XXI.—*Myricetin. Part II.*

By Arthur George Perkin, F.R.S.E.

Myricetin was first isolated from the bark of the *Myrica nagi* (Trans., 1896, **69**, 1287), and subsequently was found to be present in the leaves of *Rhus coriaria*, *cotinus*, and *metopium*, in the *Myrica gale*, *Pistachia lentiscus*, and *Hæmatoxylon campeachianum*. Its molecular weight is represented by the formula $C_{15}H_{10}O_8$; it forms crystalline acid compounds, an hexa-acetyl derivative, and by fusion with alkali yields phloroglucinol and gallic acid; these facts, together with the similarity of its dyeing properties and those of quercetin, indicate that it has the constitution of an hydroxyquercetin. The quantity of colouring matter available for the above experiments was very small, as the *Myrica nagi* contained but 0·27 per cent., and sumach only 0·11 per cent.; moreover, the stock of the former, a material not easy to obtain, was soon exhausted. Although attempts to accumulate

sufficient myricetin were made from time to time, they had to be abandoned, and it is only lately, owing to the kindness of Professor E. Joshitake, of Tokio, that an extract of the *Myrica nagi* was obtained, by means of which the following work could be carried out.

Experimental.

The extract, a brownish-black, brittle mass, was treated with ten times its weight of hot water, and when cold the clear liquid was decanted, the residue again washed twice in a similar manner, and drained on a porous tile. It was digested with boiling alcohol, filtered from insoluble matter, and the filtrate evaporated until crystals separated; these were collected by means of the pump,* washed, first with a little alcohol and then repeatedly with increasingly dilute alcohol until the washings were almost colourless. The yellowish-brown residue was crystallised from dilute alcohol, then converted into its acetyl compound, and the latter, when pure, decomposed with acid in the usual manner. It was incidentally determined that the melting point, 204—206°, previously given for acetylmyricetin, is somewhat too low, and should be 211—212°. An analysis of myricetin was again made:

0·1332 gave 0·2744 CO_2 and 0·0389 H_2O. C = 56·18; H = 3·24.
$C_{15}H_{10}O_8$ requires C = 56·60; H = 3·14 per cent.

When crystallised from dilute alcohol, and allowed to dry, myricetin has the formula $C_{15}H_{10}O_8,H_2O$, and this water of crystallisation is best removed by heating at 160°, although it is almost entirely evolved at 100°:

0·5367 at 160° lost 0·0290 H_2O. Found 5·40.
0·4686 „ 160° „ 0·0249 H_2O. „ 5·31.
Theory requires H_2O = 5·35 per cent.

Myricetin melts between 355° and 360°. Owing, however, to the darkening of the tube, it was difficult to be certain to one degree, although 357° is probably correct.

Bromine Compound.—By the action of bromine on myricetin suspended in glacial acetic acid, a compound was previously obtained which had the percentage composition of tetrabromomyricetin (*loc. cit.*). Owing to its soluble nature and peculiar dyeing properties, some doubt as to its constitution was expressed, it being possible that during the reaction a decomposition had ensued. To determine this point, the bromine compound was digested for several hours with boiling hydriodic acid and the product treated with sodium bisul-

* Filtrate A (see p. 207).

phite solution. The resulting yellow precipitate crystallised from dilute alcohol in needles which had all the properties of myricetin and gave a colourless acetyl derivative melting at 211—212°. The compound in question was thus without doubt *tetrabromomyricetin.*

Methylation of Myricetin.

Four grams of myricetin, dissolved in boiling methyl alcohol containing excess of methyl iodide, were treated drop by drop with a solution of eight grams of caustic potash in methyl alcohol, the addition extending over a day and a half. This procedure was adopted with the object of preventing an oxidation of the myricetin, which readily occurs in the presence of alkali. After removal of unattacked methyl iodide and the greater portion of the alcohol by distillation, the residue was treated with water, extracted with ether, and the ethereal solution washed with dilute caustic potash solution. On evaporation, a semicrystalline product remained which was purified by repeated crystallisation from alcohol:

0·1163 gave 0·2630 CO_2 and 0·0574 H_2O. C = 61·67; H = 5·48.
0·1134 „ 0·2553 CO_2 „ 0·0549 H_2O. C = 61·40; H = 5·37.
0·1000 „ 0·3040 AgI. CH_3 = 19·40.
$C_{15}H_5O_8(CH_3)_5$ requires C = 61·85; H = 5·15; CH_3 = 19·33 per cent.

