1920, **117**, 316). Test-tube experiments have convinced us that this ketone yields a flavonol derivative when it is heated with veratric anhydride and sodium veratrate (compare Allan and Robinson, J., 1924, **125**, 2192 and later communications).

Flavylium Salts derived from 1 : 2 : 3 : 5-*Tetrahydroxybenzene.*

Condensation of anisoylacetone and 2 : 6-dimethoxyquinol (XIV) in formic acid solution by means of hydrogen chloride gave (XXV), the alternative, a 4-anisyl-2-methylbenzopyrylium derivative, being excluded by the ready decomposition of the salt by alkalis with formation of *p*-acetylanisole and by analogy with the ascertained behaviour of benzoylacetone, for example, on condensation with phloroglucinol.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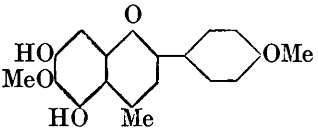
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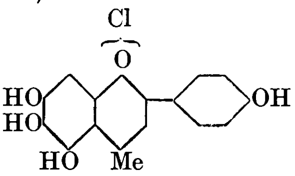
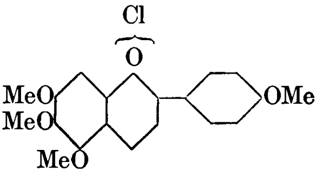
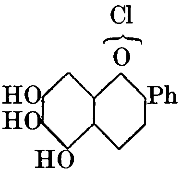

(XXVII.)

Anisoylacetone and iretol yield (XXVI) and on demethylation both

(XXV) and (XXVI) give 5 : 6 : 7 : 4′-*tetrahydroxy*-4-*methylflavylium chloride* (XXVII). Similarly 5 : 6 : 7 : 4′-*tetramethoxy*-4-*methylflavylium chloride* was obtained from antiarol and anisoylacetone. The action of hydrogen chloride on a mixture of antiarolaldehyde (XVII) and *p*-acetylanisole in acetic acid solution led to the formation of 5 : 6 : 7 : 4′-*tetramethoxyflavylium chloride* (XXVIII); 5 : 7-dihydroxy-6 : 4′-dimethoxyflavylium chloride (XI) was obtained from iretol and anisoylacetaldehyde. On demethylation with hydriodic acid both salts (proof of structure of XI) gave *scutellareinidin iodide*; the *chloride* (VI) obtained from this was, as already stated, identified with carajuretin hydrochloride.

(XXVIII.)





(XXIX.)

Antiarolaldehyde, acetophenone, and hydrogen chloride yield 5 : 6 : 7-*trimethoxyflavylium chloride* and on demethylation the salt (XXIX) was obtained. This is the flavylium salt corresponding to the flavone baicalein (Shibata, Iwata, and Nakamura, *Acta Phytochim.*, 1923, **1**, 105; Bargellini, *Gazzetta*, 1919, **49**, ii, 47) and may be termed *baicaleinidin chloride.*

EXPERIMENTAL.

Carajurin.—Finely powdered carajura (100 g.) was extracted with boiling benzene to remove wax, which was found to interfere with the isolation of the colouring matters, and then digested with a mixture of water (600 c.c.) and concentrated hydrochloric acid (65 c.c.) at 95° for 15 minutes. After cooling, the dull red mass was collected, washed, and dried in the air and finally at 100° (A., 65 g.). Partial evaporation of the filtrate led to the separation of a red powder containing very little colouring matter and consisting chiefly of calcium oxalate; evaporation to dryness then gave a viscid residue containing organic matter and soluble salts of calcium, magnesium, and potassium, the former in preponderating amount.

The product A was extracted with boiling alcohol; the dull chocolate-coloured residue (ash, 26·5%) contained sand, and organic matter having a peaty nature. The orange-red alcoholic solution was evaporated to dryness on pure sand, and the powdered mass extracted with benzene for several hours in a Soxhlet apparatus (residue, B). The extract, after treatment with a little animal charcoal, was filtered and concentrated; crystals were gradually deposited and the substance, after twice crystallising from benzene containing a trace of pyridine, was obtained in garnet-coloured needles, m. p. 205—207° (yield, 2·5 g.) (Found : C, 69·2, 68·6, 68·7, 68·1*, 68·1*; H, 4·7, 4·8, 4·9, 4·9*, 4·8* respectively; MeO, 19·8, 20·2, 20·6*, 20·4*, 20·5*. $C_{18}H_{16}O_5$ requires C, 69·2; H, 5·1; 2MeO, 19·9%. $C_{17}H_{14}O_5$ requires C, 68·4; H, 4·7; 2MeO, 20·8%).

Carajurin is sparingly soluble in hot benzene and alcohol, but is more readily soluble in pyridine; it does not dissolve in boiling dilute aqueous ammonia (distinction from carajuretin) and dissolves sparingly in dilute aqueous caustic alkalis to orange-red solutions which become brown on keeping. The solubility of carajurin in cold dilute aqueous sodium hydroxide is best demonstrated by its immediate complete extraction by the alkali from a dilute benzene solution. Carajurin and alcoholic lead acetate give a solution which slowly deposits pale red needles, whereas alcoholic ferric chloride gives a brownish-violet solution which becomes brown on the addition of an excess of the reagent.

Carajurin hydrogen sulphate. A hot solution of carajurin in acetic acid containing sulphuric acid gave a gelatinous precipitate on cooling, but when a trace of water was added to the hot liquid, fine, orange-yellow needles separated; these were collected and washed with acetic acid (Found : C, 50·7; H, 4·4. $C_{17}H_{14}O_5,H_2SO_4$ requires C, 51·5; H, 4·1%). Further analyses gave conflicting results, but owing to the necessity for conserving our material the matter was not pursued. The salt is readily soluble in boiling water, but decomposition occurs and the solution soon deposits red crystals of carajurin, m. p. 204—206°.

The *hydrochloride* crystallises from acetic acid in glistening, orange leaflets and from 8% hydrochloric acid in woolly balls of orange filaments which, when quickly heated, darken at 120° and partly fuse at about 196°, becoming black. On prolonged heating at 100° or on boiling with water it yields carajurin. It is, however, stable in aqueous solution in the presence of a slight excess of hydrochloric acid.

Action of Bromine on Carajurin.—When a solution of bromine (0·4 g.) in acetic acid (2·1 c.c.) was added to one of carajurin (0·23 g.) in boiling acetic acid (18 c.c.), crystals at once separated (yield, 0·46 g.) (Found: Br, 50·8. $C_{17}H_{14}O_5Br_4$ requires Br, 51·7%). The glistening, orange-red leaflets darkened at 195° and had become a black powder at 300°; on boiling with water, hydrogen bromide passed into solution. This tetrabromide (0·3185 g.) dissolved when boiled with acetone (10 c.c.), but red needles quickly separated and

* Indicates micro-analysis throughout.

the odour of bromoacetone became apparent. The product (yield, 75·3% of the weight of tetrabromide; in another experiment, 74·1%) evidently consisted of a dibromocarajurin (Found: Br, 35·2. $C_{17}H_{12}O_5Br_2$ requires Br, 35·2%); it did not melt, but became a carbonaceous mass at 300°. It dissolved in dilute alkalis to red solutions that became brown on keeping. Theoretically a carajurin tetrabromide (or a dibromocarajurin dibromide, $C_{17}H_{12}O_5Br_4$) should give 74% of its weight of dibromocarajurin.

