Especially interesting is phenacyl lactate, m. p. 96°, which is obtained in good yield, since this acid is important and difficult to identify.

The initial purity of the phenacyl esters is usually high, the first melting point seldom being more than one or two degrees lower than the final.

So far as our study goes, phenacyl bromide appears as a convenient and useful reagent for the identification of acids, superior in some cases to *p*-nitrobenzyl bromide.

Summary.

It has been found that phenacyl bromide may serve as a convenient reagent for the identification of acids. It is easily prepared and it readily forms esters of acids when boiled, in dilute alcohol solution, with the alkali salts of the acids. Many of these esters are solids easily purified by recrystallization from dilute alcohol and have convenient melting points.

The following esters of phenacyl alcohol have been prepared and studied and their properties tabulated:

Acetate (40°)
Aconitate (90°)
o-Aminobenzoate (181–2°)
Benzoate (118.5°)
p-Bromobenzoate (87°)
Cinnamate (140.5°)
Citraconate (108.5°)
Citrate (104°)
m-Cresotate (116.5°)
o-Cresotate (138.5°)
p-Cresotate (145.5°)
Fumarate (197.5°)
Glutarate (104.5°)
Itaconate (79.5°)
Lactate (96°)
Malate (106°)
Maleate (119°)
Mandelate
p-Nitrobenzoate (128.4°)
Palmitate (52.5°)
Pyrotartarate (101.5°)
Saccharate (120°)
Salicylate (110°)
Stearate (64°)
Succinate (148°)
Tartrate (130°)

BALTIMORE, MARYLAND.

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY, No. 316.]

THE SYNTHESIS OF AMINOFLAVONES, OF FLAVONE-AZO-BETA-NAPHTHOL DYES, AND OF OTHER FLAVONE DERIVATIVES.[1]

BY MARSTON TAYLOR BOGERT AND JOSEPH K. MARCUS.

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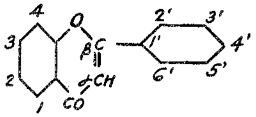
Introductory.

Many of the yellow coloring matters occurring in the plant kingdom have been shown to be hydroxy derivatives of flavone (benz-2-phenyl-γ-pyrone) (I). Aside from the general interest attaching to these compounds



(I)

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[1] The subject matter of this article forms part of a dissertation submitted by Joseph K. Marcus to the Faculty of Pure Science of Columbia University in partial fulfillment of the requirements of the degree of Doctor of Philosophy.

because of their ubiquitous occurrence in nature, they are of particular importance by reason of the successful commercial application of some of them as fast dyes, *i. e.*, quercetin (1,3,3′,4′-α-pentahydroxyflavone) the yellow dyestuff in quercitron bark, and morin (1,3,2′,4′-α-pentahydroxyflavone) which, together with maclurin (a pentahydroxybenzophenone), constitutes the coloring matter of old fustic.

In view of the strong chromophoric character of the benz-2-phenyl-γ-pyrone nucleus displayed in these compounds, it was considered of interest to extend the investigation of the flavone series to the preparation and study of the amino derivatives, in order to record the auxochromic effect of the amino group on the flavone nucleus, and to couple the diazotized amines with β-naphthol. Further, the methods which have been used hitherto for the preparation of flavone involve either the use of materials which are difficult to obtain in quantity or the employment of a long succession of reactions in which the yields at some points are disappointing.[1] Thus it seemed desirable to devise a new method for making compounds of this series which would not possess the disadvantages above named. With these objects in view, the investigation reported in this paper was undertaken.

The work was successful in regard to (A) the preparation of amino flavones, and (B) the production of azo-flavone dyes; but did not lead to (C) any better method for making flavone or its derivatives.

(A) Three monoaminoflavones, 2′-aminoflavone, 3′-aminoflavone and 4′-aminoflavone, were obtained by the reduction of a mixture of mononitroflavones. The isomeric nitro compounds were not isolated because they possessed too little difference of solubility in the solvents tried to give a satisfactory separation. The isolation of the individual aminoflavones, however, was effected by taking advantage of their differing basicities and solubilities.