Myricetin pentamethyl ether forms very pale yellow, almost colourless, hair-like needles melting at 138—139°, and is sparingly soluble in cold alcohol. On acetylation in the usual manner, it gives an acetyl derivative which crystallises from alcohol in colourless needles melting at 167—170°. Decomposition with acid indicated the presence of one acetyl group:

0·4342 gave 0·3895 regenerated ether. Found 89·70.
Theory for loss of one acetyl group requires 90·23 per cent.

Myricetin thus contains one hydroxyl group which resists methylation, and is consequently in the ortho-position to a carbonyl group. On treatment with alcoholic potash, the pentamethyl ether yields a yellow potassium salt readily decomposed by water.

On digestion with alcoholic potash at 170° for three hours, myricetin pentamethyl ether was decomposed, and from the product of the reaction an acid and a phenol were isolated. The acid crystallised in colourless needles melting at 164—167°, and was found to be *gallic acid trimethyl ether.*

The viscous, readily soluble phenol yielded an azobenzene derivative which crystallised from a mixture of alcohol and acetic acid in orange-red leaflets melting at 250—252°. This compound is identical with that given by rhamnetin, quercetin tetramethyl ether (Proc.,

1900, 181), and luteolin trimethyl ether under similar conditions and is consequently *disazobenzene phloroglucinol monomethyl ether*. The phenol is thus phloroglucinol monomethyl ether.

Ethylation of Myricetin.

Five grams of myricetin dissolved in a boiling mixture of alcohol and ethyl iodide were treated during 12 hours with a solution of 9·5 grams of caustic potash in alcohol, drop by drop. The product of the reaction insoluble in alkali was purified by crystallisation from alcohol:

0·1064 gave 0·2600 CO_2 and 0·0682 H_2O. C = 66·64; H = 7·12.
0·1124 „ 0·2730 CO_2 „ 0·0710 H_2O. C = 66·24; H = 7·01.
$C_{15}H_4O_8(C_2H_5)_6$ requires C = 66·66; H = 6·99 per cent.

It forms almost colourless needles melting at 149—151°, sparingly soluble in cold alcohol. This compound does not contain a free hydroxyl group, for after digestion with acetic anhydride and sodium acetate, its melting point and percentage composition (found C = 66·56; H = 7·01) were unaltered. Further, this product, on treatment with sulphuric acid, sustained no loss, 0·4112 and 0·8174 yielding respectively 0·4116 and 0·8173 gram of unchanged substance. It is thus without doubt *myricetin hexaethyl ether*.

When decomposed with alcoholic potash at 170°, it yielded, like the methyl ether, an acid and a phenol. The former crystallised from water in colourless needles or leaflets melting at 111—112°. It was found to be *gallic acid triethyl ether*:

0·1093 gave 0·2460 CO_2 and 0·0717 H_2O. C = 61·38; H = 7·28.
Theory requires C = 61·41; H = 7·09 per cent.

The phenol dissolved in dilute sodium carbonate solution gave, with diazobenzene sulphate, a bright yellow precipitate, which was collected, washed, dried, and purified by several crystallisations from benzene. It formed glistening, bright yellow needles melting at 163—165°, but on account of its ready solubility in the usual solvents, sufficient was not available for analysis. From analogy, however, it is probably *azobenzenephloroglucinol diethyl ether*.

When fisetin tetramethyl ether is decomposed with boiling alcoholic potash, it yields veratric acid and fisetol dimethyl ether,

$$OH\cdot C_6H_3(OCH_3)\cdot CO\cdot CH_2\cdot OCH_3,$$

a fact which enabled Herzig (*Monatsh.*, 1891, **12**, 187) to determine the constitution of fisetin. At this lower temperature, myricetin hexaethyl ether is also decomposed, but the products were identical with those given by alcoholic potash at 170°, and it thus appears likely that the anticipated phloroglucinol derivative is too unstable to be produced by

this method. The matter is worthy of further experiment, but owing to lack of raw material this at present is impossible.