A curious result was obtained when the bromination was effected in commercial acetic acid solution, red needles, apparently consisting of a crude tribromocarajurin, being isolated (Found: Br, 46·4. Calc.: Br, 44·9%).

Fission of Carajurin with Alkalis.—By fusing carajurin with 10 parts of sodium hydroxide and a little water at 200°, dissolving the melt in water, acidifying the solution and extracting it with ether, a crystalline product was obtained containing *p*-hydroxybenzoic acid and a colourless, crystalline substance, m. p. 185—187°, which was sparingly soluble in water and gave no coloration with ferric chloride.

A dilute solution of carajurin in dilute aqueous-alcoholic potassium hydroxide was rapidly distilled. The red liquid became orange-yellow (opening of the heterocyclic ring) and at a later stage a dark oil separated. When the alkali became quite concentrated, a colourless oil distilled in the steam, and this was isolated by means of ether and identified as *p*-acetylanisole by conversion into the semicarbazone, m. p. 197°, alone or mixed with an authentic specimen.

O-*Triacetyldihydrocarajurinol.*—The red solution of carajurin (0·2 g.) and pyridine (0·6 c.c.) in acetic anhydride was kept for 3 days and then mixed with ice-cold dilute sulphuric acid. The pink precipitate was collected, washed, dried in the air, and dissolved in a very small volume of hot acetone. Crystals (0·07 g.) separated on keeping, and were obtained, on recrystallisation from methyl alcohol (charcoal), in colourless leaflets, m. p. 142° (Found*: C, 62·3; H, 5·1. $C_{23}H_{22}O_9$ requires C, 62·4; H, 5·0%). When this substance was boiled with a mixture of alcohol and concentrated hydrochloric acid, an orange-yellow solution of an oxonium salt was obtained; the addition of sodium acetate produced a red colour, and the pigment (probably carajurin) could be extracted by benzene, giving a red solution.

A second acetylated carajurin derivative, probably *O*-acetylcarajurin, was obtained by the prolonged action of cold acetic anhydride and a trace of sulphuric acid on the colouring matter; it crystallised in orange needles, m. p. 190—191°, but has not been closely examined.

Carajuretin.—After the methoxyl estimations (those carried out on the normal scale, not those in which Pregl's micro-method was used) the hydriodic acid was found to contain red needles of *carajuretin hydriodide.* These were collected, washed with sulphurous acid and then with water, and dried at 100° (Found : I, 31·6. $C_{15}H_{10}O_5$,HI requires I, 31·9%) (yield, 133·5% on the weight of carajurin employed. Calc., 134·1%). When hydriodic acid was added to a solution of this salt in hot alcohol, characteristic, fan-shaped clusters of fine, red needles separated.

The hydriodide dissolved at once in a small volume of cold pyridine and crystals soon separated from the solution; after the addition of boiling water and cooling, the scarlet needles were collected (yield, 68% on the weight of carajuretin hydriodide. Calc., 67·8%). The substance was recrystallised by concentrating a solution in much boiling alcohol and then adding boiling water, and *carajuretin* was thus obtained as a woolly mass of red needles that became black at 330° without exhibiting a melting point (Found : C, 66·7 ; H, 4·1. $C_{15}H_{10}O_5$ requires C, 66·7 ; H, 3·7%).

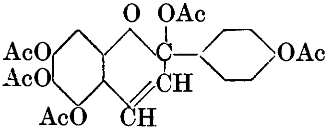
Carajuretin gives a fine crimson solution, becoming brown in the air, in aqueous ammonia or aqueous sodium carbonate. It gives a violet coloration with alcoholic ferric chloride, a dull reddish-violet precipitate with alcoholic lead acetate, and a deposit, probably of a monopotassium salt, with alcoholic potassium acetate. The substance combines with sulphuric acid in acetic acid solution to give the *hydrogen sulphate*, orange-yellow needles that can be crystallised from dilute sulphuric acid but are decomposed, with liberation of sulphuric acid (and probably carajuretin), on boiling with water.

The *hydrochloride* has been carefully examined for the sake of the comparison with the synthetical scutellareinidin chloride. Carajuretin hydriodide (0·9 g.) in hot alcoholic solution (100 c.c.) was decomposed by means of precipitated silver chloride. The filtered solution, mixed with a little hydrochloric acid, was concentrated; it then deposited prisms (0·53 g.) having an intense steel-blue lustre (Found* in material dried at 100° : C, 55·3, 55·5 ; H, 4·3, 4·2 ; Cl, 11·3, 11·0. $C_{15}H_{10}O_5$,HCl,H_2O requires C, 55·5 ; H, 4·0 ; Cl, 10·9%). The pure salt is sparingly soluble in alcohol to a brownish-orange solution; slightly impure specimens are readily soluble. Addition of a trace of ferric chloride to the alcoholic solution produces an intense brownish-violet coloration, which becomes reddish-brown on the addition of water. Addition of sodium carbonate to the alcoholic solution gives a fine permanganate-coloured liquid that becomes bluer on dilution with alcohol. The solution in aqueous sodium carbonate has a damson colour. The salt is sparingly soluble in cold 0·5% hydrochloric acid, but dissolves in the hot solvent;

on the addition of an equal volume of cold concentrated hydrochloric acid lustreless, woolly, orange needles are deposited, but if the liquid is heated, causing redissolution, and cooled very slowly, the substance separates completely in characteristic, elongated, rhombic prisms with a steel-blue lustre. These crystals are reddish-orange when viewed by transmitted light under the microscope and give a red smear on paper. Similarly the evaporation of an alcoholic solution of the chloride containing some 10% aqueous hydrochloric acid gives woolly needles that change in contact with the solvent into glistening, rhombic prisms. The salt is sparingly soluble in cold 7% sulphuric acid, but dissolves on heating: a gelatinous precipitate separates as the solution cools; on keeping, especially if warm, the amorphous material is replaced by very slender, orange-red needles. If aqueous perchloric acid (*d* 1·2) is added to the hot solution in 7% sulphuric acid, the *hydrogen perchlorate* quickly separates in clusters of short, orange-red needles exhibiting a bright metallic reflex.

The addition of bromine to a hot solution of carajuretin in acetic acid causes the immediate precipitation of minute, orange-red needles; these give hydrogen bromide to boiling water.

