635. *The Occurrence of 2-Benzyl-2-hydroxycoumaran-3-ones in Quebracho Tannin Extract.*

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The isolation and identification of the crystalline 2-benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one from commercial Quebracho tannin extract is now detailed. The structure of the compound has been confirmed by dehydration to the corresponding benzylidenecoumaran-3-one (aurone) and by synthesis from ω-hydroxyresacetophenone and isovanillin.

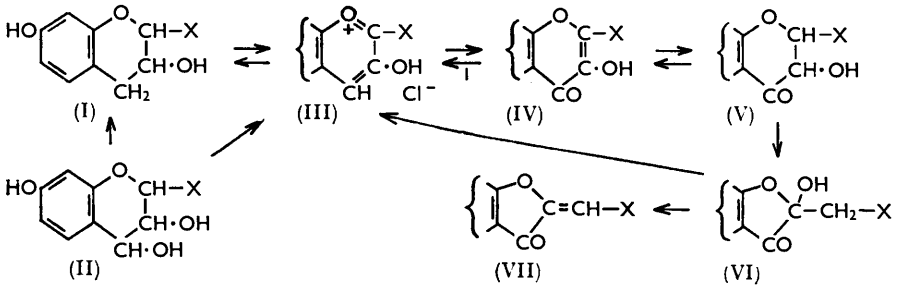
2-Benzyl-2,6,3′,4′-tetrahydroxycoumaran-3-one is also present in the above tannin but was less amenable to investigation.

THE existence of two 2-benzyl-2-hydroxycoumaran-3-ones in Quebracho tannin extract (the aqueous heartwood extract of *Schinopsis balansae* and *S. lorentzii*) has been announced [1,2] and throws new light on the biogenetic relations of C_6–C_3–C_6 compounds. The family Anacardiaceae is remarkable for the occurrence in species of the *Schinopsis* and *Rhus* genera of biogenetically related compounds having a common hydroxylation pattern and differing only in the state of oxidation of the central ring. These are fisetin (3,7,3′,4′-tetrahydroxyflavone) from Quebracho extract,[3] which also contains 4-methoxyfisetin, 3,7,4′-trihydroxyflavone, and 3,7,3′,4′,5′-pentahydroxyflavone (robinetin);[4] also fustin (3,7,3′,4′-tetrahydroxyflavanone) from the heartwood of *Rhus succedanea*,[5] sulphuretin (6,3′,4′-trihydroxyaurone) from the wood of *Rhus cotinus*,[1] and leucofisetinidin (3,4,7,3′,4′-pentahydroxyflavan) from *Schinopsis balansae* and *S. lorentzii*.[1] * The present 2-benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one (and the 2,6,3′,4′-tetrahydroxy-analogue) has a similar overall hydroxylation pattern; the 4′-methoxy-group is comparatively rare in Nature but has already been recorded [4] for Quebracho in the case of 3,7,3′-trihydroxy-4′-methoxyflavone. In no other botanical family have so many C_{15} compounds of identical hydroxylation pattern been isolated although in several cases two components occur, differing only in the oxidation level of the C_3 portion.

The structural relations between the various flavonoid compounds mentioned above is shown in the following scheme, the arrows indicating known conversions *in vitro*.

* This observation was announced by the present authors [1,2] in 1957 despite absence of reference to it in later communications.[6]

[1] King and White, *Proc. Chem. Soc.*, 1957, 341.
[2] King and White, *J. Soc. Leather Trades' Chemists*, 1957, **41**, 368.
[3] Perkin and Gunnel, *J.*, 1896, **69**, 1304.
[4] Kirby and White, *Biochem. J.*, 1955, **60**, 582.
[5] Oyamada, *Annalen*, 1939, **538**, 44.
[6] Roux, *Chem. and Ind.*, 1958, 161; Freudenberg and Weinges, *Annalen*, 1958, **613**, 61; Weinges, *ibid.*, 1958, **615**, 203; Roux and Evelyn, *Biochem. J.*, 1958, **69**, 530.



X = 3,4-$(HO)_2C_6H_3$.

