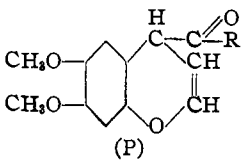
was recrystallized from 50% alcohol and melted at 152°. A mixture of the synthetic material and derrisic acid showed no depression of the melting point.

Summary

The reactions involving the formation of derritol, rotenol, dehydrorotenone and derrisic acid from rotenone are explained on the basis of their oxidation products. All of these reactions are concerned with the methoxyl containing part of the rotenone molecule which is best expressed by the formula (P).



(P)

WASHINGTON, D. C.

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, UNIVERSITY OF BRISTOL]

THE EXHAUSTIVE O-METHYLATION OF QUERCETIN

BY A. S. GOMM AND M. NIERENSTEIN

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Pentamethylquercetin (III) was first prepared by Waliaschko[1] by converting quercetin (I) into trimethylquercetin by means of dimethyl sulfate and alkali and by the action of dimethyl sulfate on the potassium salt of trimethylquercetin. Later, Wunderlich[2] showed that Waliaschko's trimethylquercetin was the 7,3′,4′-trimethyl ether, as monomethylphloroglucinol and veratric acid are obtained on hydrolysis with alkali and since it is known that an hydroxyl group in the *peri*-position (position 5 in quercetin) to a carbonyl is refractory to methylation.[3]

Doubt was, however, thrown by Herzig[4] on Waliaschko's trimethylquercetin, and Herzig expressed the opinion that it was probably 3,7,3′,4′-tetramethylquercetin (II). We have repeated Waliaschko's methylation, which we found to proceed in every respect as described by him, and we have at the same time confirmed Herzig's contention. Waliaschko's trimethylquercetin is thus shown to be 3,7,3′,4′-tetramethylquercetin (m. p. 159–160°; Waliaschko and Wunderlich give m. p. 154°), which would also obviously yield monomethylphloroglucinol and veratric acid on hydrolysis as recorded by Wunderlich.[5]

The methylation of quercetin in the presence of alkali is, however, open to the danger of nuclear methylation, as shown by Perkin,[6] and this can be

[1] Waliaschko, *Archiv. Pharm.*, **242**, 225 (1904); *Ber.*, **42**, 727 (1909).

[2] Wunderlich, *Archiv. Pharm.*, **246**, 241 (1908).

[3] See, for example, Kostanecki and Dreher, *Ber.*, **26**, 76 (1893); Schunck and Marschlewski, *J. Chem. Soc.*, **65**, 185 (1894); Perkin, *ibid.*, **103**, 1632 (1913).

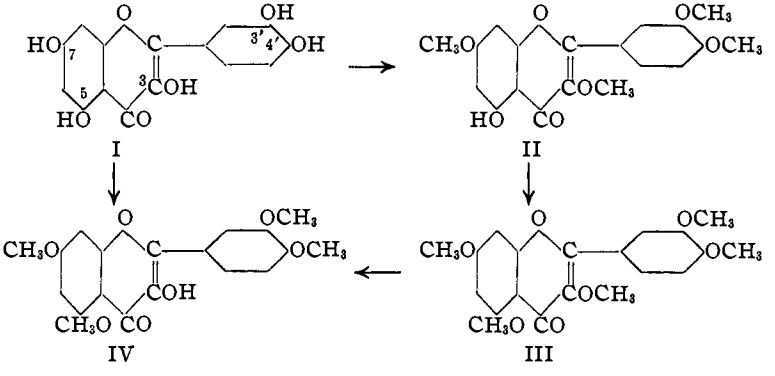
[4] Herzig, *Monatsh.*, **33**, 685 (1912).

[5] See Watson, Sen and Medhi, *J. Chem. Soc.*, **107**, 1482 (1915), who have thus used tetramethylquercetin and not the supposed trimethyl derivative in their work.

[6] Perkin, *J. Chem. Soc.*, **103**, 1632 (1913).

avoided, according to Freudenberg,[7] by methylating pentaacetylquercetin with dimethyl sulfate and potassium hydroxide, when a 75 to 80% yield of pentamethylquercetin (m. p. 147–149°) is obtained. Our results on repeating Freudenberg's methylation on several occasions do not confirm this, as we have only been able to obtain 3,7,3′,4′-tetramethylquercetin (m. p. 159–160°).[8] Since Freudenberg relies entirely on the melting point for the identity of his substance, he has apparently mistaken impure 3,7,3′,4′-tetramethylquercetin for pentamethylquercetin. In the course of this investigation we have met with preparations of the tetramethyl derivative melting as low as 145°, when not quite pure.

