oxygen when placed in contact with air or pure oxygen. This absorption of oxygen is quite rapid, as much as 3.8 equivalents per molecule of hydroquinone used, having been absorbed in 24 hours. The total quantity of oxygen consumed is large, the amount varying from 5.6 to 9.8 equivalents per molecule of hydroquinone.

2. With all the primary amines studied, and with dimethylamine, this oxidation caused the separation of brilliant red crystals, which were found to be *bis*(alkylamino)quinones. The yields of these diaminoquinones varied from 14 to 53% on the basis of the hydroquinone used.

3. Much more oxygen gas was consumed than was required for the formation of the *bis*(alkylamino)quinone which separated, the excess being as high as 14 equivalents per molecule of hydroquinone not used to form the *bis*(alkylamino)quinone. The side reaction consuming this extra oxygen has not been determined, but the results have shown that it is not due to the oxidation of alcohol, to a further oxidation of *bis*(alkylamino)-quinone, or to the accumulation of hydrogen peroxide in the solution.

4. This oxidation of hydroquinone in the presence of aliphatic amines furnishes a new, simple and quite efficient method for the preparation of *bis*(alkylamino)quinones, which compounds as a class have heretofore received little study.

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[Contribution from the Department of Chemistry, University of Bristol]

# THE ACTION OF DIAZOMETHANE ON SOME AROMATIC ACYL CHLORIDES

## II. SYNTHESIS OF FISETOL

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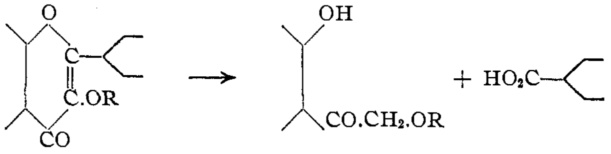
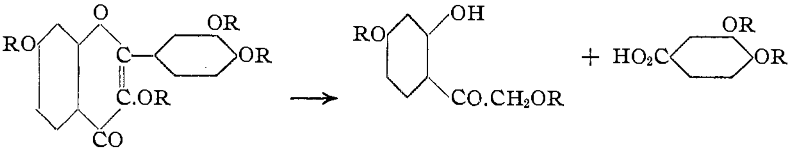
Completely alkylated flavonols (I) are disintegrated by alcoholic potassium hydroxide as follows.



I II III

The production of these disintegration products, especially of those which are derived from Formula II, has served as a basis for the formulas which have been assigned to the following flavonols: fisetin, quercetin, datiscetin, myricetin, quercetagetin and gossypetin. These formulas have been confirmed by synthesis in the case of fisetin,[1] quercetin[2] and datiscetin.[3] On the other hand, myricetin has so far not been synthesized,[4] whereas the syntheses of 5,6,7,3′,4′-pentahydroxy-flavonol[5] have shown that it is neither quercetagetin nor gossypetin as assumed by A. G. Perkin.[7] We have, therefore, as a preliminary to the syntheses of quercetagetin and gossypetin, elaborated what seems to be a general method for the preparation of the disintegration products, which are derived from Formula II.

In the present communication we describe the synthesis of fisetol (IX) which had been obtained by Herzig[8] in the form of its dialkyl derivatives (V) from completely alkylated fisetin (IV).



IV V

The scheme adopted by us for the preparation of fisetol (IX) is the extension of the reaction described by Clibbens and Nierenstein[9] and Staudinger and Mächling,[10] according to which aromatic acyl chlorides, when reacted upon with diazomethane, yield ω-chloro-acetophenones: $R.CO.Cl + CH_2N_2 = R.CO.CH_2.Cl + N_2$. Diacetyl-β-resorcoyl chloride (VI) was converted by this reaction into ω-chloro-2,4-diacetoxy-acetophenone (VII) from which ω,2,4-triacetoxy-acetophenone (VIII) was obtained on boiling with acetic anhydride and sodium acetate.[11] This latter substance on treatment with alcoholic ammonia[12] gave fisetol (IX).

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[1] Kostanecki, Lampe and Tambor, *Ber.*, **37**, 784 (1904).

[2] Kostanecki, Lampe and Tambor, *Ber.*, **37**, 1402 (1904).

[3] Bargellini and Peratoner, *Gazz. chim. ital.*, **49**, 64 (1919).

[4] Attempts to synthesize myricetin will shortly be described by H. F. Dean and M. Nierenstien.

[5] Nierenstein and Wheldale, *Ber.*, **44**, 3487 (1911). Nierenstein, *J. Chem. Soc.*, **107**, 869 (1915); **111**, 4 (1917).

Reference must here be made to a clerical error on p. 7 of the last quoted paper by Nierenstein. The melting point of 2,3,4,6-tetramethoxy-acetophenone is there given as 92–93°, whereas the correct melting point is 42–43°, which agrees with the melting point 43–45° found by Bargellini[6] for this substance.

[6] Bargellini, *Gazz. chim. ital.*, **49**, 55 (1919).

[7] Perkin, *J. Chem. Soc.*, **75**, 145 (1899); **95**, 2181 (1909); **103**, 209 (1913); **109**, 145 (1916).