O-*Penta-acetyldihydrocarajuretinol*,



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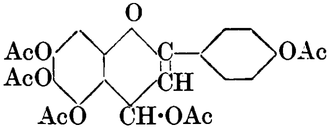


—A mixture of carajuretin (0·2 g.), pyridine (0·7 c.c.), and acetic anhydride (0·8 c.c.) was kept for 5 days; the red liquid was then added to ice-cold, dilute sulphuric acid and the pink precipitate was collected, washed, and dried on tile. An acetone solution of this product, after treatment with charcoal, was filtered and evaporated to dryness; the residue was dissolved in the minimum volume of boiling alcohol, and the solution allowed to cool. The cloudiness which then appeared was cleared by the addition of acetone drop by drop as required, and after 2 days the crystals (0·07 g.) were collected and twice recrystallised from benzene (charcoal). The colourless, prismatic needles, m. p. 156—157°, thus obtained were sparingly soluble in cold benzene and readily soluble in acetone (Found* : C, 60·3; H, 4·5. $C_{25}H_{22}O_{11}$ requires C, 60·2; H, 4·4%). This derivative discoloured on keeping in a specimen tube; it was reconverted into carajuretin hydrochloride by hydrolysis with alcoholic-aqueous hydrochloric acid and the characteristic lustrous, rhombic prisms of the salt were obtained. An acetyl estimation was carried out by Freudenberg's micro-analytical method (*Annalen*, 1923, **433**, 230; Freudenberg and Weber, *Z. angew. Chem.*, 1925, **38**, 280) [Found: Ac, 42·8. $C_{15}H_7O(OAc)_5$ requires Ac, 43·2%].

Carajurone.—The residue B (see p. 3022) in the Soxhlet tube after removal of carajurin was extracted with boiling acetone and, after treatment with charcoal and filtration, the solution was concentrated to a small volume. Dark, granular material separated and this was washed with a little benzene and crystallised from acetone. *Carajurone* was thus obtained as an indistinctly crystalline, scarlet mass, m. p. 183—186° (decomp.) (Found* in material dried at 105° in a high vacuum: C, 67·1; H, 4·3; MeO, 11·6. $C_{16}H_{12}O_5$ requires C, 67·6; H, 4·2; 1MeO, 11·1%) (an earlier analysis gave MeO, 11·4%).

Carajurone dissolves in aqueous sodium carbonate to a brownish-red solution, the colour of which is neither so intense nor so persistent on dilution as that obtained from carajuretin under similar conditions. The ferric chloride reaction in alcoholic solution closely resembles that given by carajurin; alcoholic lead acetate gives a maroon-coloured precipitate. The substance combines with strong acids, forming oxonium salts the solutions of which are brownish-orange, and there can be little doubt that it is carajuretin monomethyl ether. Definite evidence respecting the position of the methoxyl group, on this hypothesis, was not obtained, but the perceptible odour of *p*-acetylanisole observed on boiling a solution in concentrated aqueous sodium hydroxide is an indication that the methoxyl is in position 4′. The vapour evolved on destructive distillation of carajurone has an odour resembling that of *p*-hydroxybenzaldehyde.

Dyeing Properties.—Owing to its sparing solubility in water, crystalline carajurin dyes mordanted wool and cotton with difficulty; to overcome this, an alcoholic solution was poured into much water and satisfactory dyeings were then secured. The following comparative results were obtained on mordanted wool:

	Chromium.	Aluminium.	Tin.	Iron.
Carajurin.	Deep maroon.	Dull brownish-red.	Bright scarlet.	Deep violet-maroon.
Carajurone.	Deep maroon.	Dull brownish-red.	Dull scarlet.	Deep violet-maroon.
Carajuretin.	Brown.	Dull brownish-orange.	Brownish-scarlet.	Brownish-maroon.

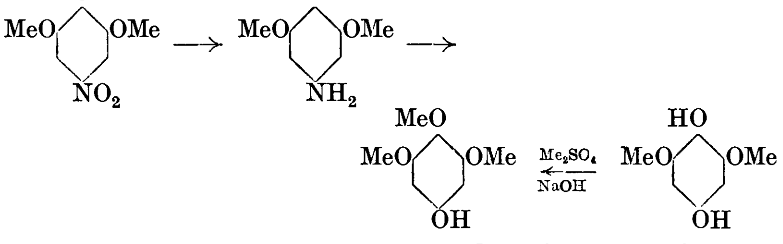
Pyrogallol Trimethyl Ether.—The following modification of Ullmann's method (*Annalen*, 1903, **327**, 116) for the methylation of pyrogallol gives an 86% yield of a colourless product that does not require the subsequent treatment with ether recommended by Ullmann.

Aqueous sodium hydroxide (150 c.c. containing 60 g. of sodium hydroxide) was gradually added from a tap-funnel during 3—4 hours to a mixture of pyrogallol (42 g.), methyl sulphate (189 g.), and alcohol (100 c.c.) agitated vigorously by means of a gas-tight stirrer and contained in a flask (reflux condenser) from which air was excluded by hydrogen. After the completion of the reaction the vessel was cooled in an ice-bath and the addition of water (150 c.c.) caused the separation of the ether in glistening, white prisms, m. p. 47°. The average yield in many experiments was 48 g.

Antiarol (XVI).—2 : 6-Dimethoxybenzoquinone (24 g.) was obtained by Graebe and Hess's method (*Annalen*, 1905, **340**, 237; compare Will, *Ber.*, 1888, **21**, 608) from nitric acid (*d* 1·2) in 95% alcohol and pyrogallol trimethyl ether (40 g.).

Dimethoxyquinol, m. p. 160° (literature, 158°), was obtained by reduction of the quinone in 87% yield. It is stated to be easily soluble in ether, but we found that 100 c.c. of dry ether dissolved only 0·4 g. of the phenol. It is readily soluble in acetone, the simple alcohols, and acetic acid in the cold, but it is very sparingly soluble in carbon disulphide, nitrobenzene, benzene, toluene, chloroform, *iso*amyl ether, and light petroleum in the cold. It is partly on this account that we experienced so much difficulty in the preparation of an aldehyde from this phenol.

Will (*loc. cit.*; compare Bargellini and Bini, *Gazzetta*, 1911, **41**, ii, 8) obtained a trimethoxyphenol as a by-product in the preparation of 1 : 2 : 3 : 5-tetramethoxybenzene by methylation of 2 : 6-dimethoxyquinol with methyl iodide and methyl-alcoholic potassium hydroxide. The constitution of this substance was apparently first determined by Schlör (*Diss.*, 1889; compare Graebe and Suter, *Annalen*, 1905, **340**, 224; Kiliani on antiarol from *antiaris toxicaria*, *Arch. Pharm.*, 1896, **234**, 444; Thoms and Siebelung, *Ber.*, 1911, **44**, 2124), and as it was a matter of considerable importance in the present investigation we confirmed the relations exhibited in the scheme, using the method of mixed melting points.