The position of the amino group in each one of the three aminoflavones which were synthesized was determined by conversion of the amine, through its diazonium compound, into the corresponding phenol.

Two of the phenols thus obtained were found to be identical with 3′-hydroxyflavone[2] and 4′-hydroxyflavone,[3] which were both previously prepared by St. v. Kostanecki by another method. The third phenol proved to be 2′-hydroxyflavone which has been hitherto unknown.

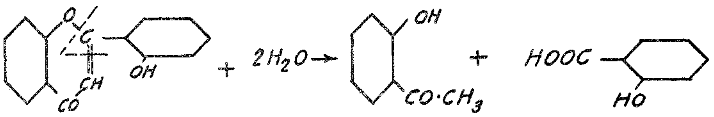
The position of the hydroxyl group in 2′-hydroxyflavone was determined by decomposing it with sodium ethoxide[4] into salicylic acid and *o*-hydroxyacetophenone (II).

[1] *Ber.*, **37**, 2635 (1904); **31**, 1760 (1898); **33**, 333 (1900); **46**, 2188 (1913); **47**, 2229 (1914).

[2] *Ibid.*, **34**, 1692 (1901).

[3] *Ibid.*, **33**, 2516 (1900).

[4] *Ibid.*, **31**, 702 (1898).



(II)

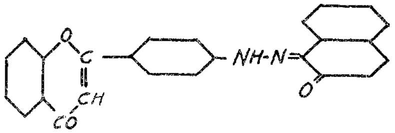
The noteworthy characteristics of the amines are:

1. They are all yellow; the 2′-amine being pale yellow; the 3′-amine, lemon-yellow; and the 4′-amine, golden yellow—thus the amino group seems to exert a stronger auxochromic influence than the hydroxyl group on the flavone nucleus, since 2′-hydroxyflavone, 3′-hydroxyflavone, and 4′-hydroxyflavone all are white. 3′-Aminoflavone and 4′-aminoflavone were found to dye wool and silk directly a light yellow color.

2. The 4′-aminoflavone stands out in sharp contrast to the other two amines, especially in those properties relating to color effect, *i. e.*, its color is a deeper yellow than that of the other amines; it produces an intense fluorescence in certain solvents (the unusual nature of the fluorescent property of this amine is that it seems to be manifested only in solvents, which contain the hydroxyl group), whereas the 2′- and 3′-isomers show no fluorescence in any solvent; its reduction with magnesium in alcoholic hydrochloric acid solution produces an intensely purple colored solution, in contrast to the light orange color developed in each case by similar treatment of the other two amines,[1] a bright red dye is obtained by coupling the diazotized 4′-aminoflavone with β-naphthol, whereas the 2′- and 3′-amines when treated in the same way give two orange dyes.

Noteworthy also are the nitration products of flavone. Although the individual nitro derivatives were not isolated, an ultimate analysis of the nitration mixture indicated that it was composed of mononitroflavones; and this was corroborated by the subsequent isolation of three monoamines (above) which were derived from the nitroflavone mixture. The following compounds, then, must have resulted from the nitration of flavone: 2′-nitroflavone, 3′-nitroflavone and 4′-nitroflavone. Thus, all the possible mononitro products arising from substitution in the phenyl nucleus of flavone have been formed, and none in which the "benz" ring has been attacked. This may be a case of steric hindrance; and it would be of interest to learn whether further nitration of mononitroflavone would be limited to the phenyl nucleus.

(B) A bright red dye of Structure III, fast to light and alkalis, was



(III)

obtained by coupling the diazotized 4′-aminoflavone with β-naphthol; and two orange dyes of Structures IV and V, of like fastness, resulted

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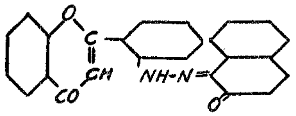
[1] Anthocyan formation possibly takes place in this reaction.

by the similar coupling of each of the diazotized 2'- and 3'-aminoflavones, respectively.