In view of these results, we were attracted by the method of Herzig[9] in which nuclear methylation is definitely excluded by the methylation of quercetin (I) with diazomethane, when 5,7,3′,4′-tetramethylquercetin (IV) and pentamethylquercetin (III) are produced.



In the light of recent work, the methylation of the hydroxyl group in the *peri*-position with diazomethane is in itself very remarkable,[10] and on methylating quercetin with diazomethane in ethereal and alcoholic suspension or in dioxane solution, we only obtained 3,7,3′,4′-tetramethylquercetin (II) and neither 5,7,3′,4′-tetramethylquercetin (IV) nor pentamethylquercetin (III) could be detected. It is impossible to reconcile our results with those of Herzig, and the position is still more aggravated by the fact that Herzig gives no details of his procedure. Methylation with diazomethane is well known to be erratic,[11] and it suggested itself to us that Herzig's results may perhaps be due to the presence of methylamine in the diazomethane prepared from nitrosomethylurethan as used by

[7] Freudenberg, *Ann.*, **433**, 236 (1923).

[8] See, however, Tsujimura, *Sci. Papers, Inst. Phys. and Chem. Res.* (*Tokyo*), **10**, 261 (1929), who seems to have had no difficulty in repeating Freudenberg's method.

[9] Herzig, *Monatsh.*, **33**, 690 (1912).

[10] See Perkin and Story, *J. Chem. Soc.*, 1407 (1929).

[11] See, for example, Meerwein and Hinz, *Ann.*, **484**, 1 (1930).

him.[12] We found, however, that the addition of methylamine had no influence on the course of the reaction.

In view of our experience with the different methods for the preparation of pentamethylquercetin, we now describe a procedure which we have found to be reliable.

Experimental

3,7,3′,4′-Tetramethylquercetin.—Into a solution of 6.4 g. of quercetin (crystallized from 50% acetic acid and dried at 110°) in 90 cc. of dioxane, an ethereal solution of diazomethane from 22 cc. of nitrosomethylurethan is distilled over a period of one hour and fifty minutes. A modified apparatus of Malkin and Nierenstein[13] is used, in which Flask B is replaced by a stout, wide-mouthed bottle fitted with a mercury sealed stirrer and outlet to which is attached a bulb-condensor and a glacial acetic acid trap. Stirring is continued for some time after all the diazomethane is added, when the red-colored solution turns gradually lighter and becomes finally light yellowish-brown after ninety hours' standing. On removal of the ether and subsequently of the dioxane *in vacuo*, a residue is obtained which on triturating with warm alcohol gives 4.0 g. (57% of the theoretical) of a solid melting at 150–152°,[14] and this melting point is raised to 159–160° (the highest m. p. given in the literature is 156–157°) on several crystallizations from absolute alcohol. Faintly yellow colored needles are obtained which, if quickly crystallized, appear quite colorless. These properties, including unaltered mixed melting points, are given by the products prepared according to Waliaschko and Freudenberg.

Anal. Subs., 3.729, 2.883 mg.: AgI, 9.685, 7.550 mg. Calcd. for $C_{19}H_{18}O_7$: CH_3O, 34.64. Found: CH_3O, 34.31, 34.60.

On acetylation by boiling with acetic anhydride, the *acetyl* derivative is obtained as colorless needles from absolute alcohol, m. p. 169–170°, which is slightly higher than 167–168° given in the literature. If exposed to sunlight the product becomes slightly colored.

Anal. Subs., 2.869, 3.043 mg.: AgI, 6.700, 7.045 mg. Calcd. for $C_{21}H_{20}O_8$: CH_3O, 31.00. Found: CH_3O, 30.83, 30.58.