(I) Flavanol. (II) Leucoanthocyanidin. (III) Anthocyanidin. (IV) Flavonol. (V) Dihydroflavonol. (VI) 2-Benzyl-2-hydroxycoumaran-3-one. (VII) Aurone.

I, *Via* the reduced acetate.

The general reactivity of the hydroxylated 2-benzylcoumaran-3-ones resembles that of the catechins and leucoanthocyanidins and this new group of polyphenols must, therefore, enter into considerations of the nature of the precursors of the condensed tannins. The synthesis and characterisation of the examples now recorded in Quebracho extract presented particular difficulties, mainly because recorded work on substances of this type has concerned examples lacking hydroxyl groups other than in the 2-position, or possessing a 4-hydroxyl group capable of hydrogen-bonding with the 3-keto-group, factors which affect considerably the reactivity and ease of synthesis of these substances.

2-Benzyl-2-hydroxycoumaran-3-ones have been suggested [7] as intermediates in the synthesis of aurones from dihydroflavanols. 2-Benzyl-2-hydroxycoumaran-3-one itself resulted when Gripenberg [8] treated 3-hydroxyflavanone with alcoholic potassium hydroxide and he identified as 2-benzyl-2-hydroxy-4,6-dimethoxycoumaran-3-one the " apoalpinone monomethyl ether " similarly obtained by Lindstedt [9] from pinobanksin dimethyl ether (3-hydroxy-5,7-dimethoxyflavanone). Zwingelstein and Jouanneteau [10] used aqueous alkali to convert quercetin into 2-benzyl-2,4,6,3′,4′-pentahydroxycoumaran-3-one. We applied these techniques to fisetin but obtained no 2-benzyl-2,6,3′,4′-tetrahydroxycoumaran-3-one, presumably because of the absence of a 5-hydroxyl group and presence of other reactive hydroxyl groups in fisetin. With a view to obtaining the 2-benzyl-4′-methoxy-compound we attempted to convert 4′-methoxyfisetin first into the corresponding flavanone by treatment with sodium dithionite,[11] but again the reaction failed, as it did also with fisetin (again absence of 5-hydroxyl group since substances with this group are converted readily into dihydro-derivatives).

However, the required fustin (3,7,3′,4′-tetrahydroxyflavanone) occurs naturally and was synthesised by treating 3,4,2′,4′-tetrahydroxychalcone with alkaline hydrogen peroxide under conditions used by Anand *et al.*[12] Boiling alcoholic potassium hydroxide converted it into a complex mixture containing very small amounts of the required 2-benzyl-2,6,3′,4′-tetrahydroxycoumaran-3-one. Curiously, when Jouanneteau *et al.*[13] applied a similar treatment to taxifolin (dihydroquercetin) the product had no 2-hydroxyl group but was 2-benzyl-4,6,3′,4′-tetrahydroxycoumaran-3-one.

An alternative approach is to treat α-hydroxy- or α-methoxy-chalcones with mineral acid. Gripenberg[8] thus obtained 2-benzyl-2-hydroxycoumaran-3-one from 2′-hydroxy-α-methoxychalcone, and Enebäck and Gripenberg [14] synthesised 2-benzyl-2-methoxycoumaran-3-one

[7] Molhs, Coillard, and Mentzner, *Bull. Soc. chim. France*, 1954, 1397.
[8] Gripenberg, *Acta Chem. Scand.*, 1950, **4**, 1323.
[9] Lindstedt, *Acta Chem. Scand.*, 1950, **4**, 772.
[10] Zwingelstein and Jouanneteau, *Compt. rend.*, 1955, **240**, 981.
[11] Pew, *J. Amer. Chem. Soc.*, 1948, **70**, 3031.
[12] Anand, Iyer, and Venkataraman, *Proc. Indian Acad. Sci.*, 1949, **29**, *A*, 203.
[13] Jouanneteau, Zwingelstein, and Mentzner, *Compt. rend.*, 1954, **239**, 1514.
[14] Enebäck and Gripenberg, *Acta Chem. Scand.*, 1957, **11**, 866.

from the same source although they failed to obtain it by methylating its 2-hydroxy-analogue. Tsukamoto and Tominaga [15] later established that certain α-methoxychalcones can be converted simultaneously into 2-benzyl-2-hydroxy- and -2-methoxy-coumaranones, but our treatment of 3,2′,4′-trihydroxy-α,4-dimethoxychalcone with acid gave only a dimethoxy-derivative * (ultraviolet spectrum almost identical with that of 2-benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one), no 2-hydroxy-analogue being obtained.