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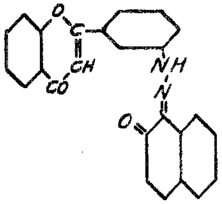
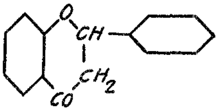


(V)

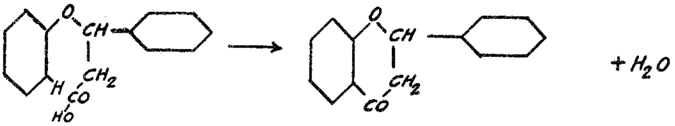
(C) St. v. Kostanecki[1] showed that flavone may be conveniently prepared by successive treatments of flavanone (VI), with bromine and potassium



(VI)

hydroxide. But, since the formation of flavanone, as carried out by the same investigator, involves the use of *o*-hydroxyanisole which is difficult to obtain in quantity, the following attempt was made to synthesize it from cinnamic acid which is readily available:

β-Phenoxyhydrocinnamic acid was prepared by the action of phenol on β-bromohydrocinnamic acid, which in turn was obtained from cinnamic acid and hydrogen bromide. The hope that the action of anhydrous aluminum chloride on β-phenoxyhydrocinnamyl chloride would effect an internal condensation to form flavanone (VII), similar to the condensation of β-phenoxycinnamyl chloride to form flavone,[2] was not realized. An attempt was also made to accomplish the internal condensation of free β-phenoxyhydrocinnamic acid by the employment of concd. sulfuric acid as a dehydrating agent, but the result was the formation of a disulfo-β-phenoxyhydrocinnamic acid instead. Further failure to effect condensation of the free acid resulted from the use of other dehydrating agents such as phosphorus pentoxide, anhydrous zinc chloride or fuming stannic chloride.



(VII)

Because of the well-known influence of the nitro group in a benzene ring

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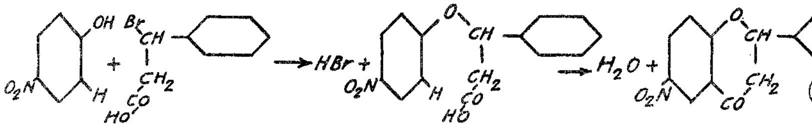
[1] *Ber.*, 37, 2635 (1904).

[2] *Ibid.*, 46, 2188 (1913)

on the lability of the hydrogen atom lying in the meta position to it, it was considered probable that flavanone ring formation would be successful with β-*p*-nitrophenoxyhydrocinnamic acid. With the purpose of obtaining the latter substance, *p*-nitrophenol was heated with β-bromohydrocinnamic acid, but instead of the expected acid, a compound which possesses the empirical formula for, and is believed to be, 2-nitroflavanone was obtained. The course of the reaction was doubtless a preliminary metathesis between *p*-nitrophenol and β-bromohydrocinnamic to form hydrogen bromide and the expected acid which immediately condensed to form 2-nitroflavanone with the elimination of water (VIII). However, in view of the small yield (2% of the calculated amount) of the nitro flavanone obtained, the third part of the investigation must be considered successful only insofar that one flavanone derivative has been prepared in poor yield by a new rapid method. Not enough of the compound was obtained to convert to the nitroflavone.



(VIII)

The procedure adopted in this paper for the preparation of flavone is a modification of the one devised by Ruhemann.[1] It was found that the interaction of ethylphenylpropiolate with sodium phenolate gave not one, as stated by Ruhemann, but two esters which on saponification yielded two isomeric acids, one of which corresponds with the β-phenoxycinnamic acid described by the above worker and the other of which has been shown to be either β-*o*-hydroxyphenylcinnamic acid or β-*p*-hydroxyphenylcinnamic acid.

The phenylpropiolic acid used in the flavone synthesis was prepared by a modification of the method described by Sudborough and Thompson.[2]

The other compounds which were prepared for the purpose of characterization of the aminoflavones or hydroxyflavones are: 2′-diacetylaminoflavone, 3′-diacetylaminoflavone 4′-diacetylaminoflavone, 2′-acetoxyflavone, 3′-acetoxyflavone and 4′-acetoxyflavone.

Experimental.

I and II.