The following conditions were employed for the semi-methylation of 2 : 6-dimethoxyquinol, the object aimed at being the complete conversion of the quinol into antiarol and tetramethoxybenzene, because both substances were required and the separation of antiarol from dimethoxyquinol was difficult. A solution of sodium hydroxide (20 g.) in water (140 c.c.) was added to 2 : 6-dimethoxyquinol (34 g.) in a flask from which air was excluded by hydrogen. Methyl sulphate (32 g.) was then added in one portion with vigorous shaking, which was continued for 10—15 minutes and at intervals for 1 hour. 11 G. of 1 : 2 : 3 : 5-tetramethoxybenzene were isolated, and the alkali-soluble fraction (20 g.) was crystallised from ten times its weight of water and thus obtained in flat, white needles, m. p. 146° (yield 16·5 g.), and free from unchanged dimethoxyquinol.

Sodium antiarolate crystallised in silky, snow-white needles when a solution of antiarol in moderately concentrated aqueous sodium hydroxide was cooled.

O-*Acetylantiarol* (3 : 4 : 5-*trimethoxyphenyl acetate*), obtained by the action of boiling acetic anhydride and sodium acetate on the phenol, crystallised from not too much alcohol in colourless, transparent, elongated prisms, m. p. 74° (Found: C, 58·5; H, 6·3; MeO*, 40·8, 40·8, 40·7. $C_{11}H_{14}O_5$ requires C, 58·4; H, 6·2; 3MeO, 41·2%). The micro-analytical estimations of methoxyl in this readily purified substance gave slightly low results, and as those of carajurin were carried out in the same apparatus we considered that a similar small error would affect those determinations also. The first indication that carajurin has the formula $C_{17}H_{14}O_5$ rather than $C_{18}H_{16}O_5$ was obtained in this way.

3 : 6-*Dihydroxy*-2 : 4-*dimethoxybenzaldehyde* (XV).—Dry hydrogen cyanide in a stream of carbon dioxide and, by another delivery tube, a stream of hydrogen chloride, were simultaneously introduced into a warm solution of 2 : 6-dimethoxyquinol (3·5 g.) in ethyl acetate (100 c.c.). The slow passage of hydrogen chloride was continued for 2 hours and the flask was then stoppered and kept in the ice-chest. Next day, water was added to the reddish-green, dichroic solution so as to dissolve the small, dark-green deposit and the red, aqueous solution was then separated from the colourless ethyl acetate layer and boiled for a few minutes with passage of sulphur dioxide. On cooling, clumps of fine needles separated and these crystallised from hot water, containing sulphur dioxide, in very pale brown, feathery needles, m. p. 135—136° (Found: MeO*, 30·7. $C_9H_{10}O_5$ requires 2MeO, 31·3%). This substance, the yield of which was extremely poor, gives a sparingly soluble semicarbazone, and a golden-yellow solution in aqueous sodium hydroxide. It develops a green coloration, brown with excess of the reagent, on the addition of ferric chloride to its alcoholic solution.

Antiarolaldehyde (XVII).—In this experiment the use of sufficient ether to dissolve the antiarol was found inadvisable and the quantities were so adjusted that all the phenol passed into solution before the separation of aldimine hydrochloride commenced. Hydrogen cyanide (from 10 g. of potassium cyanide), carried over in a slow stream of carbon dioxide, was introduced into a solution and suspension of finely powdered antiarol (6 g.) in anhydrous ether (300 c.c.), and a moderately rapid stream of hydrogen chloride led into the mixture (reflux condenser), which was frequently shaken. After 3 hours, glistening, white crystals began to be deposited and after 2 hours more, the stream of gas was interrupted and the vessel stoppered and kept over-night. The ethereal solution was decanted and the aldimine hydrochloride decomposed by heating on the steam-bath with water (30 c.c.) for a few minutes. The aldehyde, which separated as an oil and crystallised on cooling (4·7 g.), was recrystallised by the addition of warm water to its solution in hot methyl alcohol (yield, 4·45 g.). It was obtained in elongated, flat, white prisms, m. p. 65° (Found : C, 56·8; H, 5·8. $C_{10}H_{12}O_5$ requires C, 56·6; H, 5·7%). *Antiarolaldehyde* is slightly soluble in boiling water to a colourless solution, which becomes turbid on cooling and then deposits beautiful, star-shaped aggregates of needles. It is readily soluble in ether, alcohol, benzene, chloroform, acetic acid, and acetone. In aqueous or alcoholic solution it develops an intense brownish-violet coloration on the addition of ferric chloride; its solution in aqueous sodium hydroxide has a greenish-yellow colour. The *semicarbazone*, prepared in the usual manner, crystallised from 80% alcohol in slender, colourless needles that became yellow at 210° and melted with effervescence at 245° (Found : N, 15·4. $C_{11}H_{15}O_5N_3$ requires N, 15·6%).

Iretol Monomethyl Ether (XXI).—Picric acid (50 g.) gave recrystallised picryl chloride (30 g.) according to Jackson and Gazzolo's method (*Amer. Chem. J.*, 1900, **23**, 384); the addition of benzene in the crystallisation from alcohol, recommended by these authors, was found to be unnecessary.

Jackson and Boos (*Amer. Chem. J.*, 1898, **20**, 444) showed that the scarlet compound obtained by the action of sodium methoxide on picryl chloride yields methyl picrate on decomposition with water, but the method does not appear to have been used for the preparation of the substance in quantity. The following conditions gave good results. Sodium (4 g.) was dissolved in methyl alcohol (120 c.c.), and the solution added with shaking to one of picryl chloride (20 g.) in methyl alcohol (40 c.c.). After a short time, 80—100 c.c. of the methyl alcohol were distilled away and hydrochloric acid was added to the residue until it became yellow (acid reaction). Precipitation of the ether was completed by water and after one crystallisation of the product from 60 c.c. of methyl alcohol it had m. p. 67—68° (yield, 18 g.) (Buttle and Hewitt, J., 1909, **95**, 1759, assign the m. p. 68° to the pure ether).

The conversion of methyl picrate into iretol was carried out by Kohner's method (*Monatsh.*, 1899, **20**, 928), and de Laire and Tiemann's work (*loc. cit.*) on the monomethylation of iretol from irigenin was confirmed with the synthetical material.

4 : 5-*Dimethoxyresorcinol* (XXIII).—The nitration of 4-nitroguaiacol (Pollecoff and Robinson, J., 1918, **113**, 647) required very careful control and the following method was used. Nitric acid (100 c.c.; *d* 1·42), cooled in ice to 0—3°, was mechanically stirred, finely powdered 4-nitroguaiacol (10 g.) was added in one portion, and 50 c.c. of nitric acid (*d* 1·42) at 0° were used to wash the stirrer and the sides of the container. The temperature rose and when it reached 11—12°, usually in 2 or 3 minutes, a large volume of water was added, precipitating the dinitroguaiacol as a bulky, yellow, crystalline mass (yield, 10·5 g.; m. p. 121—122°; the pure substance has m. p. 123°).