Using Saiyad, Nadkarni, and Wheeler's method [16] for the synthesis of chalcones we then condensed ω-hydroxyresacetophenone with isovanillin in the presence of aqueous potassium hydroxide: we obtained, among other products, 2-benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one directly; the expected α-hydroxychalcone is presumably unstable and rearranges immediately. The synthesis, although unexpected, served to establish finally the identity of the crystalline product from Quebracho extract,[1,2] this being the first record of the existence in Nature of compounds of this general structure.†

2-Benzyl-2-hydroxycoumaranones in Quebracho.—Two compounds resulted when the acetone-soluble portion of Quebracho extract was extracted with ether, and the water-soluble portion of this ether extract chromatographed on powdered-cellulose columns with dilute acetic acid as eluant. Neither the acetates not the methoxy-derivatives crystallised but the general structures became clear when treatment with concentrated sulphuric acid converted one into the aurone sulphuretin, and the other into 6,3′-dihydroxy-4′-methoxyaurone. Both this and its parent 2-benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one gave a bright scarlet colour when dissolved in glacial acetic acid containing a trace of sulphuric acid, a reaction found to have structural significance.[18] Further evidence for the general structure is that treatment of the reduced acetate of 2-benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one with hot propan-2-ol–hydrogen chloride [19] gave the same anthocyanidin as did the reduced acetate of fisetin 4′-methyl ether under the same conditions.

Experimental

Isolation of 2-Benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one.—Quebracho extract (1·5 kg.), dried in a vacuum over P_2O_5, was shaken with dry acetone (2 l.) for 24 hr., and the solution centrifuged off. This process was twice repeated. The combined extracts were concentrated to s.g. 0·975 and stirred with an equal volume of ether. The next morning the solution was decanted and taken to dryness; the residue was redissolved in acetone to a solution of s.g. 0·975 and again treated with ether (2 l.). After being kept overnight the solution was removed and taken to dryness. This product (110 g.) was dissolved in water (750 ml.) and extracted continuously with ether until the extract was colourless. The ether extract was taken to dryness and the product (15 g.) dissolved in warm 5% acetic acid (30 ml.). The flavonoid material which separated on cooling was filtered off and the filtrate chromatographed on a column of " Solka Floc " (30″ × 2″) with 5% acetic acid as the solvent. When the effluent reacted with the ferricyanide or diazotised benzidine polyphenol reagent,[20] samples (15 ml.) were collected and refrigerated overnight. 2-Benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one separated as clumps of white crystals in several successive tubes, usually nos. 6—12. A spot of solution from each tube was chromatographed on paper in 6% acetic acid and examined in ultraviolet light after being sprayed with the benzidine reagent. This showed the presence of the coumaranone up to tube 14, accompanied by the closely related 2-benzyl-2,6,3′,4′-tetrahydroxycoumaran-3-one. The crystals were filtered off and the filtrates and contents of the remaining tubes known to contain the benzylcoumaranones were concentrated, thus yielding

* R. A. Low synthesised the same dimethoxy-derivative at Sheffield University.

† Jones, King, and Morgan [17] have since observed a 2-benzyl-2-hydroxycoumaran-3-one in *M. eminii* wood.

[15] Tsukamoto and Tominaga, *J. Pharm. Soc. Japan*, 1953, **73**, 1172.
[16] Saiyad, Nadkarni, and Wheeler, *J.*, 1937, 1737.
[17] Jones, King, and Morgan, *Chem. and Ind.*, 1961, 346.
[18] King and White, *J.*, 1961, 3539.
[19] King and White, *J.*, 1957, 3901.
[20] White, Kirby, and Knowles, *J. Soc. Leather Trades' Chemists*, 1952, **36**, 148.

