

Institute of Dehra Dun, India, where it was carefully identified before it was despatched to England. In this connection it is worth while to remember that not only *Acacia Catechu* but also *Acacia Catechuoides* and *Acacia Sundra* are used for the manufacture of cutch, which is one of the main sources of "catechin."²²

During this investigation I was assisted by Miss E. O. Hazelton, and I wish to thank the Department of Scientific and Industrial Research for a grant which has enabled her to take part in this work. My thanks are also due to the Colston Research Society of this University for a grant which has covered the expenses of this research.

Summary

4,5,7,3',4'-Pentahydroxy-flavan has been prepared and shown to differ in every respect from *dl*-acacatechin and *dl*-*iso*-acatechin.

BRISTOL, ENGLAND

[CONTRIBUTION FROM THE UNIVERSITY OF BRISTOL]

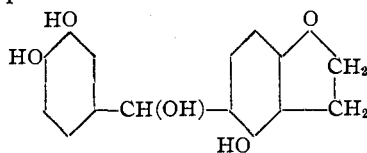
THE CONSTITUTION OF CATECHIN. VIII. α ,3,5,3',4'-PENTAHYDROXY-4-BENZYL-1,2-DIHYDROCOUMARONE

BY H. F. DEAN AND M. NIERENSTEIN

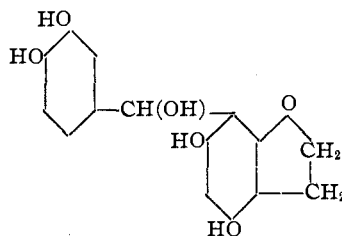
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The experiments described in the present communication were in progress in 1914, when they were suspended in consequence of the War. At that time, and for some years subsequently, Formula I proposed by Kostanecki and Lampe¹ was generally considered to represent catechin.² Consequently, the synthesis of a substance having this formula was attempted.



I



II

Both α ,3,5,3',4'-pentahydroxy-4-benzyl-1,2-dihydrocoumarone (I) and its isomer α ,3,5,3',4'-pentahydroxy-6-benzyl-1,2-dihydrocoumarone (II) have now been prepared and they have been found to differ in every

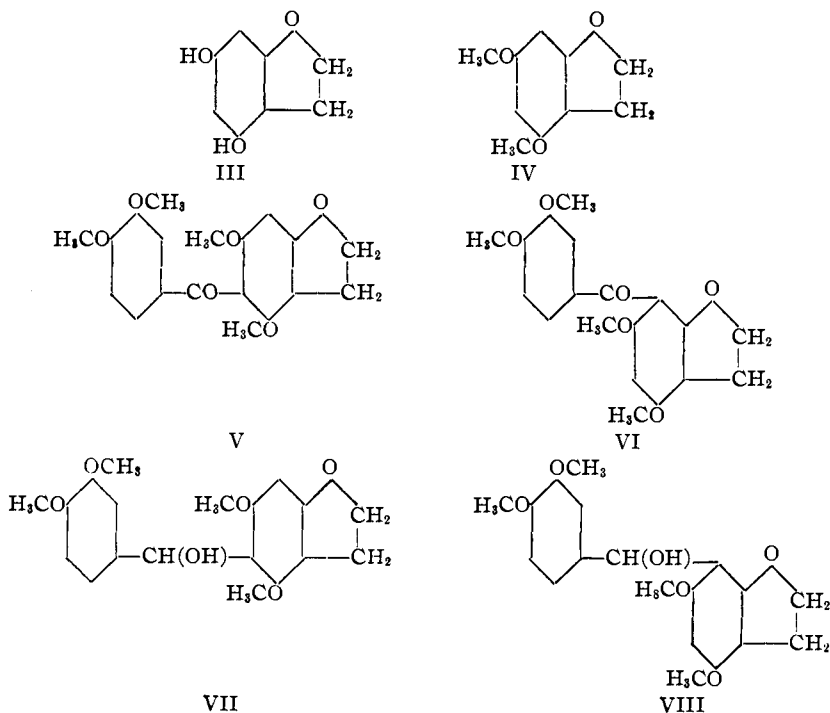
²² In view of what has been said it must be regretted that Professor Freudenberg did not see his way to accept the offer of an exchange of specimens made to him by the author two years ago.