The dinitroguaiacol (15 g.) gave 4 : 6-dinitroveratrole (13·5 g., m. p. 97—98°; the pure substance has m. p. 101—102°) when heated with potassium carbonate and methyl sulphate in nitrobenzene solution.

A mixture of 4 : 6-dinitroveratrole (15 g.), granulated tin (50 g.), concentrated hydrochloric acid (150 c.c.), and water (50 c.c.) was shaken, the reaction being started by gentle heating on the steam-bath, subsequently moderated by the addition of water (20—30 c.c.), and finally completed by short heating on the steam-bath. The filtered liquid was evaporated to dryness under diminished pressure, air having been displaced by carbon dioxide, and the residue was dissolved in water. After removal of tin as sulphide, the filtered solution was evaporated to dryness under the conditions previously employed, leaving a white, crystalline crust (15 g.). This gave the *m*-diamine reaction with nitrous acid and a purple coloration with ferric chloride in aqueous solution. A solution of this product (17 g.) and stannous chloride (3·5 g.) in air-free water (1000 c.c.) was refluxed for 48 hours in a stream of carbon dioxide. Tin was eliminated as sulphide from the filtered, yellowish solution and the liquid was then concentrated to about 150 c.c. under diminished pressure (of carbon dioxide) and extracted with ether. The combined extracts were dried with sodium sulphate and filtered and the solvent was removed, finally under diminished pressure, leaving a brown oil that solidified on rubbing and was found to be free from nitrogenous material. This was dissolved in a little water, and lead acetate added, giving a small, flocculent precipitate. Lead was eliminated as sulphide from the filtered solution, which was then evaporated to dryness under diminished pressure (carbon dioxide). The residue was dissolved in warm benzene; on slowly cooling, an oil separated; the benzene was decanted from this, and glassy crystals were then deposited. After recrystallisation from benzene the hard, transparent prisms, approximately tetrahedral in shape but possessing many facets, were dried in the air and then had m. p. 76—77°. When stored in an evacuated desiccator over calcium chloride, the crystals became at first sticky, adhering together, and then in a few days dry and friable again. The anhydrous material had m. p. 115—116° (Found*: C, 56·5; H, 5·9; MeO, 36·2. $C_8H_{10}O_4$ requires C, 56·4; H, 5·9; 2MeO, 36·5%). The solvent of crystallisation was also retained when the phenol was crystallised from chloroform; it was water, because, in a second experiment, the crude product was more thoroughly dried before the crystallisation from benzene and the crystals (1·1 g.) then melted at 105—110° and at 113° after recrystallisation.

The behaviour of this *dimethoxyresorcinol* with ferric chloride distinguishes it sharply from iretol monomethyl ether, the colorations developed in aqueous solutions being reddish-brown and blue respectively. A pine shaving, immersed in an alcoholic hydrochloric acid solution of the phenol, becomes mauve in colour.

Attempted Nuclear Acetylation of Antiarol.—There was no satisfactory outcome of experiments in which antiarol was (1) heated with acetic acid and zinc chloride, (2) treated with sulphoacetic acid at room temperature (compare Schneider and collaborators, *Ber.*, 1921, **54**, 1484, 2298, 2302; 1922, **55**, 1892), (3) boiled with acetic anhydride containing a little concentrated sulphuric acid (compare Brand and Collischonn, *J. pr. Chem.*, 1921, **103**, 338), (4) treated with acetyl chloride alone or in presence of anhydrous ferric chloride with or without carbon disulphide as solvent, (5) treated in anhydrous ether with acetonitrile (or methoxyacetonitrile) and hydrogen chloride, with or without the addition of zinc chloride.

Antiarol could not be carboxylated by means of potassium hydrogen carbonate, even in glycerol solution at 180° (stream of carbon dioxide) (compare Brunner, *Annalen*, 1907, **351**, 359); the phenol was recovered unchanged.

The relatively small nuclear reactivity of antiarol is of theoretical interest, a comparison with the much more reactive phloroglucinol dimethyl ether illustrating the depressing effect of the methoxyl group in the *m*-position to the free nuclear positions. An analogous phenomenon is the feeble reactivity of pyrogallol, in comparison with resorcinol, in the Hoesch reaction.

Acetyl chloride (10 c.c.) and then aluminium chloride (16 g.)

were added to a solution of antiarol (10 g.) in nitrobenzene (160 c.c.) and the mixture was heated for a short time on the steam-bath. The following products were isolated : (A). This was precipitated on addition of a little water to an alcoholic solution of the mixture; it crystallised from aqueous alcohol in stout, white needles, m. p. 92—93° (Found : C, 56·7, 56·7; H, 5·5, 5·7; MeO*, 24·1, 24·0. $C_{12}H_{14}O_6$ requires C, 56·7; H, 5·6; 2MeO, 24·4%). This substance, 4 : 5-*dimethoxy*-2 : 6-*diacetylresorcinol* (XVIII), is sparingly soluble in water, readily soluble in ether, and develops a deep red coloration with alcoholic ferric chloride. It dissolves in aqueous sodium hydroxide to a yellow solution and is not decomposed when the liquid is boiled.

After the separation of (A) a second substance (B) was isolated by taking advantage of its relatively sparing solubility in ether. It was only obtained in small amount, and crystallised from benzene in yellow prisms, m. p. 160—161° (Found* : MeO, 28·7, 28·9. $C_{10}H_{12}O_5$ requires 2MeO, 29·3%). (C) was obtained in minute amount from the ethereal solution, after separation of (A) and (B), in pearly plates, m. p. 78—84°, but owing to paucity of material it was not further investigated.

ω : 5 : 6-*Trimethoxyresacetophenone* (XXIV).—A solution of 4 : 5-dimethoxyresorcinol (0·75 g.) and methoxyacetonitrile (0·4 g.) in dry ether (30 c.c.) was saturated with hydrogen chloride and kept over-night. A clear solution resulted, but on the addition of fresh dry ether, colourless crystals were precipitated and these were separated and washed with ether. When an aqueous solution of this ketimine hydrochloride was heated on the steam-bath for a few minutes, the normal ready hydrolysis did not occur and ether extracted only a minute amount of the ketone. After being kept for several weeks, however, the aqueous solution gradually deposited yellow crystals, m. p. 128—129°. The substance crystallised from water in long, glistening, very pale yellow needles, m. p. 129—130° (Found* : C, 54·7; H, 5·9; MeO, 38·3. $C_{11}H_{14}O_6$ requires C, 54·5; H, 5·8; 3MeO, 38·4%). The ketone is readily soluble in alcohol and in boiling water; its solution in 10% aqueous sodium hydroxide is yellow, and after prolonged boiling, the unchanged substance, m. p. 129—130°, is recovered an acidification. The addition of ferric chloride to an alcoholic solution produces a holly-green coloration which fades to brown; in aqueous solution, the coloration is brownish-black.