a further small quantity of crystalline trihydroxy-4′-methoxy-compound. The concentrated filtrate from this, containing the crude tetrahydroxy-compound, was set aside for later work. The yield of *2-benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one* in typical experiments was 0·3 g. (0·02% on the wt. of extract taken); recrystallised from water this product formed white needles, m. p. 194° (Found: C, 63·6; H, 4·6; OMe, 10·1. $C_{15}H_{11}O_4$·OMe requires C, 63·7; H, 4·6; OMe, 10·3%). It gave a red-brown colour with aqueous ferric chloride solution. Fusion with potassium hydroxide produced resorcinol, guaiacol, and protocatechuic acid (under these conditions isovanillic was demethylated to protocatechuic acid). Its R_F on paper chromatograms in 6% acetic acid was 0·74 and in 14 : 1 : 5 butan-2-ol–acetic acid–water was 0·94. Under ultraviolet light the spot is dark; it becomes violet in ammonia vapour. The compound has $\lambda_{max.}$ 232, 278, and 325 mμ ($E^{1\%}_{1cm.}$ 482, 505, and 293).

The *triacetate* (obtained in pyridine–acetic anhydride) was a glass, flowing at 147° [Found: OAc, 31·2; OMe, 7·6. $C_{15}H_8O(O{\cdot}CO{\cdot}CH_3)_3$·OMe requires Ac, 30·2; OMe, 7·3%], unchanged in methoxyl content on treatment with diazomethane.

The parent 2-benzylcoumaran-3-one with (*a*) diazomethane, (*b*) dimethyl sulphate and alkali, or (*c*) diazomethane after treatment (*b*) gave a *trimethyl ether* [Found: OMe, 28·5. $C_{15}H_9O_2(OMe)_3$ requires OMe, 29·1%], one hydroxyl group being unmethylated.

2-Benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one dissolved readily in sodium hydrogen carbonate solution and was recovered unchanged on acidification. It could be titrated directly with sodium hydroxide, giving an equivalent weight of 300 (calc., 302), but the methylation experiments prove the absence of carboxyl and lactone groups. The presence and position of a tertiary hydroxyl and of the 4′-methoxyl group followed from dehydration of the compound with sulphuric acid to an aurone (see below).

Adding a drop of concentrated sulphuric acid to a very dilute solution of the coumaran-3-one or its related aurone in acetic anhydride produced a bright red colour.[18] In the former case, the normal triacetate was formed together with the aurone diacetate which resulted from simultaneous acetylation and dehydration. The aurone gave only its own diacetate. The two acetates are readily separated and demonstrated on paper chromatograms run in 25% acetic acid and sprayed with 5% aqueous sodium hydroxide as they show up as yellow spots. The R_F values were: coumaran-3-one triacetate 0·97; aurone diacetate 0·71.

Isolation of 2-Benzyl-2,6,3′,4′-tetrahydroxycoumaran-3-one.—50 ml. of final concentrated filtrate from several isolations of 2-benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one from Quebracho extract were chromatographed with 5% acetic acid on a " Solka Floc " column; the effluent was collected until paper chromatograms showed that all the tetrahydroxycoumaranone had been eluted. The part of the effluent containing this product was extracted exhaustively with ether, the extract dried, and the ether distilled off, yielding a brown glass (7·08 g.). Paper chromatography showed the presence of some gallic acid and some trihydroxy-4′-methoxycoumaranone. The product was dissolved in 2% aqueous sodium hydrogen carbonate (100 ml.) and extracted with ethyl acetate. The extract was concentrated to a glass which was dissolved in water (200 ml.) and treated with saturated (normal) lead acetate solution to precipitate the tetrahydroxycoumaranone. The precipitate was filtered off, washed with water, resuspended in water, and brought to pH 1·5 with 10% w/v sulphuric acid to remove lead as sulphate. After filtration, extraction with ethyl acetate followed by removal of the solvent left an orange-brown hygroscopic solid consisting of 2-benzyl-2,6,3′,4′-tetrahydroxycoumaran-3-one (1·913 g.) with a trace of flavanoid material. The substance is oxidised very readily in solution and it was not possible to crystallise or purify it further. It is very soluble in water, alcohol, and ether and melted at 105°. Ferric chloride solution produced a green colour. Dehydration with sulphuric acid produced the corresponding aurone, sulphuretin; treatment with sulphuric acid in acetic anhydride gave a mixture of the tetra-acetate of the coumaranone and of sulphuretin triacetate. These were again readily separated and detected on paper chromatograms run in 25% acetic acid and had R_F 0·91 (coumaranone tetra-acetate) and 0·79 (sulphuretin triacetate). Acetylation and methylation gave only glasses.