β-Phenoxycinnamic Acid, $C_6H_5C(OC_6H_5):CH.COOH$.—In attempting to prepare ethyl-β-phenoxycinnamate by Ruhemann's method,[3] it was found that in adding ethylphenylpropiolate to a "warm" (60–70°) mixture of sodium phenolate and phenol only part of the sodium phenolate dissolved, and an impure product which distilled over a wide range (between

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[1] *Ber.*, 46, 2188 (1913).

[2] *J. Chem. Soc.*, 83, 1154 (1903).

[3] *Ber.*, 24, 2582 (1891).

140 and 215° at 12 mm.), and smelled of ethylphenylpropiolate, was obtained.

It was found, however, that when ethylphenylpropiolate was added to sodium phenolate above 125°, the phenolate dissolved completely and the reaction was accompanied by an evolution of heat.

Further it was found desirable to use xylene in the preparation of the sodium phenolate.

The reaction between ehtylphenylpropiolate[1] and sodium phenolate suspended in xylene and an excess of phenol was carried out at 140–150°. The reaction product was treated according to the directions of Ruhemann.

After the excess of phenol, xylene and ether had been removed, the product gave on distillation at 18 mm., 10 g. of a rather viscous colorless liquid from 203 to 216° and 116.1 g. of a very viscous colorless oil from 216 to 219° (Ruhemann gives the b. p. of ethyl-β-phenoxycinnamate as 204 to 205° at 10 mm.). The latter fraction solidified overnight to a white crystalline mass, m. p. 37–45° (Ruhemann gives the m. p. of ethyl-β-phenoxycinnamate as 73–74°).

The 116.1 g. fraction was saponified with alcoholic sodium hydroxide, but, contrary to the finding of Ruhemann, gave not only β-phenoxycinnamic acid but also another acid. They were separated as follows:

The mixture of acids was dissolved in 250 cc. of boiling alcohol. On cooling, broad prisms came down at first, and later fine needles began to appear. At this point the warm liquid was poured off from the precipitate of prisms.

The decanted solution deposited chiefly the needle crystals, and when cool was filtered. The precipitate was recrystallized 5 times from hot ethyl alcohol and the result was 49 g. of a fluffy precipitate of fine white needles, which softened at 126° and melted at 139–140° with evolution of gas. This product was fairly pure β-phenoxycinnamic acid and was used in the preparation of flavone (*q. v.*). For purposes of comparison with the acid described by Ruhemann, some of the above product was further recrystallized (three times) from hot alcohol with the production of a pure

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[1] The ethylphenylpropiolate used in this reaction was prepared as described by Perkin (*J. Chem. Soc.*, 83, 673 (1903)). It was purified by distillation *in vacuo*.

The phenylpropiolic acid was prepared by a modification of the method of Sudborough and Thompson (*Loc. cit.*), by using ethyl dibromocinnamate instead of dibromocinnamic acid, because, as these investigators have shown, a much greater proportion of α-bromocinnamic acid is formed directly from the ester than from the free acid in the first treatment with alcoholic alkali (*Ibid.*, 77, 985 (1900)). Also the α-bromocinnamic acid, α-allobromocinnamic acid and phenylpropiolic acid were all recrystallized from benzene instead of from chloroform and petroleum ether. The ethyl dibromocinnamate was prepared by the method of Perkin.

Perkin's method for preparing phenylpropiolic acid involves fewer reactions than the method of Sudborough and Thompson, but was found to give a poor yield (33% of the amount calculated from the ethyldibromocinnamate).

substance that softened at 127° and melted at 143–145° (corr.) with decomposition. Ruhemann gives the softening point as 125° and melting point as 143°.

Subs., 0.3213: CO_2, 0.8823; H_2O, 0.1503.
Calc. for $C_{15}H_{12}O_3$: C, 75; H, 5.0. Found: C, 74.9; H, 5.2.

The compound agrees in other properties with the acid described by Ruhemann.

The precipitate of broad prisms (8 g.) was recrystallized 6 times from hot ethyl alcohol, and 1.7 g. of a pure substance softening at 169° and melting at 176–177° (corr.) was obtained. This substance is not mentioned by Ruhemann.