¹ Kostanecki and Lampe, *Ber.*, **40**, 720 (1907).

² Compare, for example, Karrer and Widmer, *Helvetica chim. Acta*, **2**, 454 (1919).

respect from catechin. This is in agreement with our knowledge of catechin.³ In this connection special reference must be made to the fact that neither Substance I nor II, nor 3,5-dihydroxy-1,2-dihydrocoumarone (III) gives the phloroglucinol test with pine-wood and hydrochloric acid, which is specific for catechin. These negative results are probably due to the greater stability of the coumaran ring as compared with the chroman ring which is present in catechin. This probably also applies to the other coumaran formulas which have been suggested for catechin.⁴

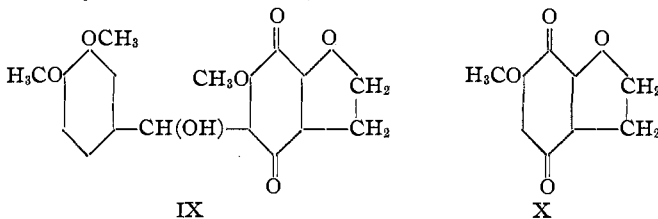
The preparation of $\alpha,3,5,3',4'$ -pentahydroxy-4-benzyl-1,2-dihydrocoumarone (I) and $\alpha,3,5,3',4'$ -pentahydroxy-6-benzyl-1,2-dihydrocoumarone (II) is carried out according to the following scheme: veratroyl chloride is condensed with 3,5-dimethoxy-1,2-dihydrocoumarone (IV) when 3,5,3',4'-tetramethoxy-4-benzoyl-1,2-dihydrocoumarone (V) and 3,5,3',4'-tetramethoxy-6-benzoyl-1,2-dihydrocoumarone (VI) are simultaneously produced; the latter are reduced to α -hydroxy-3,5,3',4'-tetramethoxy-4-benzyl-1,2-dihydrocoumarone (VII) and α -hydroxy-3,5,3',4'-tetramethoxy-6-benzyl-1,2-dihydrocoumarone (VIII), which on demethylation yield Substances I and II, respectively.



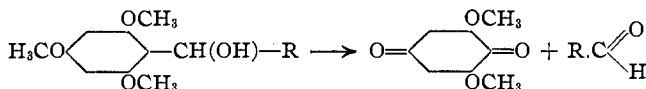
³ Nierenstein, *J. Chem. Soc.*, 117, 971 (1920).

⁴ Freudenberg, Orthner and Fikentscher, *Ann.*, 436, 287 (1924).

The relative constitution of Substances I and II is evident from the following. On oxidation, α -hydroxy-3,5,3',5'-tetramethoxy-4-benzyl-1,2-dihydrocoumarone (VII) yields α -hydroxy-5,3',4'-trimethoxy-4-benzyl-1,2-dihydro-3,6-quinocoumarone (IX), whereas α -hydroxy-3,5,3',4'-tetramethoxy-6-benzyl-1,2-dihydrocoumarone (VIII) on similar treatment undergoes fission, yielding veratric aldehyde and 5-methoxy-1,2-dihydro-3,6-quinocoumarone (X). This product is also obtained when 3,5-dimethoxy-1,2-dihydrocoumarone (IV) is oxidized under the same conditions.

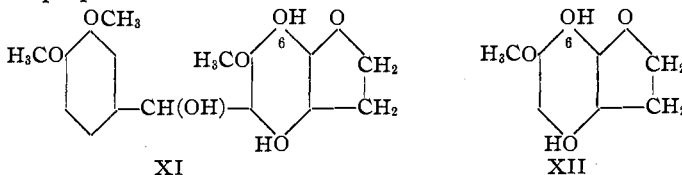


The formation of veratric aldehyde and 5-methoxy-1,2-dihydro-3,6-quinocoumarone (IX) corresponds to the production of 1,3-dimethoxy-2,6-benzoquinone and the respective aldehydes when various α -hydroxy-polymethoxy-diphenylmethanes of the phloroglucinol series are oxidized in the same manner.⁵



In this connection it is interesting to note that Kostanecki and Lampe⁶ attempted to isolate 5-methoxy-1,2-dihydro-3,6-quinocoumarone (X) from catechin-tetramethyl ether. They obtained, however, only veratric aldehyde and veratric acid. This observation together with their failure to obtain the quinocoumarone (X) is also in perfect agreement with our present knowledge of catechin.