6,3′-Dihydroxy-4′-methoxyaurone.—6-Hydroxycoumaran-3-one (4 g.) was condensed with isovanillin (4 g.) for 30 min. with ethanol (300 ml.) and concentrated hydrochloric acid (200 ml.), then poured into water (2·5 l.). The resultant sticky product was filtered off and dissolved in the minimum volume of acetone, and the solution concentrated by distillation until the *aurone* separated (4·3 g.; m. p. 230°). It recrystallised from methanol as yellow needles, m. p. 254° (Found: C, 68·1; H, 4·2; OMe, 11·7. $C_{15}H_9O_4$·OMe requires C, 67·8; H, 4·2; OMe, 11·0%).

On paper chromatograms spots fluoresce yellow-green under ultraviolet light, the colour changing to light green in ammonia vapour. Its R_F in acetic acid–water–hydrochloric acid (30 : 15 : 1) [21] is 0·76, and in butan-2-ol–acetic acid–water (14 : 1 : 5) is 0·92.

Formation of 6,3′-*Dihydroxy*-4′-*methoxyaurone from* 2-*Benzyl*-2,6,3′-*trihydroxy*-4′-*methoxycoumaran*-3-*one*.—The coumaranone (0·5 g.) was dissolved in ice-cold concentrated sulphuric acid (10 ml.), and after exactly 8 min. was poured on crushed ice (100 g.). The initial orange precipitate quickly redissolved, leaving a clear golden-yellow solution which was extracted with ethyl acetate. The extract was dried and concentrated to 1 ml., then water (50 ml.) was added and residual sulphuric acid removed by stirring with Deacidite E ion-exchange resin. The deionised solution was taken to dryness (yield 84 mg.). Paper chromatography in aqueous acetic–hydrochloric acid (see above) against synthetic 6,3′-dihydroxy-4′-methoxyaurone showed this product to be present (R_F 0·73) and also a substance (R_F 0·80) fluorescing yellow in ultraviolet light, a little sulphuretin (R_F 0·55), and some unchanged starting material (R_F 1·00). Recrystallising the crude product from ethanol–water produced pure 6,3′-dihydroxy-4′-methoxyaurone identical in chromatographic behaviour, spectrum, and decomposition temperature (238—240°) with the synthetic product.

6,3′-*Dihydroxy*-4′-*methoxyauronesulphonic Acid*.—(*a*) Aurone (1 g.) was dissolved in warm concentrated sulphuric acid (20 ml.), and the deep red solution cooled and poured into water (250 ml.). The orange precipitate soon redissolved and the solution was then passed down a column of " Solka Floc " cellulose (26 × 2 in.) previously set up with water; development was with water. The mobile orange-brown band of sulphonated aurone was collected and its volume reduced to 50 ml., yielding a red-orange solid (0·8 g.) which recrystallised from water as orange needles and after drying *in vacuo* had m. p. 258° (decomp.), $\lambda_{max.}$ 250 ($E^{1\%}_{1cm.}$ 406) and 380 mμ ($E^{1\%}_{1cm.}$ 662). Potentiometric titration of the sulphonated aurone gave an equivalent weight of 360, corresponding to 1 HSO_3 group. The acid formed an S-*benzylthiouronium salt*, m. p. 207° (from 50% aqueous alcohol) (Found: C, 51·9; H, 4·7; S, 11·4; OMe, 5·8. $C_{22}H_{19}N_2O_7S_2$·OMe,H_2O requires C, 51·7; H, 4·5; S, 11·9; OMe, 5·8%).

(*b*) 2-Benzyl-2,6,3′-trihydroxy-4′-methoxycoumarone, treated as in (*a*), gave a similar acid (of lower m. p.) affording the same salt.

