

XLIX.—*Luteolin*. Part II.

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IN a previous communication (this vol., 206), it was shown that the true formula of luteolin is $C_{15}H_{10}O_6$, a fact determined by the examination of its compounds with mineral acids and with bromine. The production of a tetracetyl and tetrabenzoyl compound also proved it to contain four hydroxyl groups, and a preliminary study of the behaviour of its alkali salt towards methylic iodide resulted in the production of a compound containing three methoxy-groups only. Since the publication of my results, Herzig (*Ber.*, 1896, **29**, 1013) has published a short paper in which he states that he is also working on luteolin, and at the same time mentions its acetyl derivative, methyl ether, and its behaviour towards fused alkalis. I must express my thanks to this gentleman for his courtesy in allowing me to see the manuscript of his paper before forwarding it for publication. As, through press of other work, I may be unable to complete my examination of this colouring matter for some little time, it appeared to me advisable to lay before the Society the net results that have been

obtained, especially as they have an important bearing on its constitution.

Ethylation of Luteolin.

One part of luteolin dissolved in a solution of 10 parts of caustic potash in ethylic alcohol, was boiled with excess of ethylic iodide and digested for 24 hours. After removal of the excess of ethylic iodide and the greater part of the alcohol by distillation, the residue was poured into water, the precipitated product dissolved in ether, and the ethereal solution, after being washed with dilute alkali, evaporated to a small bulk. The crystalline mass which separated on cooling was collected and crystallised repeatedly from alcohol until it had a constant melting point. On analysis,

0·1294 gave 0·3225 CO₂ and 0·0730 H₂O. C = 67·97; H = 6·26.

0·1555 „ (by Zeisel's method) 0·3000 AgI. C₂H₅ = 23·79.

C₁₅H₇O₃(OC₂H₅)₃ requires C = 68·11, H = 5·95, C₂H₅ = 23·51 p. c.

Luteolin triethyl ether is obtained as a glistening mass of light yellow needles melting at 131—132°, readily soluble in boiling, but almost insoluble in cold alcohol. It is insoluble in alkalis.

The residual hydriodic acid mother liquor from the Zeisel determinations was poured into water, treated with excess of sodium hydrogen sulphite solution, and the yellow flocculent precipitate which was produced was collected and crystallised from dilute alcohol. It formed a mass of light yellow needles, and was without doubt luteolin, for it yielded a colourless acetyl derivative melting at 213—215°. Herzig (*loc. cit.*) states that he has found the melting point of acetyl luteolin to be 225—227°. Feeling that it was possible some mistake might have occurred, I re-examined the melting point of my preparation, and, moreover, recrystallised it from alcohol with the result that the previous melting point, 213—215°, was not altered. By conducting the operation with rapidity, a slightly different result could be obtained, but in no case more than three degrees higher, and I therefore consider the melting point, 213—215°, to be correct. In experimenting with this tetracetyl-luteolin, I have observed that unless the product, which is of an exceedingly light and fluffy nature, is in good contact with the sides of the tube, erroneous results are liable to be obtained, and it is possible that this may account for the discrepancy above referred to.

It having been previously shown that luteolin contains four hydroxyl groups, whilst only a triethyl ether could be obtained, it appeared evident that the latter contains an hydroxyl group which resists ethylation; this being the case, it should yield an acetyl derivative.

To determine this point, one part of luteolin triethyl ether was

digested with one part of anhydrous sodium acetate and a slight excess of acetic anhydride for an hour; the solution was then poured into water and allowed to remain for 24 hours, when the colourless precipitate was collected, drained upon a porous tile, and purified by crystallisation from alcohol.

0.1196 gave 0.2934 CO₂ and 0.0654 H₂O. C = 66.90; H = 6.07.

C₁₅H₆O₃(C₂H₃O)(OC₂H₅)₃ requires C = 66.99; H = 5.82 per cent.

Monacetyl-luteolin triethyl ether crystallises in colourless needles melting at 185—186°, sparingly soluble in alcohol.

It has been shown by Kostanecki (*Monatsh.*, 1891, **12**, 318—322), with the xanthonenes and chrysin (*Ber.*, 1893, **26**, 2901), by Herzig with quercetin (*Monatsh.*, **5**, 72—93), by Schunck and Marchlewski with alizarin (*Trans.*, 1894, **65**, 185), and by myself with resorcylic acid (*Trans.*, 1895, **67**, 995), that it is not possible to ethylate by known methods the hydroxyl group occupying the ortho-position relatively to the carbonyl group in these substances. Kostanecki has, moreover, shown (*loc. cit.*), in the case of the ethers of gentisin and chrysin, that such compounds, when treated with alcoholic potash in alcoholic solution, yield intensely yellow, crystalline, potassium salts, which, however, on treatment with water, are decomposed, more or less readily, into potassium hydroxide and the free ether. Experiments with luteolin triethyl ether yielded a similar result, for, when a boiling alcoholic solution of this substance was treated with a few drops of alcoholic potash, glistening, yellow needles of the potassium salt were deposited, which, when treated with water, were at once decomposed yielding the free triethyl ether. It, therefore, appears that one of the hydroxyls in luteolin is in the ortho-position relatively to a carbonyl group.