The two quinones (IX) and (X) may be reduced to α ,3,6-trihydroxy-5,3',4'-trimethoxy-4-benzyl-1,2-dihydrocoumarone (XI) and 3,6-dihydroxy-5-methoxy-1,2-dihydrocoumarone (XII), respectively. Both of these substances are colorless products, which is contrary to the suggestion made by Nierenstein⁷ that the hydroxyl group in the 6 position possesses chromatic properties.



⁵ Koenig and Kostanecki, *Ber.*, **39**, 4027 (1906).

⁶ Kostanecki and Lampe, *Ber.*, **39**, 4017 (1906).

⁷ Nierenstein, *Ann.*, **386**, 324 (1912); **396**, 194 (1913).

Experimental Part

3,5-Dimethoxy-1,2-dihydrocoumarone (IV).—This substance is prepared by converting 3,5-dimethoxy-coumaran-2-one⁸ into the hydrazone and reducing the latter by Wolff's method.⁹

1. The HYDRAZONE of 3,5-dimethoxy-coumaran-2-one crystallizes from absolute alcohol in slightly yellow needles; m. p., 157–159°.

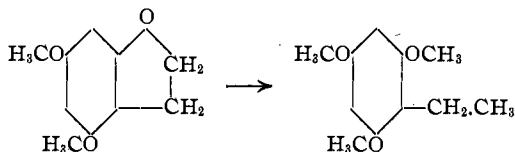
Anal. Subs., 0.1828: N, 20.4 cc. (over 33% KOH; 15° and 773 mm.). Calc. for C₁₀H₁₂O₃N₂: N, 13.4. Found: 13.3.

2. The hydrazone (5 g.) dissolved in alcohol (25 cc.) is heated with sodium ethylate (1.5 g.) in a sealed tube at 160° for 22 hours. The contents of the tube after evaporating to dryness are treated with dil. hydrochloric acid, filtered and freed from hydrochloric acid by washing with water. The substance so obtained is crystallized from dilute alcohol, from which it separates in faintly yellow needles. An absolutely colorless product is obtained after several crystallizations from 60% alcohol with the aid of animal charcoal.

3,5-Dimethoxy-1,2-dihydrocoumarone (IV) melts sharply at 109°. It is soluble in the usual organic solvents and may also be crystallized from benzene and alcohol. Ferric chloride produces a violet coloration when added to a suspension of the substance in concd. sulfuric acid. This color reaction is given by all of the coumaran derivatives described in the present communication. The average yield from eight preparations is 74%.

Anal. Subs., 0.1668: CO₂, 0.4080; H₂O, 0.1022. Calc. for C₁₀H₁₂O₃: C, 66.7; H, 6.7. Found: C, 66.7; H, 6.9.

On reduction with metallic sodium and alcohol and subsequent methylation with methyl sulfate, 2 g. of 3,5-dimethoxy-1,2-dihydrocoumarone (IV) gave 1.3 g. of 1,3,5-trimethoxy-2-ethylphloroglucinol.



The small needles crystallizing from ligroin melt at 29–30°, as found by Ryan and Walsh.¹⁰

3,5-Dihydroxy-1,2-dihydrocoumarone (III).—A solution of 2 g. of 3,5-dimethoxy-1,2-dihydrocoumarone (IV) in 20 cc. of 80% acetic acid is heated in a boiling water-bath for six hours with a solution of 2 g. of acetyl chloride in 20 cc. of glacial acetic acid. The solid formed on dilution with water is dissolved in dil. sodium hydroxide solution and the filtered solution acidified with dil. sulfuric acid. The product thus formed crystallizes from alcohol in prismatic needles; m. p., 176–178°. The average yield of three preparations is 67%.

Anal. Subs., 0.1840 (dried in a vacuum at 100° over P₂O₅ until it became constant): CO₂, 0.4264; H₂O, 0.0926. Calc. for C₉H₈O₃: C, 63.2; H, 5.2. Found: C, 63.2; H, 5.6.