6,3′-*Diacetyl*-4′-*methoxyaurone*.—6,3′-Dihydroxy-4′-methoxyaurone (0·25 g.) with acetic anhydride (10 ml.) and concentrated sulphuric acid or acetic anhydride (2 drops) and sodium acetate gave the diacetate, m. p. 165° (0·2 g.).

6,3′,4′-*Triacetylaurone* (*Sulphuretin Triacetate*).—Sulphuretin (0·25 g.) was converted into its triacetate, m. p. 167°, by preceding methods.

Formation of 6,3′-*Diacetyl*-4′-*methoxyaurone and* 2-*Benzyl*-2,6,3′-*triacetyl*-4′-*methoxycoumaran*-3-*one from* 2-*Benzyl*-2,6,3′-*trihydroxy*-4′-*methoxycoumaran*-3-*one*.—The trihydroxycoumaranone (0·23 g.) was treated with acetic anhydride (10 ml.) containing concentrated sulphuric acid (0·025 ml., the proportion giving the maximum colour). The product (0·28 g.) melted from 80° to 133° and decomposed at 155—160°. Paper chromatography showed that it was a mixture of 6,3′-diacetyl-4′-methoxyaurone and 2-benzyl-2,6,3′-triacetyl-4′-methoxycoumaran-3-one, and slow crystallisation from ethanol gave needles of the aurone, m. p. 161°. The mixed acetates (0·5 g.) were boiled with N-ethanolic potassium hydroxide (5 ml.) for 5 min. A brown product separated during several days and was filtered off and dried (0·17 g.). Paper chromatography in acetic acid–water–hydrochloric acid (30 : 15 : 1) showed it to be 2-benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one with 6,3′-dihydroxy-4′-methoxyaurone and a flavone-like material. This product was dissolved in 5% sodium hydroxide solution (10 ml.) and acidified with hydrochloric acid, and a brown precipitate was filtered off. The filtrate deposited further material on refrigeration for 3 days, this containing only the aurone and coumaranone. The latter was removed by boiling water, leaving pure 6,3′-dihydroxy-4′-methoxyaurone (65 mg.). The filtrate was taken to dryness and the residue extracted with ethanol, the extract yielding 62 mg. of product. This product was chromatographed on a " Solka Floc " column under the conditions used in isolating the parent coumaranone from Quebracho extract; the appropriate portion of eluant gave crystalline 2-benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one (54 mg.).

Treatment of 2-*Benzyl*-2,6,3′,4′-*tetrahydroxycoumaran*-3-*one with Acetic Anhydride and Sulphuric Acid*.—The tetrahydroxy-coumaranone (0·27 g.) was acetylated as above, the product dissolved in chloroform, and the extract dried and evaporated, giving a golden oil (0·34 g.). This

[21] Bate-Smith, *Biochem. J.*, 1954, **58**, 122.

was dissolved in ethanol (2 ml.) and gave pale yellow needles on refrigeration for 3 days. The crystals were filtered off and air-dried (16 mg.; m. p. 165°). They were sulphuretin triacetate but paper chromatography showed the presence of traces of contaminants. Deacetylation as above produced only sulphuretin.

ω-Hydroxyresactophenone (*Fisetol*).—The product prepared by the method of Karrer and Biedermann [22] crystallised from water as needles, m. p. 191° (Found: C, 56·9; H, 4·9. Calc. for $C_8H_8O_4$: C, 57·2; H, 4·8%).

Synthesis of 2-Benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one.—Fisetol (1·24 g.) and isovanillin (1·1 g.) in ethanol (10 ml.) were treated with potassium hydroxide (10 g.) in water (7 ml.) on a boiling-water bath for 10 min., kept overnight, and acidified with concentrated hydrochloric acid. A sticky product separated after 3 days' refrigeration; the supernatant liquid was distilled off and the residue was treated with small volumes of glacial acetic acid to extract the product from accompanying salt. Water was then added to the total extract until precipitation was imminent and the solution was then chromatographed on a column of " Solka Floc " cellulose (26 × 2 in.) with 5% acetic acid as the eluant. Sixty 15-ml. fractions were collected, a paper-chromatographic check showing the presence of 2-benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one in tubes 25—35. The product crystallised during several days in tubes 26—30 and was filtered off. The filtrates were concentrated with the contents of tubes 25 and 31—35, yielding a further crop (total yield, 106 mg., 4·9%). The m. p. and mixed m. p. with the natural trihydroxycoumaranone was 194° (Found: C, 63·8; H, 4·5; OMe, 10·3. Calc. for $C_{15}H_{11}O_5$·OMe: C, 63·7; H, 4·6; OMe, 10·3%), and $\lambda_{max.}$ were 232 ($E^{1\%}_{1cm.}$ 457), 278 ($E^{1\%}_{1cm.}$ 480), and 325 mμ ($E^{1\%}_{1cm.}$ 275).