Decomposition of Luteolin with Fused Alkalis.

It was previously shown (*loc. cit.*) that when luteolin is fused with potassium hydroxide, protocatechuic acid and a nearly colourless crystalline substance melting at 210° are the principal products. As this gives no coloration with chloride of iron, it was considered not to be phloroglucinol, although its melting point* indicated this substance. Herzig has stated (private communication and *loc. cit.*) that with small quantities of phloroglucinol the ferric chloride reaction was not trustworthy, a fact of which I was not aware, and that my substance was very probably phloroglucinol, as he had obtained evidence of its presence in the products of the action of fused alkali on luteolin by means of the fir wood and hydrochloric acid test. A small quantity

* The melting point of phloroglucinol varies according to the rapidity with which it is heated; on slowly heating (Baeyer, *Ber.*, 1886, **19**, 2186) it melts at 200—209°, and when quickly heated at 217—219°.

of luteolin was therefore again treated with fused alkali, and the products of the reaction separated as before; a solution of the substance melting at 210° gave the phloroglucinol reaction by the fir wood test. Luteolin, therefore, on fusion with alkali yields protocathechuic acid and phloroglucinol.

Decomposition of Luteolin Triethyl Ether with Alcoholic Potash.

Although only a small quantity of the triethyl ether was available it was of interest to determine whether it would yield protocathechuic acid diethyl ether on treatment with alcoholic potash, as the ethyl ethers of both quercetin and fisetin yield this compound under such circumstances.

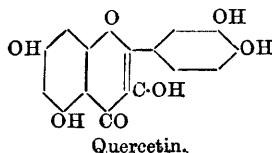
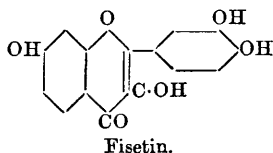
The triethyl ether was, therefore, heated with 10 parts of alcoholic potash in a sealed tube at $130-140^{\circ}$ for two hours, it having been previously found that it was but little attacked by digestion at 100° . The light brown liquid obtained was poured into water, extracted with ether which removed a trace of a light yellow substance, and the solution saturated with carbonic anhydride. After extraction with ether, the liquid was neutralised with acid, and the colourless precipitate collected and purified by crystallisation from alcohol. A mass of colourless needles was thus obtained which melted at $165-166^{\circ}$, and had all the properties of protocathechuic acid diethyl ether.

The ethereal extract of the liquid that had been treated with carbonic anhydride, on evaporation, yielded a light brown oily residue, which gave the phloroglucinol reaction. The quantity, however, was too small to admit of purification.

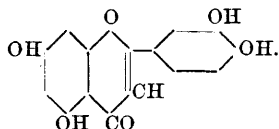
As previously stated, preliminary experiments on the methylation of luteolin resulted in the isolation of a methylic ether melting at $191-192^{\circ}$; this closely resembles the ethylic ether, in that it has now been found to have the formula $C_{15}H_7O_3(OCH_3)_3$, and to yield a monacetyl derivative, $C_{15}H_6O_3(OCH_3)_3 \cdot C_2H_3O$ (melting at $174-175^{\circ}$), and a yellow potassium salt. I hope shortly to be able to complete my examination of this substance.

Theoretical Considerations.

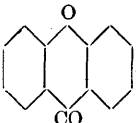
Fisetin and quercetin have been shown by Herzig (*Ber.*, 1895, **28**, 293) and Kostanecki (*ibid.*, 2302) to be derivatives of phenylated pheno- γ -pyrone, quercetin being a hydroxy-fisetin, thus



In the previous communication, a resemblance between luteolin and fisetin was pointed out in that they both had the same formula, contained four hydroxyl groups, and yielded dibromo-derivatives. Moreover, on fusion with potash, both give protocatechuic acid as one of their decomposition products, and they also combine with acids. On the other hand, as shown in this communication, in its alkyl derivatives luteolin more closely resembles quercetin, in that the latter, unlike fisetin, contains a hydroxyl in the ortho-position relatively to a carbonyl group. Quercetin also, on fusion with alkali, yields not only protocatechuic acid, but also phloroglucinol. It should also be remarked that when the ethylic ethers of luteolin and quercetin are digested with alcoholic potash, in each case the diethylic ether of protocatechuic acid is produced, showing that in the original molecule the hydroxyl groups of the catechol are intact, whereas one of those of the phloroglucinol nucleus is not. Most probably, therefore, the constitution of luteolin must be thus represented



this formula differing only from that of quercetin in that it contains no hydroxyl group in the pyrone ring. In other words, quercetin is also a hydroxy-luteolin. The acid compounds of luteolin appear to support this formula, for a further study of the behaviour of the natural yellow colouring matters towards acids, an account of which, I hope shortly to lay before the Society, has so far resulted in the fact

that no members of the xanthone, , or benzophenone

class, have been yet found which possess the property of combining with mineral acids, and it appears probable that this is a general reaction for the yellow colouring matters of the pheno- γ -pyrone class.

The absence in luteolin of a hydroxyl group in the pyrone ring may account for the greater permanency of its shades upon mordanted fabrics, as compared with those obtained with quercetin and fisetin.

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