The DIACETYL DERIVATIVE crystallizes from alcohol in needles; m. p., 177°. Al-

⁸ Blom and Tambor, *Ber.*, **38**, 3590 (1905). Dumont and Tambor, *Ber.*, **43**, 1969 (1910).

⁹ Wolff, *Ann.*, **394**, 86 (1912); **420**, 275 (1920).

¹⁰ Ryan and Walsh, *Sci. Proc. Roy. Dublin Soc.*, **15**, 119 (1916).

though there is practically no difference in the melting points of the two substances, they give definite depressions of 16–18° on admixture.

Anal. Subs., 0.1424 (dried in a vacuum at 100° over P₂O₅): CO₂, 0.3169; H₂O, 0.0812. Calc. for C₁₂H₁₂O₅: C, 61.0; H, 5.1. Found: C, 60.7; H, 6.4.

5-Methyl-1,2-dihydro-3,6-quinocoumarone (X).—To a carefully cooled solution of 5 g. of 3,5-dimethoxy-1,2-dihydrocoumarone (IV) in 25 cc. of glacial acetic acid, 5 g. of chromic acid dissolved in 30 cc. of the same solvent is slowly added, any increase in temperature being carefully avoided. After the mixture has stood on ice for 24 hours it is poured into ice water, when a red, sandy precipitate is obtained which crystallizes from glacial acetic acid in salmon-colored, microscopical needles that melt and decompose at 168–170°. When an acetic acid solution of the substance is boiled with tolylene-3,4-diamine no azine formation is observed, thus excluding the possibility of an *ortho*-quinone structure.

Anal. Subs., 0.1431 (dried at 100° in a vacuum over P₂O₅): CO₂, 0.3154; H₂O, 0.0568. Calc. for C₉H₈O₄: C, 60.0; H, 4.4. Found: C, 60.1; H, 4.5.

3,6-Dihydroxy-5-methoxy-1,2-dihydrocoumarone (XII).—Two g. of the quinone in glacial acetic acid solution is reduced with zinc dust. The solid formed on precipitation with water crystallizes from alcohol in colorless, prismatic needles; m. p., 191–192°.

Anal. Subs., 0.1641: CO₂, 0.3556; H₂O, 0.0786. Calc. for C₉H₁₀O₄: C, 59.3; H, 5.5. Found: C, 59.1; H, 5.4.

The DIACETYL DERIVATIVE crystallizes from alcohol in needles; m. p., 207–209°.

Anal. Subs., 0.1332: CO₂, 0.2850; H₂O, 0.0633. Calc. for C₁₃H₁₄O₆: C, 58.6; H, 5.2. Found: C, 58.4; H, 5.3.

3,5,3',4'-Tetramethoxy-4-benzoyl-1,2-dihydrocoumarone (V) and 3,5,3',4'-Tetramethoxy-6-benzoyl-1,2-dihydrocoumarone (VI).—These substances are simultaneously formed when 25 g. of 3,5-dimethoxy-1,2-dihydrocoumarone (IV) dissolved in 75 cc. of dry chloroform is condensed with 27.8 g. of veratroyl chloride in 25 cc. of the same solvent. The actual condensation is carried out by adding 15 g. of freshly prepared aluminum chloride to the warm chloroform mixture and heating the solution in a water-bath at 60°, until the evolution of hydrochloric acid practically ceases. The mixture is then evaporated to dryness in a vacuum and the solid left decomposed with ice water, containing hydrochloric acid. The solid thus obtained is extracted several times with boiling alcohol, the alcoholic solution filtered and poured into water, when a white, bulky precipitate consisting of Substances V and VI is formed.

Much difficulty was experienced in separating the two substances, but finally the following method was found to give excellent results. The finely powdered mixture is carefully dried over phosphorus pentoxide, thoroughly mixed with dry, white sand and this mixture extracted in a Soxhlet apparatus with (1) ligroin (b. p., 65–70°) which removes Substance VI and (2) with dry benzene, by which Substance V is dissolved from the sand. The extraction with ligroin is a lengthy process, requiring five to six days, and it is discontinued only when a few drops of the overflow leave no residue on evaporation. The same procedure is adopted for the benzene extraction.