Subs., 0.2110: CO_2, 0.5806; H_2O, 0.0968.
Calc. for $C_{15}H_{12}O_3$: C, 75.0; H, 5.0. Found: C, 75.1; H, 5.1.

This compound gives positive tests for the phenolic hydroxyl group with Liebermann's reagent and with a solution of titanium dioxide in conc. sulfuric acid. It does not give a coloration in water or alcohol solution with ferric chloride.

The compound dissolves in concentrated sulfuric acid, forming a bright yellow solution. It decolorizes a chloroform solution of bromine, is soluble in hot ethyl alcohol, toluene or ligroin (100–110°), and is insoluble in hot water or carbon disulfide.

From its properties it is believed to be either β-*o*-hydroxyphenylcinnamic acid or β-*p*-hydroxyphenylcinnamic acid. Lack of a sufficient quantity of the substance prevented further investigation to decide between the ortho-and para-structures.

Flavone (Benz-2-phenyl-γ-pyrone).—This substance was prepared, with few modifications, by the method of Ruhemann,[1] in which the acid chloride of β-phenoxycinnamic acid is treated with anhydrous aluminum chloride. It was found that the quantities of benzene and aluminum chloride, indicated by Ruhemann, could be cut down without affecting the yield of flavone. 320 g. of benzene and 60 g. of anhydrous aluminum chloride were used for 30.5 g. of β-phenoxycinnamic acid. The crude flavone was recrystallized from ligroin (100–110°). The yield of flavone was 85%.

Nitration of Flavone.—All attempts to limit the action of nitric acid on flavone to the formation of only one nitroflavone failed.

60.5 g. of flavone was dissolved in 60 cc. of glacial acetic acid, and 180 cc. sulfuric acid (1.84) was slowly added. 32 cc. (3 cc. more than the theoretical amount required for the formation of a mononitroflavone) of a glacial acetic acid solution of nitric acid (1.5) containing 0.58 g. of nitric acid per cc. of solution was slowly added, while cooling, to the above flavone mixture. After standing at the ice-box temperature for three days,

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[1] *Loc. cit.*

the solution was poured into ice and water. The faint yellow precipitate that came down was filtered, well washed with water, and dried over sulfuric acid *in vacuo*. The 69 g. of nitroflavone thus obtained was dissolved in 350 cc. of boiling glacial acetic acid, and on cooling, the pale yellow solution deposited 39 g. of a white crystalline product, which when dry, melted from 174 to 205°. Some of this product was prepared for analysis by another crystallization from glacial acetic acid. M. p. 175–206°.

Subs., 0.3112: CO_2, 0.7677; H_2O, 0.0871.
Calc. for $C_{15}H_9O_4N$: C, 67.4; H, 3.3. Found: C, 67.3; H, 3.2.
Subs., 0.2813: 13.6 cc. nitrogen at 23°, 752 mm.
Calc. for $C_{15}H_9O_4N$: N, 5.2. Found: 5.4.

The analysis together with the wide range of melting point indicates that the material was composed of a mixture of mononitroflavones, and its subsequent conversion (*q. v.*) into 3′-aminoflavone and 4′-aminoflavone proved that it consisted of 3′-nitroflavone and 4′-nitroflavone.

This mononitroflavone mixture is very soluble in cold pyridine or aniline, slightly soluble in hot ether or ligroin (b. p. 100–110°), and moderately soluble in the other common organic solvents when hot.

To the hot glacial acetic acid filtrate from the above 3′- and 4′-nitroflavones was added 200 cc. of hot water, and on standing overnight, 19 g. of a white crystalline product came down, which, when dry, melted at 143 to 168°. Some of this product was prepared for analysis by another crystallization from glacial acetic acid, m. p. 148–170°.

Subs., 0.3121: CO_2, 0.7709; H_2O, 0.0976.
Calc. for $C_{15}H_9O_4N$: C, 67.4; H, 3.3. Found: C, 67.4; H, 3.5.
Subs., 0.2464: Nitrogen 11.7 cc. at 25°, 759 mm.
Calc. for $C_{15}H_9O_4N$: N, 5.2. Found: 5.3.