Pentamethylquercetin.—To a suspension of 5 g. of carefully purified 3,7,3′,4′-tetramethylquercetin in 14 cc. of dimethyl sulfate, freed from acid by washing, is slowly added 11 g. of finely powdered potassium hydroxide, the reaction being carried out in a silver dish. During the addition of the potassium hydroxide the product is continuously stirred with a pestle. The reaction mixture turns bright yellow and then changes to brown as the suspension liquefies with the evolution of heat, and finally becomes white when the product suddenly solidifies. It is kept in a desiccator for twenty-four hours, transferred into hot water and well stirred and left standing for several hours. The colorless product (m. p. 148°) thus obtained (4.9 g. = 94% of the theoretical) crystallizes from absolute alcohol in needles which melt at 151–152°, and this melting point remains unaltered on further crystallization. The alcoholic solution

[12] See Herzig, *Ber.*, **56**, 221 (1923). In this paper Herzig uses for the first time a fractionation column to avoid contamination with methylamine. This precaution is always adopted in this Laboratory; see Malkin and Nierenstein, THIS JOURNAL, **52**, 1508 (1930).

[13] Malkin and Nierenstein, THIS JOURNAL, **52**, 1508 (1930).

[14] The alcoholic filtrate gives on concentration an oil from which on further methylation with diazomethane as above some more tetramethylquercetin is obtained. The production of this oil is remarkable and requires further study.

remains colorless on the addition of alcoholic potash, whereas the slightest trace of tetramethylquercetin if present produces a bright yellow color. It is very sensitive to light.

Anal. Subs., 5.000, 4.930 mg.: CO_2, 11.810, 11.670; H_2O, 2.51, 2.46 mg. Subs., 2.846, 2.079 mg.: AgI, 8.985, 6.560 mg. Calcd. for $C_{20}H_{20}O_7$: C, 64.52; H, 5.38; CH_3O, 41.67. Found: C, 64.44, 64.59; H, 5.62, 5.58; CH_3O, 41.71, 41.68.

Summary

A method is described for the preparation of pentamethylquercetin, in which quercetin is converted in dioxane solution with the aid of diazomethane into 3,7,3′,4′-tetramethylquercetin, from which pentamethylquercetin is obtained through the agency of dimethyl sulfate and solid potassium hydroxide.

BRISTOL, ENGLAND

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE COLLEGE OF LIBERAL ARTS, NORTHWESTERN UNIVERSITY]

THE REACTIVITY OF THE METHYLATED SUGARS. V. THE ACTION OF DILUTE ALKALI ON TRIMETHYL-*l*-ARABINOSE[1]

BY HARRY T. NEHER WITH W. LEE LEWIS

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In 1895 Lobry de Bruyn and van Ekenstein[2] published their first papers on the interconversion of sugars by alkali, changes since studied by a number of investigators. In an extensive study of the action of alkali and alkaline oxidizing agents on the sugars, Nef[3] found that he could best explain the complicated system of products which he found, by assuming the existence of a sugar enol, such as was first proposed by Fischer[4] and used by Wohl and Neuberg[5] in explanation of some of their work on glyceric aldehyde. Recent work by W. L. Evans[6] on the behavior of a number of reducing sugars in relatively strong alkali, both in the presence of oxidizing agents and in their absence, has strongly supported the enol theory.

In previous papers[7] in this series, the blocking effect of methyl groups upon enolization has been demonstrated. In the present paper these conceptions have been extended to trimethyl-*l*-arabinose.

[1] Abstracted from a dissertation submitted by Harry T. Neher to the Graduate School of Northwestern University, in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

[2] Lobry de Bruyn and van Ekenstein, *Rec. trav. chim.*, **14**, 156, 203, 213 (1895).

[3] Nef, *Ann.*, **357**, 214 (1907); **376**, 1 (1910); **403**, 204 (1914).

[4] Fischer, *Ber.*, **28**, 1149 (1895).

[5] Wohl and Neuberg, *ibid.*, **33**, 3099 (1900).

[6] Evans, *Chem. Rev.*, **6**, 281 (1929).

[7] (a) Gustus with Lewis, THIS JOURNAL, **49**, 1512 (1927); (b) Wolfrom with Lewis, *ibid.*, **50**, 837 (1928); (c) Greene with Lewis, *ibid.*, **50**, 2813 (1928); (d) Gross with Lewis, *ibid.*, **53**, 2772 (1931).