3,5,3',4'-Tetramethoxy-4-benzoyl-1,2-dihydrocoumarone (V), of which 26.4 g. was obtained, crystallizes from alcohol in small needles; m. p., 148°.

Anal. Subs., 0.1006 (dried in a vacuum at 100° over P₂O₅): CO₂, 0.2444; H₂O, 0.0562. Calc. for C₁₉H₂₀O₆: C, 66.3; H, 5.8. Found: C, 66.3; H, 6.3.

When 1 g. of the substance dissolved in glacial acetic acid is heated with 1 g. of phenylhydrazine for four hours a calculated yield of the *phenylhydrazone* is obtained. It crystallizes from acetic acid in pale yellow needles that melt and decompose at 218–222°.

Anal. Subs., 0.3966: N, 22 cc. (over 33% KOH; 23°, 763 mm.). Calc. for $C_{25}H_{26}O_5N_2$: N, 6.4. Found: 6.5.

3,5,3',4'-Tetramethoxy-6-benzoyl-1,2-dihydrocoumarone (VI) crystallizes in small needles from alcohol; m. p., 132–133°.

Anal. Subs., 0.1035 (dried in a vacuum at 100° over P_2O_5): CO_2 , 0.2519; H_2O , 0.0587. Calc. for $C_{19}H_{20}O_6$: C, 66.3; H, 5.8. Found: C, 66.4; H, 6.3.

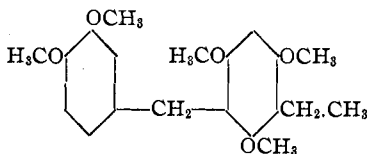
The PHENYL HYDRAZONE, which is prepared in the same manner as that of Substance V, crystallizes from acetic acid; m. p. (decomp.), 204–207°.

Anal. Subs., 0.1693: N, 9.7 cc. (over 33% KOH; 17°, 759 mm.). Calc. for $C_{25}H_{26}O_5N_2$: N, 6.4. Found: 6.6.

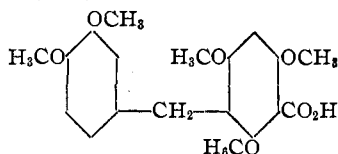
α -Hydroxy-3,5,3',4'-tetramethoxy-4-benzyl-1,2-dihydrocoumarone (VII).—A solution of 22 g. of 3,5,3',4'-tetramethoxy-4-benzoyl-1,2-dihydrocoumarone (V) in 500 cc. of alcohol is heated on a water-bath for 12 hours with 30 g. of sodium hydroxide dissolved in 50 cc. of water and 250 g. of zinc dust. The filtered solution is concentrated to about 75 cc. and diluted with a large quantity of water, whereupon 6.5 g. of unchanged 3,5,3',4'-tetramethoxy-4-benzoyl-1,2-dihydrocoumarone (V) is recovered, which is reduced in the same manner, proportional amounts of alcohol, sodium hydroxide and zinc dust being used. The second reduction leaves only 0.4 g. of unchanged 3,5,3',4'-tetramethoxy-4-benzoyl-1,2-dihydrocoumarone. The alkaline filtrates from the unchanged ketone (VI) give on acidification with dil. sulfuric acid a bulky precipitate which crystallizes from alcohol in small needles, melting at 124–126°. α -Hydroxy-3,5,3',4'-tetramethoxy-4-benzyl-1,2-dihydrocoumarone (VII) is soluble in the usual organic solvents but it may also be crystallized from carbon tetrachloride, from which it separates in small needles; m. p., 124–126°; a yield nearly that calculated is obtained.

Anal. Subs., 0.1431: CO_2 , 0.3447; H_2O , 0.0801. Calc. for $C_{19}H_{22}O_6$: C, 65.9; H, 6.3. Found: C, 65.7; H, 6.2.

On reduction with metallic sodium and alcohol and subsequent methylation with methyl sulfate 2 g. of α -hydroxy-3,5,3',4'-tetramethoxy-4-benzyl-1,2-dihydrocoumarone (VII) gives 1.1 g. of 2,4,6,3',4'-pentamethoxy-3-ethyl-diphenylmethane (XIII), from which on oxidation with potassium permanganate in alkaline solution 0.8 g. of 2,4,6,3',4'-pentamethoxy-diphenyl-methane-3-carboxylic acid (XIV) is obtained.