The conversion of this product into 2′-aminoflavone and 3′-aminoflavone (*q. v.*), together with its analysis, proved that it was composed of a mixture of 2′-nitroflavone and 3′-nitroflavone. No 4′-nitroflavone was present in this product as was indirectly proved by the absence of fluorescence in an amyl alcohol or other solution of the amine mixture derived therefrom. The presence of 4′-aminoflavone would have caused an intense blue or green fluorescence.

Solubilities, similar to those of the mixture of 3′- and 4′-nitroflavones, are possessed by this product.

2′-Aminoflavone.—This was obtained by reduction, with stannous chloride, of the mixture of 2′- and 3′-nitroflavones, and subsequent separation of the two amines thus formed by means of the difference in solubility in water of their hydrochlorides.

19 g. of the mixture of 2′- and 3′-nitroflavones was suspended in 250 cc. of boiling alcohol and 134 cc. of stannous chloride solution containing 24 g. of tin and 40 g. of hydrogen chloride (theory requires 24. g of tin

and 14 g. of hydrogen chloride) was added. In two minutes all had dissolved to a clear orange solution. 5 cc. more of the stannous chloride was added and the solution boiled for 10 minutes. On cooling, orange colored microscopic crystals came down. The mixture was left in the ice box overnight and then filtered, and the precipitate dried in the air. The orange powder (34 g.) was added to two liters of hot water and most of it dissolved, leaving a gelatinous white precipitate of tin hydroxides in suspension. The mixture was saturated with hydrogen sulfide, and the tin sulfides were removed by filtration. The yellow filtrate was made alkaline with dil. sodium carbonate, whereupon a yellow precipitate was formed. This was filtered, washed with water and dried over sulfuric acid. Yield, 13 g. This product gave no fluorescence in amyl alcohol or other solution which showed that 4′-aminoflavone was absent.

The 13 g. of yellow substance was then suspended in 150 cc. of 5% hydrochloric acid and the mixture boiled and stirred for 5 minutes, whereupon some of the solid went into solution. 5 cc. of conc. hydrochloric acid was added, the boiling continued for 5 minutes; and as soon as the mixture had cooled to room temperature, it was filtered. The precipitate consisted of the hydrochlorides of 2′-aminoflavone mixed with a little 3′-aminoflavone. The filtrate contained 3′-aminoflavone mixed with a considerable amount of 2′-aminoflavone.

The precipitate was suspended in an excess of dil. sodium carbonate solution, heated on the water bath and stirred for 15 minutes until the hydrochloride was completely converted to the free amine, which was filtered, washed, and dried over sulfuric acid. Yield, 7 g. Two crystallizations from hot acetone gave thin silky pale yellow needles, which melted at 149.5–150.5° (corr.) to a yellow liquid.

Subs., 0.2132: CO_2, 0.5931; H_2O, 0.0901.
Calc. for $C_{15}H_{11}O_2N$: C, 75.9; H, 4.6. Found: C, 75.9; H, 4.7.
Subs., 0.2512: N, 13.1 cc. at 19°, 765 mm.
Calc. for $C_{15}H_{11}O_2N$: N, 5.9. Found: 6.0.

Subsequent conversion of this amine, by decomposition with water of its diazonium salt, into the corresponding phenol which, in turn, was converted into salicylic acid and *o*-hydroxyacetophenone, proved that the amino group occupied the 2′-position in the flavone nucleus.

The substance gives a positive isonitrile test showing it to be a primary amine. It is slightly soluble in hot conc. hydrochloric acid and moderately so in the same hot dil. acid. It is soluble in cold conc. sulfuric acid, forming a colorless solution. From its solution in hot 20% sulfuric acid, on cooling, colorless straight thick bars come down. It dissolves in conc. nitric acid, forming a yellow solution. It reduces a solution of potassium permanganate and dil. sulfuric acid in the cold. In warm dil. sulfuric solution it gives a black amorphous precipitate with potassium dichromate.