3,2′,4′-Trihydroxy-α,4-dimethoxychalcone.—ω-Methoxyresacetophenone (1·8 g.) was warmed with isovanillin (1·5 g.) in ethanol (2 ml.) until homogeneous. Potassium hydroxide (17 g.) in water (12 ml.) was added and the mixture heated on a boiling-water bath for 10 min., then kept overnight at room temperature, diluted with an equal volume of water, and acidified with 50% w/v hydrochloric acid. The resulting sticky brown mass was washed with hot water and recrystallised twice from aqueous methanol, giving the *chalcone* (0·52 g.), m. p. 153° [Found: C, 60·7; H, 5·6; OMe, 20·3; H_2O, 5·4. $C_{15}H_{10}O_4(OMe)_2,H_2O$ requires C, 61·0; H, 5·4; OMe, 18·6; H_2O 5·4%].

2-Benzyl-6,3′-dihydroxy-2,4′-dimethoxycoumaran-3-one.—3,2′,4′-Trihydroxy-α,4-dimethoxychalcone (0·81 g.) was refluxed in ethanol (100 ml.) containing 2N-sulphuric acid (20 ml.) for 27 hr. The solution was subjected to paper chromatography (6% acetic acid); spraying with bisdiazotised benzidine gave a red, R_F 0·74, and a yellow spot, R_F 0·79. Both spots absorbed ultraviolet light before spraying and became dark violet when exposed to ammonia vapour. The ethanol was distilled from the reaction mixture and the remaining aqueous solution extracted with ether. The combined extracts were extracted twice with N-sodium hydroxide (20 ml.). Acidification of the alkaline extract with dilute hydrochloric acid gave an oil mixed with solid. This mixture was boiled with charcoal in water, giving a solution which, during several days at 0°, deposited first a sticky solid and then white crystals (22 mg.), m. p. 153°, giving the red spot of R_F 0·79 [Found: C, 59·9; H, 5·6; OMe, 18·3; loss at 100°, 5·6. $C_{15}H_{10}O_4(OMe)_2,H_2O$ requires C, 61·0; H, 5·4; OMe, 18·6; H_2O, 5·4%], $\lambda_{max.}$ 226 ($E^{1\%}_{1cm.}$ 442), 230 ($E^{1\%}_{1cm.}$ 436), 282 ($E^{1\%}_{1cm.}$ 552), and 325 mμ ($E^{1\%}_{1cm.}$ 265). This *product* gave the same scarlet reaction as 2-benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one with acetic anhydride and sulphuric acid, but less intensely. No product corresponding to the spot of R_F 0·74 was isolated.

Synthesis of 2-Benzyl-2,6,3′,4′-tetrahydroxycoumaran-3-one.—Fustin (0·1 g.) was refluxed for 10 min. in methanol (10 ml.) containing potassium hydroxide (1 g.). The solution was cooled and acidified and the methanol distilled off. The remaining aqueous suspension was extracted with ether (5 × 10 ml.) and the dried, filtered extracts were taken to dryness, giving a golden, amorphous, hygroscopic solid (61 mg.). This was shown by paper chromatography, alone and in conjunction with a natural sample, to contain a high proportion of the required 2-benzylcoumaranone and treatment of this product with sulphuric acid yielded sulphuretin.

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See also p. 3234.]
[*Received, January 18th*, 1961.]

[22] Karrer and Biedermann, *Helv. Chim. Acta*, 1927, **10**, 441.