XIII



XIV

Both substances melt correctly at 91–92° and 108°, respectively, and neither of these melting points is depressed on admixture with specimens of these substances described previously.¹¹

α -Acetoxy-3,5,3',4'-tetramethoxy-4-benzyl-1,2-dihydrocoumarone crystallizes from alcohol in needles; m. p., 147–148°.

Anal. Subs., 0.1548: CO_2 , 0.3682; H_2O , 0.0870. Calc. for $C_{21}H_{24}O_7$: C, 65.0; H, 6.2. Found: C, 64.8; H, 6.2.

α -Hydroxy-5,3',4'-trimethoxy-4-benzyl-1,2-dihydro-3,6-quinocoumarone (IX).—Five g. of α -hydroxy-3,5,3',4'-tetramethoxy-4-benzyl-1,2-dihydrocoumarone (VII) is oxidized by the same method as that described in the case of 3,5-dimethoxy-1,2-dihydro-

¹¹ Ref. 3, p. 975.

coumarone (IV). The quinone crystallizes from acetic acid in red needles; m. p. (decomp.), 272–275°; yield, 64%. It does not react with tolylene-3,4-diamine to form an azine.

Anal. Subs., 0.1216: CO₂, 0.2780; H₂O, 0.0592. Calc. for C₁₈H₁₆O₇: C, 62.4; H, 5.2. Found: C, 62.2; H, 5.5.

The MONO-ACETYL DERIVATIVE crystallizes from alcohol in faintly yellow needles; m. p., 297–299°.

Anal. Subs., 0.1486: CO₂, 0.3348; H₂O, 0.0777. Calc. for C₂₀H₂₀O₈: C, 61.8; H, 5.1. Found: C, 61.5; H, 5.8.

α ,3,6-Trihydroxy-5,3',4'-trimethoxy-4-benzyl-1,2-dihydrocoumarone (XI).—A solution of 3 g. of the quinone (IX) in 75 cc. of acetic anhydride is heated for six hours with 35 g. of zinc dust that had been dried for a short time at 100°. The precipitate formed on the addition of water to the cold filtered solution is dissolved in alcohol and the solution boiled for a short time with dil. sulfuric acid and then again precipitated with water. The solid is treated with dilute alkali in an atmosphere of hydrogen, the solution filtered and acidified with dil. sulfuric acid. The product crystallizes from dil. alcohol in colorless, prismatic needles; m. p. (decomp.), about 197–202°; yield, 51%.

It is of interest to note that the solutions of both α ,3,6-trihydroxy-5,3',4'-trimethoxy-4-benzyl-1,2-dihydrocoumarone (XI) and 3,6-dihydroxy-5-methoxy-1,2-dihydrocoumarone (XII) in potassium and sodium hydroxides are yellow, which is somewhat unexpected.

Anal. Subs., 0.1636: CO₂, 0.3722; H₂O, 0.0802. Calc. for C₁₈H₂₀O₇: C, 62.1; H, 5.7. Found: C, 62.2; H, 5.7.

The TRIACETYL DERIVATIVE crystallizes from alcohol and acetone in small plates; m. p., 217–218°.

Anal. Subs., 0.1291: CO₂, 0.2890; H₂O, 0.0684. Calc. for C₂₄H₂₆O₁₀: C, 60.8; H, 5.5. Found: C, 61.0; H, 5.9.