Anisoylacetone.—Besthorn and Jaegli (*Ber*., 1894, **27**, 810) employed alcohol-free sodium ethoxide for the condensation of *p*-acetylanisole and ethyl acetate. We have used sodamide as the condensing agent. Finely powdered sodamide (4 g.) was added to a mixture of *p*-acetylanisole (15 g.), ethyl acetate (22 g.), and dry ether (70 c.c.). A brisk reaction (reflux) supervened and the mixture was occasionally shaken during an hour and then warmed for a few minutes on the steam-bath. The sodium salt was separated and after acidification of its aqueous solution with acetic acid, a product, m. p. 55—56°, was isolated (8·1 g.). After crystallisation from methyl alcohol the m. p. was 57° (literature, 54·5°).

6-*Hydroxy*-5 : 7 : 4′-*trimethoxy*-4-*methylflavylium Chloride* (XXV). —A mixture of 2 : 6-dimethoxyquinol (3·4 g.), anisoylacetone (4 g.), and formic acid (50 c.c.; 98—100%) was saturated with hydrogen chloride for several hours and next day the oxonium salt was precipitated as a red, crystalline powder (5·5 g.) by the addition of ether. The *chloride* crystallised from dilute hydrochloric acid in stellar aggregates of slender, red needles (Found in material dried in a vacuum over potassium hydroxide: C, 58·4; H, 5·7. $C_{19}H_{19}O_5Cl,1{\cdot}5H_2O$ requires C, 58·5; H, 5·7%). On heating, the salt lost water at 120° and then melted with decomposition at 139° to 145° according to the rate of heating. It dissolves in hot water to a red solution and in hot dilute hydrochloric acid to an orange solution. Addition of sodium carbonate to an aqueous solution gives a deep red liquid tinged with purple; on keeping, it becomes turbid and yellow. The reaction with sodium hydroxide is similar, but the change is more rapid. Sodium acetate, added to an aqueous solution, gives the pseudo-base as a dirty grey precipitate. The intensely golden-yellow solution in sulphuric acid does not exhibit fluorescence. Ferric chloride gives no characteristic reaction. After a solution of the salt in 20% aqueous potassium hydroxide had been refluxed for 1 hour (atmosphere of hydrogen), *p*-acetylanisole was isolated from the products by means of ether. The semicarbazone crystallised from alcohol in needles, m. p. 197°, alone or mixed with an authentic specimen. The *ferrichloride* crystallised from acetic acid in flat, elongated prisms, m. p. 205°, that are reddish-brown by reflected light and pale orange-brown by transmitted light (Found: C, 43·7; H, 3·8. $C_{19}H_{19}O_5Cl_4Fe$ requires C, 43·4; H, 3·7%).

5 : 7-*Dihydroxy*-6 : 4′-*dimethoxy*-4-*methylflavylium Chloride* (XXVI).—A moderately rapid stream of hydrogen chloride was passed through a mixture of iretol (1·6 g.), anisoylacetone (2 g.), and formic acid (30 c.c.; *d* 1·2) for 2 hours. The glistening, red prisms that separated (3·25 g.) crystallised from 3% hydrochloric acid (1 g. required about 400 c.c.) in shining, red needles, which became duller on being kept in a vacuum over sodium hydroxide for 3 days (Found: C, 60·0; H, 5·2. $C_{18}H_{17}O_5Cl,0{\cdot}5H_2O$ requires

C, 60·4; H, 5·1%). This specimen darkened rapidly at 100—105°, was very dark at 120°, shrank at 135°, became black at 150°, and melted with vigorous decomposition at 208°. On the other hand, an air-dried specimen lost water at 120°, but the salt darkened very slowly; it blackened from 170° to 190° and melted with vigorous decomposition at 208°.

The chloride is moderately readily soluble in water and alcohol, giving bright red solutions, and is sparingly soluble in dilute hydrochloric acid, the solution being reddish-orange. The reddish-yellow solution in sulphuric acid becomes deep red on warming. Sodium carbonate, added to an aqueous solution, gives a purplish-red coloration, persistent even on boiling, but with sodium hydroxide the red colour changes to yellow and on boiling the odour of *p*-acetylanisole becomes apparent. This salt exhibits no characteristic ferric chloride reaction, a fact of interest in connexion with the constitution of carajurin.

Addition of sodium acetate to a solution of the chloride caused the separation of the red anhydro-base as an oil, which solidified and was soluble in hot benzene to a deep red solution.

The *ferrichloride* crystallised from acetic acid in compact, rhombic prisms, m. p. 180—181° with slight previous darkening (Found: C, 42·3; H, 3·5. $C_{18}H_{17}O_5Cl_4Fe$ requires C, 42·3; H, 3·4%). The crystals were red in mass, exhibited a blue metallic lustre, and appeared brown when viewed by transmitted light.

5 : 6 : 7 : 4′-*Tetramethoxy-4-methylflavylium Ferrichloride*.—A mixture of antiarol (2·7 g.), anisoylacetone (3 g.), and formic acid (35 c.c.; *d* 1·2) was treated with hydrogen chloride for 6 hours, and the saturated solution then kept for several days. The *chloride*, precipitated by ether (4·6 g.), crystallised from dilute hydrochloric acid in slender, silky, orange-red needles, m. p. 143—144° (decomp. and previous darkening). The *ferrichloride* crystallised from acetic acid in golden-yellow needles, m. p. 176° (Found: C, 44·5; H, 4·0. $C_{20}H_{21}O_5Cl_4Fe$ requires C, 44·5; H, 3·9%).

5 : 6 : 7 : 4′-*Tetrahydroxy-4-methylflavylium Chloride* (XXVII).—(A) *From the trimethyl ether* (XXV). In our earlier experiments we obtained a specimen of the demethylated chloride in the usual manner; it formed reddish-brown prisms exhibiting a bluish-green lustre (Found: C, 57·8; H, 4·7; Cl, 10·3; loss at 105—110° in a high vacuum, 2·7. $C_{16}H_{13}O_5Cl,0{\cdot}5H_2O$ requires C, 58·3; H, 4·3; Cl, 10·8; H_2O, 2·7%. The monomethyl ether, $C_{17}H_{15}O_5Cl,H_2O$, requires C, 57·9; H, 4·9; Cl, 10·1; H_2O, 5·1%). It was clearly impossible to be sure that demethylation was complete and the process was therefore investigated quantitatively. A specimen of the initial material (XXV) was twice crystallised from 7%

hydrochloric acid and dried in a vacuum desiccator over sodium hydroxide; it differed somewhat from that described above and, on heating, lost water at 120° and melted at 142—143° with effervescence (Found: C, 49·9; H, 6·0%). We suspect that this product may have had the composition $C_{19}H_{19}O_5Cl,HCl,3H_2O$, which requires C, 50·3; H, 5·8%, but it was sufficient for our purpose that the analysis indicated that it contained 71·4% of the anhydro-base $C_{19}H_{18}O_5$. When the salt (0·3156 g.), mixed with phenol (8·0 g.) and hydriodic acid (20 c.c.; *d* 1·7), was heated at 135—145° in an atmosphere of carbon dioxide, demethylation was complete after 3 hours (Found: MeO, 19·8. Calc.: MeO, 20·4%), and this was confirmed in two further experiments. In the absence of phenol, however, demethylation was incomplete (Found: MeO, 17·7%). The *iodide* was isolated, after the addition of ether, in lustrous, brownish-red, diamond-shaped plates that appeared pale brown by transmitted light. Addition of hydriodic acid to its hot solution in alcohol caused the separation of characteristic, glistening, radiating clusters of flat, red needles. On heating, it began to shrink and darken at 278° and melted with decomposition at 290°. When treated with pyridine (compare the behaviour of the lower homologue carajuretin hydriodide, p. 3025), the salt dissolved, but on stirring, needle crystals, changing to prisms, separated. The anhydro-base could not be isolated in a sufficiently pure form for analysis.