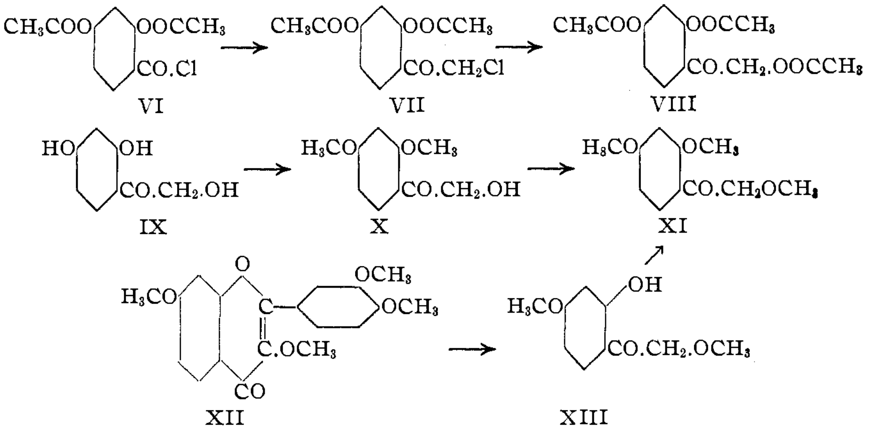
[8] Herzig, *Monatsh.*, **12**, 184 (1891); **14**, 51 (1893).

[9] Clibbens and Nierenstein, *J. Chem. Soc.*, **107**, 1491 (1915).

[10] Staudinger and Mächling, *Ber.*, **49**, 1973 (1916).

[11] Tambor and Dubois, *Ber.*, **51**, 748 (1918).

[12] (a) Nierenstein, *Ber.*, **43**, 1688 (1910). (b) Fischer and Bergmann, *Ber.*, **50**, 1066 (1917).



The fisetol (IX) thus obtained gave the same data as found for fisetol, previously synthesized by Sonn and Falkenheim[13] by a different, but not generally applicable, method. For further identification trimethyl-fisetol (XI) was prepared from fisetol (IX). Diazomethane was used as a methylating reagent, when fisetol was only partially methylated, 2,4-dimethyl-fisetol (X) being produced, since on oxidation in alkaline solution with permanganate, 2,4-dimethyl-β-resorcylic acid was formed. Trimethyl-fisetol (XI) was then obtained by methylating 2,4-dimethyl-fisetol (X) with methyl iodide and silver oxide. Trimethyl-fisetol (XI) was also prepared by hydrolyzing tetramethyl-fisetin (V), when ω,4-dimethyl-fisetol (XIII) was recovered. This latter substance gave, on methylation with dimethyl sulfate and alkali, trimethyl-fisetol (XI) which was in every respect identical with trimethyl-fisetol from synthetic fisetol.

## Experimental Part

### ω-Chloro-2,4-diacetoxy-acetophenone (VII)

The intermediate products required in the preparation of this substance are prepared as follows.

1. β-Resorcylic acid is prepared according to the method of Bistrzycki and Kostanecki[14] as modified by Clibbens and Nierenstein.[15]

2. 2,4-Diacetyl-β-resorcylic acid is prepared according to the method of Bergmann and Dangschat.[16]

3. Diacetyl-β-resorcoyl-chloride (VI) is prepared by the action of an excess of thionyl chloride on a gently warmed suspension of diacetyl-β-resorcylic acid in chloroform. The oil left on evaporation of the chloroform in a vacuum solidifies on standing

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[13] Sonn and Falkenheim, *Ber.*, **55**, 2975 (1922). This paper gives a summary of the attempts which have been made to synthesize fisetol.

[14] Bistrzycki and Kostanecki, *Ber.*, **18**, 1985 (1885).

[15] Ref. 9, p. 1494.

[16] Bergmann and Dangschat, *Ber.*, **52**, 379 (1919).

in ice. It crystallizes from ligroin in small needles; m. p., 37°. Pacsu,[17] who has also prepared diacetyl-β-resorcoyl-chloride, describes it as an oil; b. p., 170° (12 mm.).

*Anal.* Subs., 0.1781: AgCl, 0.0984. Calc. for $C_{11}H_9O_6Cl$: Cl, 13.8. Found: 13.6.

Six g. of diacetyl-β-resorcoyl chloride (1) in ether (Grignard) is treated with an excess of diazomethane, prepared according to the method of Staudinger and Kupfer.[18] The solid left on evaporating the ether crystallizes from dry benzene in prismatic needles, m. p., 73°, which have the characteristic odor of the chloromethyl ketones; yield, 98%.

*Anal.* Subs., 0.1973: AgCl, 0.1034. Subs., 0.2452: $CO_2$, 0.4762; $H_2O$, 0.0998. Calc. for $C_{12}H_{11}O_5Cl$: C, 53.2; H, 4.1; Cl, 13.1. Found: C, 53.0; H, 4.5; Cl, 13.0.