α ,3,5,3',4'-Pentahydroxy-4-benzyl-1,2-dihydrocoumarone (I).—A solution of 8 g. of α -hydroxy-3,5,3',4'-tetramethoxy-4-benzyl-1,2-dihydrocoumarone (VII) in 50 cc. of 80% acetic acid is heated in a water-bath for eight hours with a solution of 8 g. of acetyl chloride in 50 cc. of glacial acetic acid. The solid formed on dilution with water is collected and treated with dil. alkali, hydrogen being passed through the solution. The alkaline solution is quickly filtered and acidified at once with dil. sulfuric acid. The precipitate crystallizes from water in prismatic needles; m. p., 200–201°. As will be seen, this melting point agrees fairly well with that of *dl*-acacatechin, which melts at 203–205° and it must therefore be noted that mixed melting points of α ,3,5,3',4'-pentahydroxy-4-benzyl-1,2-dihydrocoumarone (I) with *dl*-acacatechin give depressions of 16–29°. α ,3,5,3',4'-Pentahydroxy-4-benzyl-1,2-dihydrocoumarone is soluble in alcohol and ethyl acetate, but insoluble in benzene, ligroin, etc. It may also be crystallized from alcohol, from which it separates in needles; m. p., 200–201°. The aqueous solution of Substance I gives with ferric chloride a green coloration which is not changed on the addition of sodium acetate. It differs in this respect from catechin which also gives a green coloration with ferric chloride which changes, however, into violet on the addition of sodium acetate. Substance I does not give the phloroglucinol test with pine-wood and hydrochloric acid, as already pointed out in the introduction.

α ,3,5,3',4'-Pentahydroxy-4-benzyl-1,2-dihydrocoumarone (I) is remarkably resistant to alkali, in which property it again differs from catechin. Two g. of Substance I when heated for 40 minutes at 120° with 3 g. of solid potassium hydroxide and a little water gave no trace of phloroglucinol, protocatechuic acid being the only disintegration product, which could be identified with any degree of certainty.

Anal. Subs., 0.1450 (dried over P_2O_5 at 100° in a vacuum): H_2O , 0.0295. Calc. for $C_{15}H_{14}O_6 \cdot 4H_2O$: H_2O , 19.9. Found: 20.2.

Subs., 0.1420 (dried over P_2O_5 at 100° in a vacuum): CO_2 , 0.3230; H_2O , 0.0609. Calc. for $C_{15}H_{14}O_6$: C, 62.1; H, 4.8. Found: C, 62.0; H, 4.8.

The PENTA-ACETYL DERIVATIVE crystallizes from alcohol in small needles; m. p., 157–158°. This melting point is depressed by 23–41° on admixture with penta-acetyl-*dl*-acacatechin (m. p., 160°).

Anal. Subs., 0.0620: CO_2 , 0.1368; H_2O , 0.0279. Calc. for $C_{25}H_{24}O_{11}$: C, 60.0; H, 4.8. Found: C, 60.0; H, 5.1.

α -Hydroxy-3,5,3',4'-tetramethoxy-6-benzyl-1,2-dihydrocoumarone (VIII).—A solution of 7 g. of 3,5,3',4'-tetramethoxy-6-benzyl-1,2-dihydrocoumarone (VI) in 100 cc. of alcohol is heated on a boiling water-bath for 12 hours with 10 g. of potassium hydroxide dissolved in water, and 20 g. of zinc dust, the subsequent procedure being the same as that described for Substance VII. The resulting product (VIII) crystallizes from alcohol in small needles; m. p., 127–128°; yield, that calculated.

Anal. Subs., 0.1709: CO_2 , 0.4099; H_2O , 0.1057. Calc. for $C_{15}H_{22}O_6$: C, 65.9; H, 6.3. Found: C, 65.5; H, 6.6.

Oxidation of α -Hydroxy-3,5,3',4'-tetramethoxy-6-benzyl-1,2-dihydrocoumarone (VIII).—When oxidized with chromic acid in acetic acid solution, 2 g. of Substance VIII gave 0.7 g. of 5-methoxy-1,2-dihydro-3,6-quinocoumarone (X) and a small quantity of veratric aldehyde.

The former (X) crystallized from glacial acetic acid and melted at 168° , as previously observed.

Anal. Subs., 0.1139: CO_2 , 0.2492; H_2O , 0.0462. Calc. for $C_9H_8O_4$: C, 60.0; H, 4.4. Found: C, 59.8; H, 4.6.

The veratric aldehyde was obtained on neutralizing the filtrate from the crude quinone and steam distillation. The cloudy distillate was extracted with ether and the solid left on evaporation of the ether crystallized from ligroin. The aldehyde was obtained in small needles, m. p., 46–47°, and this melting point was not depressed on admixture with authentic veratric aldehyde.

α -Acetoxy-3,5,3',4'-tetramethoxy-6-benzyl-1,2-dihydrocoumarone crystallizes in needles from alcohol; m. p., 136–137°.