The *chloride* was prepared from the iodide in alcoholic solution in the usual manner by means of silver chloride. It was twice recrystallised by the addition of concentrated hydrochloric acid to its alcoholic solution, which was then concentrated and cooled, and was obtained in reddish-brown, oblique, frequently twinned prisms. The smaller crystals appeared reddish-brown, but the larger ones had a bluish-green metallic reflex (Found in material dried in a vacuum over sodium hydroxide: C, 58·5; H, 4·5. $C_{16}H_{13}O_5Cl,0·5H_2O$ requires C, 58·3; H, 4·3%). A specimen was again crystallised (Found: C, 58·6; H, 4·4%). The salt gradually darkened above 200°, lost its lustre at about 255°, and became very dark at 270°, but did not melt at 320°. It is sparingly soluble in cold water and moderately readily soluble in hot water to a red solution. Other properties are mentioned below.

(B) *From the dimethyl ether* (XXVI). The chloride (0·3—0·4 g.) was demethylated by means of hydriodic acid (20 c.c.; *d* 1·7) in presence of phenol (8 g.) for 3 hours at 135—145° with passage of carbon dioxide. The methyl iodide was absorbed in pyridine (Found: MeO, 16·7, 16·6. Calc.: MeO, 17·3%). The isolated *iodide* had all the properties mentioned above under (A), but the *chloride*, in this case very sparingly soluble in alcohol, crystallised in well-formed, hexagonal tablets, reddish-brown by transmitted light and exhibiting a splendid green lustre (Found : C, 59·9 ; H, 4·1. $C_{16}H_{13}O_5Cl$ requires C, 59·9; H, 4·1%). The crystals separated from a hot solution during the distillation of the alcohol and this may account for their anhydrous character, but the superficial difference between this specimen and the one obtained as above under (A) was sufficiently great to give us at first the impression that the substances were structurally different. Further experiments and comparison with the analogous case of scutellareinidin chloride have made it clear that the chlorides from (A) and (B) were, in fact, identical, although the latter was the purer specimen. The behaviour on heating was the same as that cited above (under A) and all the reactions and solubility relations of the two specimens were found to be identical. The salt is a homologue of carajuretin hydrochloride and in some of its properties resembles this substance. A solution in aqueous sodium carbonate has a brownish-cherry-red colour, but on dilution with alcohol the change of shade towards blue is not so pronounced as is the case with carajuretin. The damson solution in aqueous sodium hydroxide is not so intensely coloured as an equivalent solution of carajuretin and when it fades it becomes more brownish-yellow. The colour reaction with ferric chloride in alcoholic solution was brownish-red; the violet tinge observed with carajuretin was absent. For purposes of comparison of the specimens prepared as under (A) and (B), the behaviour of the salt with acetone, chloroform, sodium acetate, ammonia, concentrated hydrochloric and sulphuric acids was observed, but the details need not be recorded.

5 : 6 : 7 : 4′-*Tetramethoxyflavylium Chloride* (XXVIII).—A mixture of antiarolaldehyde (4·2 g.), *p*-acetylanisole (3 g.), and acetic acid (10 c.c.) was saturated with hydrogen chloride at 60° for 6 hours; on cooling and keeping, bright red needles were copiously deposited (6·5 g.). On heating, the salt lost water at 100—120°, darkened at 140°, and had m. p. 145—146° (decomp.). It is sparingly soluble in cold water, acetone, or dilute hydrochloric acid, more readily soluble in alcohol, and all its solutions have a golden-yellow colour. The amber-yellow solution in concentrated sulphuric acid did not fluoresce and on heating became bright red and then deep red. The *ferrichloride* crystallised from acetic acid in orange, elongated prisms, m. p. 170° (Found: C, 43·5; H, 3·8. $C_{19}H_{19}O_5Cl_4Fe$ requires C, 43·4; H, 3·7%).

5 : 6 : 7 : 4′-*Tetrahydroxyflavylium Chloride* (*Scutellareinidin Chloride, Carajuretin Hydrochloride*) (VI).—A mixture of tetramethoxyflavylium chloride (2·5 g.), phenol (8 g.), and hydriodic

acid (70 c.c.; *d* 1·7) was boiled in an atmosphere of carbon dioxide for 20—30 minutes. The salt passed into solution, but glistening, deep red crystals slowly separated again and, after cooling, these were isolated (2·2 g.). The substance decomposed from 200—270° without melting.

The iodide was converted in the usual manner into the *chloride*, which crystallised from alcohol, containing concentrated hydrochloric acid, in shining, reddish-brown plates exhibiting a green reflex (Found: C, 59·3, 59·5; H, 4·1, 4·1. $C_{16}H_{13}O_5Cl$ requires C, 59·9; H, 4·1%). As a result of later work we now regard this substance as consisting essentially of a *scutellareinidin chloride monomethyl ether*. It does not melt below 285°.

Demethylations were then effected in which the amount of methyl iodide produced was estimated. The 5 : 6 : 7 : 4′-tetramethoxyflavylium chloride employed was crystallised from 10% hydrochloric acid and obtained in hair-fine, red needles which were dried in a vacuum over sodium hydroxide. As before, the m. p. was 145—146° (decomp.), but the chlorine content (11·3%) indicated a complex constitution ($C_{19}H_{19}O_5Cl$ requires Cl, 9·8%). The theoretical methoxyl content was therefore calculated from the results of combustions (Found: C, 55·2, 55·4; H, 5·7, 5·8; and hence complete demethylation requires MeO, 30·1%). The salt (0·3038 g.) was heated at 135—145° with hydriodic acid (20 c.c.; *d* 1·7) for 2·5 hours (Found: MeO, 22·9. Calc.: for 3MeO, 22·6%); in later experiments the quantities of the salt and of hydriodic acid were similar. Addition of 2 g. of phenol raised the methoxyl eliminated to 24·6%; 6 g. raised it to 28·3%; and using 8 g. of phenol and heating for 3 hours, we found MeO, 29·5% in two experiments. The last conditions were accordingly employed in the preparation of scutellareinidin iodide, and the phenol and hydriodic acid were always heated together at 135—140° to remove impurities before the introduction of the flavylium salt. The *iodide* was collected after the addition of ether and had all the properties previously mentioned as characteristic of carajuretin hydriodide. The *chloride* crystallised from alcohol–concentrated hydrochloric acid in reddish-brown, rhombic tablets exhibiting a dark green metallic lustre (Found in material dried in a vacuum over sodium hydroxide: C, 58·6; H, 3·8. $C_{15}H_{11}O_5Cl$ requires C, 58·7; H, 3·6%). This specimen, therefore, was anhydrous, whereas carajuretin hydrochloride crystallised with $1H_2O$; nevertheless a direct comparison showed that the substances were identical, and this is a further example of the small reliance to be placed on the extent of hydration of flavylium salts as a guide to their individuality. Another case is mentioned above and it may be recalled that Malkin and