### ω,2,4-Triacetoxy-acetophenone (VIII)

A solution of 5 g. of ω-chloro-2,4-diacetoxy-acetophenone (VII) in 25 cc. of acetic anhydride is boiled with 10 g. of anhydrous sodium acetate for ten hours. The solid obtained on diluting with water crystallizes from alcohol in needles; m. p., 129°; yield, 96%.

*Anal.* Subs., 0.1553: $CO_2$, 0.3248; $H_2O$, 0.0688. Calc. for $C_{14}H_{14}O_7$: C, 57.1; H, 4.8. Found: C, 57.0; H, 5.0.

### Fisetol (IX)

To a solution of 3 g. of ω,2,4-triacetoxy-acetophenone (VIII) in 25 cc. of dry methyl alcohol is added 75 cc. of 5 *N* dry alcoholic ammonia, which is prepared by passing dry ammonia into methyl alcohol which had been refluxed for ten days over calcium oxide. The solution is left standing for eight days in the cold, when ammonium acetate commences to crystallize after 24 hours' standing. The solution is filtered and concentrated in a vacuum to about 50 cc., when a further amount of ammonium acetate crystallizes. It is again filtered and evaporated to dryness in a vacuum. It crystallizes from water slightly acidulated with hydrochloric acid in small prismatic needles which melt at 189°, as found by Sonn and Falkenheim.[19] The properties of our fisetol agree with those described by these workers.

*Anal.* Subs., 0.1378: $CO_2$, 0.2895; $H_2O$, 0.0584. Calc. for $C_8H_8O_4$: C, 57.1; H, 4.8. Found: C, 57.2; H, 4.8.

The PHENYLHYDRAZONE melts at 109° with decomposition, as found by Sonn and Falkenheim.

*Anal.* Subs., 0.2695: 24.4 cc. of N (17°, 765 mm.; over 33% KOH). Calc. for $C_{14}H_{14}O_3N_2$: N, 10.9. Found: 11.0.

### 2,4-Dimethyl-fisetol (X)

To a suspension of 1.5 g. of fisetol (IX) in dry ether is added an excess of an ethereal solution of diazomethane prepared from nitroso-methylurethan. The solid left on evaporating the ether crystallizes from benzene in small silky needles; m. p., 131°. Slater and Stephen[20] who have prepared this substance by a different method give its melting point as 127–129°, with decomposition. They state, however: "the purest sample of the compound obtained melted and decomposed at 127–129°, but there was insufficient for an analysis." This may, perhaps, account for the difference between the two melting points of this substance.

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[17] Pacsu, *Ber.*, **56**, 413 (1923).

[18] Staudinger and Kupfer, *Ber.*, **45**, 501 (1912).

[19] Ref. 13, p. 2984.

[20] Slater and Stephen, *J. Chem. Soc.*, **117**, 316 (1920).

*Anal.* Subs., 0.1640: $CO_2$, 0.3679; $H_2O$, 0.0960. Calc. for $C_{10}H_{12}O_4$: C, 61.2; H, 6.1. Found: C, 61.2; H, 6.5.

### Oxidation of 2,4-Dimethyl-fisetol (X) to 2,4-Dimethyl-β-resorcylic Acid

A solution of about 0.3 g. of 2,4-dimethyl-fisetol (X) in 10 cc. of 5% potassium hydroxide is heated for five hours on a boiling water-bath with 15 cc. of *N* potassium permanganate solution. The filtered liquid is acidified with dil. sulfuric acid which contains a little sulfur dioxide, and the solid formed dissolved in ether. The ethereal solution is shaken with aqueous sodium bicarbonate saturated with carbon dioxide. The solid formed on acidifying the aqueous extract crystallizes from water in needles which melt at 108–109°; this melting point is not depressed on admixture with authentic 2,4-dimethyl-β-resorcylic acid.

### ω,2,4-Trimethyl-fisetol (XI)

1. A solution of 1 g. of 2,4-dimethyl-fisetol (X) in 50 cc. of ether is heated for ten hours with 3 cc. of methyl iodide and 5 g. of silver oxide. The filtered solution is evaporated to dryness and the residue crystallized from alcohol, when fine, silky needles are obtained; m. p., 61–62°.

*Anal.* Subs., 0.1014: $CO_2$, 0.2329; $H_2O$, 0.0602. Calc. for $C_{11}H_{14}O_4$: C, 62.8; H, 6.7. Found: C, 62.7; H, 6.6.

2. A solution of 1 g. of ω,4-dimethyl-fisetol (XIII), prepared by hydrolyzing tetramethyl-fisetin (XII), in a little alcohol is methylated by the addition of 5 cc. of methyl sulfate and 5 cc. of 20% alcoholic potassium hydroxide, both reagents being added hot. The solid formed by the addition of water is crystallized several times from alcohol with the aid of animal charcoal giving fine, silky needles; m. p., 61–62°. The melting point of neither of these two preparations is depressed on admixture with the other.

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

### Summary

1. Fisetol has been synthesized and it has been found to give the same data as the synthetic fisetol prepared by Sonn and Falkenheim by a different method.

2. The trimethyl derivative from synthetic fisetol has been shown to be identical with trimethyl-fisetol from tetramethyl-fisetin.

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