Anal. Subs., 0.1357: CO_2 , 0.3222; H_2O , 0.0748. Calc. for $C_{21}H_{24}O_7$: C, 65.0; H, 6.2. Found: C, 64.8; H, 6.3.

$\alpha,3,5,3',4'$ -Pentahydroxy-6-benzyl-1,2-dihydrocoumarone (II).—Four g. of α -hydroxy-3,5,3',4'-tetramethoxy-6-benzyl-1,2-dihydrocoumarone (VIII) is demethylated in the same manner as Substance VII, the reagents being used in correspondingly smaller quantities. The product crystallizes from water in small needles, m. p. 187–188°, and resembles $\alpha,3,5,3',4'$ -pentahydroxy-4-benzyl-1,2-dihydrocoumarone (I) in its general properties.

Anal. Subs., 0.3246 (dried at 100° in a vacuum over P_2O_5): H_2O , 0.0651. Calc. for $C_{15}H_{14}O_6 \cdot 4H_2O$: H_2O , 19.9. Found: 20.0.

Subs., 0.1653 (dried at 100° in a vacuum over P_2O_5): CO_2 , 0.3787; H_2O , 0.0722. Calc. for $C_{15}H_{14}O_6$: C, 62.1; H, 4.8. Found: C, 62.3; H, 4.9.

The PENTA-ACETYL DERIVATIVE crystallizes from alcohol; m. p., 151–152°.

Anal. Subs., 0.1130: CO_2 , 0.2491; H_2O , 0.0524 g. Calc. for $C_{25}H_{24}O_{11}$: C, 60.0; H, 4.8. Found: C, 60.1; H, 5.1.

In conclusion we wish to thank the Colston Research Society of the University of Bristol for grants which have covered the expenses of this investigation.

Summary

1. $\alpha,3,5,3',4'$ -Pentahydroxy-4-benzyl-1,2-dihydrocoumarone (the Kostanecki formula for catechin) and $\alpha,3,5,3',4'$ -pentahydroxy-6-benzyl-1,2-dihydrocoumarone have been prepared and are shown to differ in every respect from catechin.

2. These two 1,2-dihydrocoumarones, also 3,5-dihydroxy-1,2-dihydrocoumarone, show great stability as compared with catechin and there is reason to believe that substances having a coumaran constitution, as suggested by Freudenberg for catechin, will probably show the stability of these 1,2-dihydrocoumarones.

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[CONTRIBUTION FROM THE STERLING CHEMISTRY LABORATORY OF YALE UNIVERSITY]

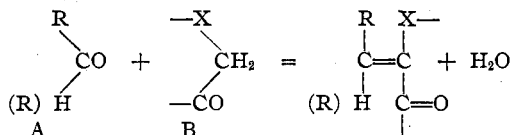
CONDENSATION REACTIONS OF CYCLIC KETONES. I. THE ACTION OF ISATIN AND ISATIN ALPHA CHLORIDE UPON CERTAIN HYDANTOINS¹

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The interaction of aldehydes or ketones with the activated methylene group of substances having the configuration $-\text{CO}-\text{CH}_2-\text{NH}-$ (or S) has frequently been observed. This type of condensation is accompanied by the elimination of water, and is usually effected by glacial acetic acid,³ or acetic anhydride, with or without sodium acetate.



Among the most important representatives of B are hippuric acid, the hydantoin, rhodanic acid and its derivatives, isothiohydantoin, dioxo-thiazoles, indoxyl, thio-indoxyl and diketopiperazine.⁴

The ease with which the carbonyl group will combine with these substances is greatly influenced by the molecular configuration of the compound in which it is present. Indeed, in this regard, certain generalizations may be made as follows.

(A) **Aldehydes.**—Nucleus aromatic aldehydes are conspicuously capable of undergoing this reaction and a large number have been investigated.

¹ This paper is constructed from Part I of the Dissertation presented to the Faculty of the Graduate School of Yale University by Henry R. Henze in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

² Holder of the National Aniline and Chemical Company Fellowship.

³ The discussion is therefore restricted to condensations carried out in acid media.

⁴ Sasaki, *Ber.*, **54**, 163, 2056 (1921).