Robinson (J., 1925, **127**, 1190) obtained two specimens of pelargonidin chloride 3 : 4′-dimethyl ether, only one of which persistently crystallised in a hydrated form. All the reactions and properties given above under the heading " carajuretin hydrochloride " were also found to be characteristic of scutellareinidin chloride and a specimen of the latter having the steel-blue appearance of the former was obtained by repeated crystallisation. Finally, scutellareinidin chloride was converted into an acetyl derivative of the pseudo-base as previously described for the carajuretin derivative. The substance had m. p. 156—157°, alone or mixed with *O*-penta-acetyldihydrocarajuretinol, and the other properties of the specimens exhibited no divergences.

5 : 7-*Dihydroxy*-6 : 4′-*dimethoxyflavylium Chloride* (XI).—A solution of *p*-anisyl β-hydroxyvinyl ketone (from 4 g. of the copper derivative) in dry ether (100 c.c.) was added to one of iretol (2·2 g.) in dry ether (200 c.c.), and the mixture saturated with hydrogen chloride for 6 hours. The red solid was separated (4 g.) and extracted with very dilute hydrochloric acid; the filtered solutions deposited microscopic red crystals, which were recrystallised from 9% hydrochloric acid, only 0·18 g. of the pure salt being obtained. The salt was also obtained and in rather better yield by using dry ethyl acetate as the solvent; it crystallised in minute, red needles (Found* : MeO, 17·4. $C_{17}H_{15}O_5Cl,H_2O$ requires 2MeO, 17·6%). It did not melt at 260° and was moderately readily soluble in alcohol and in water to red solutions that gave no distinctive coloration with ferric chloride. A further distinction from carajurin hydrochloride was the solubility in aqueous sodium carbonate to a red solution.

The chloride (0·16 g.) was added to phenol (4 g.) and hydriodic acid (10 c.c.; *d* 1·7), and the mixture boiled with passage of carbon dioxide for 1·5 hours. After cooling and addition of ether, the demethylated iodide (0·13 g. of maroon needles) was collected and transformed into the chloride in the usual manner. This salt (yield, 0·08 g.) crystallised from alcohol–concentrated hydrochloric acid in clumps of dark reddish-brown, flat prisms or plates having a bluish-green reflex. On solution in 0·5% hydrochloric acid and addition of concentrated hydrochloric acid, woolly, orange-red needles were obtained and on reheating and slow cooling, glistening, rhombic prisms exhibiting a steel-blue reflex were deposited. The colour of the acid solutions, the solubility relations, and the reactions with alkalis and with ferric chloride were all identical with those of scutellareinidin chloride and carajuretin hydrochloride. The preparation of *O*-penta-acetyldihydrocarajuretinol could not be attempted in this case owing to paucity of material and the poor yield in the acetylation.

5 : 6 : 7-*Trimethoxyflavylium Salts.*—A mixture of antiaroldehyde (5·6 g.), acetophenone (3·2 g.), and acetic acid (10 c.c.) was saturated with hydrogen chloride at 65—70° for 6—7 hours. After keeping for 12 hours, the flavylium chloride was precipitated by the addition of ether as a reddish-brown, crystalline mass; this crystallised from 9% hydrochloric acid (100 c.c.) in slender, golden-yellow, silky needles (yield, 8·2 g.) which darkened at 110° and had m. p. 124—125° (decomp.). The salt is readily soluble in hot water, hot dilute hydrochloric acid, cold alcohol, or acetone to golden-yellow solutions. Its amber-yellow solution in sulphuric acid becomes bright red and then deep red on heating; consequently this reaction, shared with many other substances described in this communication, is due to the tetrahydroxybenzene nucleus. The cream-coloured pseudo-base is precipitated by the addition of sodium acetate or sodium carbonate to an aqueous solution of the chloride. The *ferrichloride* crystallises from acetic acid in well-formed, deep red prisms, m. p. 151°, exhibiting a bluish glance and appearing brownish-yellow by transmitted light (Found: C, 43·9; H, 3·5. $C_{18}H_{17}O_4Cl_4Fe$ requires C, 43·7; H, 3·5%). The derivative is readily soluble in acetone to a red solution.

5 : 6 : 7-*Trihydroxyflavylium Chloride* (*Baicaleinidin Chloride*) (XXIX).—5 : 6 : 7-Trimethoxyflavylium chloride (3 g.) and phenol (10 g.) were added to hydriodic acid (70 c.c.; *d* 1·7) and the mixture was gently boiled in a stream of carbon dioxide for 1 hour. In this case the salt remained in solution during the operation and we attribute the complete demethylation observed to this circumstance. After cooling, the iodide crystallised and was collected and washed with ether (yield, 1·5 g.); it formed long, transparent prisms, reddish-brown by reflected and pale brown by transmitted light. It sintered above 225° and had m. p. 254° (decomp.). The conversion into the *chloride* was carried out in dilute alcoholic solution by means of precipitated silver chloride; after concentration the salt separated in bluish-red, metallic-looking crystals (1·8 g.) and was recrystallised from 9% hydrochloric acid (500 c.c.). The glistening, dark maroon, elongated prisms with rectangular ends were dried in a vacuum over sodium hydroxide, causing them to become opaque and lustreless (Found: C, 59·6, 59·6; H, 4·0, 4·1. $C_{15}H_{11}O_4Cl,0{\cdot}5H_2O$ requires C, 60·1; H, 4·0%). A specimen was boiled with hydriodic acid (*d* 1·7) and phenol for 4 hours, but no trace of methyl iodide was produced. The salt darkened above 220° and at 250—252° appeared to soften and decompose, leaving a black mass which did not melt at 320°. The chloride is sparingly soluble in water to a brownish-yellow solution and gives a reddish-brown coloration with sodium hydroxide, sodium carbonate, and

even with sodium acetate. The brownish-red alcoholic solution becomes much more intensely reddish-brown on the addition of ferric chloride.

We desire to thank the Royal Society for a grant which defrayed a part of the cost of the investigation.

THE UNIVERSITIES OF LEEDS AND
MANCHESTER.

[*Received, October* 18*th*, 1927.]