Monopotassium Myricetin.—When a boiling solution of myricetin in absolute alcohol is treated with alcoholic potassium acetate, an orange-red, amorphous precipitate separates; if, however, a slightly dilute alcohol be employed, the substance is obtained in a crystalline condition. It was collected and washed with alcohol, and dried at 100°, when it assumed a dark green colour. When digested with boiling water, it is decomposed, with separation of myricetin:

Found K = 11·95. $C_{15}H_9O_8K$ requires K = 10·95 per cent.

Owing possibly to oxidation, the salt could not be obtained in a chemically pure condition, but the result is sufficient to prove that myricetin reacts in an analogous manner to quercetin and the other colouring matters of this group.

A Glucoside of Myricetin.

The alcoholic filtrate (A, p. 204) from the crude myricetin, on standing overnight, became semisolid owing to the deposition of crystals. These were drained from the black, tarry mother liquor, washed first with a little alcohol and then with 50 per cent. alcohol until the filtrate was nearly colourless. The product was dissolved in boiling water, filtered from a small quantity of myricetin, and the crystals which separated on cooling again treated in a similar manner. It was now twice crystallised from alcohol, and again from water. *Myricitrin*, the name proposed for this glucoside, crystallises from water in pale yellow, almost colourless leaflets containing one molecule of water of crystallisation; this cannot be removed at 100°, but is completely evolved at 160°:

1·0925 at 160° gave 0·0420 H_2O. Found 3·84.
1·1390 ,, 160° ,, 0·0475 H_2O. Found 4·17.
Theory requires H_2O = 3·60 per cent.
0·1185 at 100° gave 0·2205 CO_2 and 0·0520 H_2O. C = 50·74; H = 4·87.
0·1098 ,, 160 ,, 0·2098 CO_2 ,, 0·0445 H_2O. C = 52·10; H = 4·50.
0·1150 ,, 160 ,, 0·2181 CO_2 ,, 0·0475 H_2O. C = 51·72; H = 4·59.
$C_{21}H_{22}O_{13},H_2O$ requires C = 50·40; H = 4·80 per cent.
$C_{21}H_{22}O_{13}$,, C = 52·28; H = 4·56 ,,

When slowly heated, it sinters at 197° and melts at 199—200°, and is sparingly soluble in water and absolute alcohol. It dissolves in dilute alkaline solutions with a pale yellow colour having a faint green tint and this solution rapidly becomes brown on exposure to air. Aqueous lead acetate gives a gelatinous, orange-yellow precipitate, and alcoholic ferric chloride a deep, greenish-black coloration. In appearance, it

cannot be distinguished from quercitrin, and the dyeing properties of the two substances are almost identical:

	Chromium.	Aluminium.	Tin.	Iron.
Quercitrin.	Full brown-yellow.	Full golden-yellow.	Lemon-yellow.	Deep olive.
Myricitrin.	Full brown-yellow.	Full golden-yellow.	Lemon-yellow.	Brown-olive

Decomposition of the Glucoside.—One gram (approx.) of myricitrin, dissolved in 500 c.c. of water, was treated with 1 c.c. of sulphuric acid and digested at the boiling temperature for 45 minutes. Crystals of myricetin separated out, and, after standing overnight, were collected washed, and dried at 160°:

1·0835 air-dried glucoside gave 0·6915 $C_{15}H_{10}O_8$. Found 63·85.
1·1660 dried at 100° „ 0·7427 $C_{15}H_{10}O_8$. Found 63·69.
1·0380 „ „ 160° „ 0·6800 $C_{15}H_{10}O_8$. Found 65·51.
$C_{21}H_{22}O_{13},H_2O$ requires $C_{15}H_{10}O_8 = 63·60$ per cent.
$C_{21}H_{22}O_{13}$ „ $C_{15}H_{10}O_8 = 65·97$ „

The free colouring matter had all the reactions of myricetin.

The Sugar.—The acid filtrate from the myricetin was neutralised with barium carbonate, filtered, and evaporated to a small bulk. The residue yielded a crystalline osazone, which was collected, washed with a little ether, recrystallised from alcohol, and finally from alcohol and water. It formed yellow needles melting at 181—183°, and was identical in properties with *rhamnose osazone*, a sample of which was prepared for comparison from the pure sugar.

Myricitrin, on hydrolysis, thus gives myricetin and rhamnose, and this reaction may be expressed as follows:

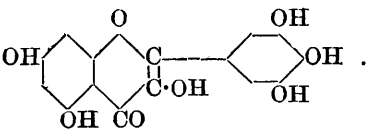
$$C_{21}H_{22}O_{13} + H_2O = C_{15}H_{10}O_8 + C_6H_{14}O_6.$$

It is analogous to quercitrin which, in a similar manner, yields rhamnose and quercetin.

$$C_{21}H_{22}O_{12} + H_2O = C_{15}H_{10}O_7 + C_6H_{14}O_6.$$

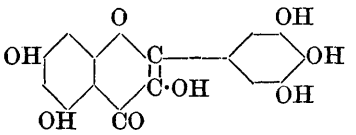
Theoretical.

The remarkable similarity between the reactions of quercetin and myricetin, previously pointed out (*loc. cit.*), is enhanced by the above results, and there seems no reason to doubt that myricetin is *hydroxyquercetin.*

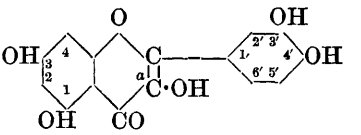


It is interesting that myricetin can so readily be fully ethylated with formation of a hexaethyl ether, whereas quercetin, although con-

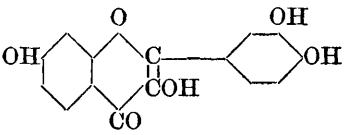
taining five hydroxyl groups, gives but a tetraethyl derivative. This distinction is not of importance, in view of the behaviour in this respect of other members of the flavone group. Apigenin (Trans., 1897, **72**, 805), $C_{15}H_7O_2(OH)_3$, has given a dimethyl and a diethyl-ether; luteolin (Trans., 1900, **77**, 1314), $C_{15}H_6O_2(OH)_4$, a dimethyl ether of methylluteolin and tetraethylluteolin (Herzig, *Ber.*, 1897, **30**, 656), and campherol, $C_{15}H_7O_2(OH_3)$, a dimethyl ether of methyl-campherol (Testoni, *Gazzetta*, 1900, **30**, ii, 327); such results are thus evidently due to the presence or absence of certain hydroxyl groups in these compounds, although in what manner they effect the reaction is not at present clear. The resemblance between the dyeing properties of quercetin and myricetin has been already alluded to, but it is most interesting that quercitrin and myricitrin should behave almost identically in this respect. These results indicate as probable that in both compounds the sugar group is present in the same position; further, it is possible, from a knowledge of the dyeing properties of some members of the flavone series, to indicate with some certainty the locality of this in myricitrin at least. The shades produced from fisetin, quercetin (Trans., 1896, **69**, 1287) and myricetin



Myricetin.

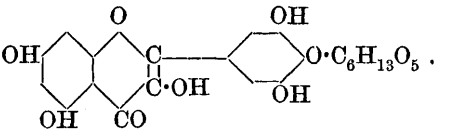


Quercetin.



Fisetin.

are similar in strength and character, and the resemblance in this respect between quercetin and rhamnetin (quercetin monomethyl ether, $OCH_3 = 3$) has also been pointed out. Consequently, it is evident that the hydroxyls 3 and 1 do not appreciably influence the colouring effect of quercetin or myricetin, the character of which is due to the orthohydroxyls they contain in conjunction with that present in the pyrone ring. Now, the dyeing properties of quercitrin and myricitrin are almost identical with those of morin, the constitution assigned to which (Trans., 1896, **68**, 792) is very similar to that of myricetin, from which the hydroxyl (4′) has been removed. It is thus likely that myricitrin has the constitution



and that that of quercitrin may be similarly expressed. The only alternative formula for myricitrin is that in which the sugar group has the position (*a*); such a compound should, by analogy, dye like luteolin, the shades of which (*loc. cit.*) do not widely differ from those given by morin. Employing the monopotassium derivatives of quercetin and myricetin (*loc. cit.*), experiments will be carried out with the hope of preparing glucosides of these colouring matters.

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