The amine is easily soluble in cold aniline, or in hot pyridine, ethyl alcohol, methyl alcohol, acetone, glacial acetic acid, chloroform, benzene, toluene, xylene, ethyl acetate, amyl alcohol, amyl acetate or nitrobenzene. It is moderately soluble in hot ligroin (100–110°), slightly soluble in hot ether, carbon disulfide, or carbon tetrachloride, insoluble in hot water or petroleum ether.

4′-Aminoflavone.—This substance was obtained by reduction with stannous chloride, of the mixture of 3′- and 4′-nitroflavones (above) and subsequent separation of the resulting amines by heating their hydrochlorides with water, which effected the solution of the 3′-aminehydrochloride and the precipitation of the free 4′-amine.

35 g. of the 3′- and 4′-nitroflavones were suspended in 800 cc. of boiling ethyl alcohol and 246 cc. of stannous chloride solution containing 42 g. of tin and 72 g. of hydrogen chloride (theory requires 44 g. of tin and 25 g. of hydrogen chloride) was added. In 5 minutes all had dissolved to a dark orange solution. 10 cc. more of the stannous chloride mixture was added and after boiling further for two minutes a heavy precipitate of orange colored microscopic crystals separated. The mixture was left in the ice box overnight and then filtered. The precipitate was divided (for convenience of manipulation of the large volumes of water used later) into three parts, and each part boiled with 3.5 liters of water for 15 minutes. Most of the precipitate went into solution leaving a mixture of a yellow flocculent solid and a white gelatinous mass which was filtered when cool.

The filtrates were saturated with hydrogen sulfide and the small amount of tin sulfide that came down was filtered off. The filtrates were made alkaline with dil. sodium carbonate and a precipitate of small yellow needles deposited. The combined dry precipitates weighed 12 g. and consisted mainly of 3′-aminoflavone mixed with a small amount of 4′-aminoflavone.

The combined precipitates (the filtrates from which deposited 3′-aminoflavone) were heated with 100 cc. of 10% hydrochloric acid, whereupon the yellow substance dissolved leaving a white mass (stannic oxide) which was removed by filtration. The filtrate was made alkaline with dil. sodium carbonate, and the yellow precipitate that came down was filtered, washed, and dried over sulfuric acid. Yield, 7 g.

The small amount of tin oxide present in this product was removed by treating it with hot pyridine in which the amine dissolved leaving a small amount of a dark residue which was removed by filtration. The pyridine filtrate on cooling deposited the amine, which, after one more crystallization from the same solvent and then another crystallization from boiling xylene, was obtained in the form of extremely long (3 cm.) golden yellow needles, which melted at 234–236° (corr.) to a yellow-brown liquid.

Subs., 0.2152: CO_2, 0.5979; H_2O, 0.0852.
Calc. for $C_{15}H_{11}O_2N$: C, 75.9; H, 4.6. Found: C, 75.8; H, 4.4.
Subs., 0.3501: N, 17.7 cc. at 18°, 761 mm.
Calc. for $C_{15}H_{11}O_2N$: N, 5.9. Found: 6.0.

The position of the amino group of this compound was determined as in the case of 2′-aminoflavone.

The solubilities of this compound are similar to those of the 2′-amine described above, except that it is easily soluble in hot aniline, and is insoluble in hot carbon disulfide.

4′-aminoflavone was found to impart an intense bluish green fluorescence to isoamyl alcohol, glycerol or ethyl alcohol; an intense blue fluorescence to ether, acetone, ethyl acetate, amyl acetate or pyridine; a faint green fluorescence to methyl alcohol or phenol. No fluorescence was observed in solutions of the amine in chloroform, benzene, toluene, xylene, ligroin, carbon tetrachloride or glacial acetic acid.

An inspection of the above solvents, excluding pyridine, shows that those which give rise to the flourescence contain the alcohol hydroxyl group (the ethyl acetate, amyl acetate, ether and acetone used, were of the ordinary "C. P." quality and so all contained impurities of alcohol). Unlike these solvents, ligroin, benzene, toluene, xylene, chloroform, glacial acetic acid or carbon tetrachlroide contain no impurities of an alcoholic nature.

In order to confirm more definitely the relationship between the presence of the alcohol group and the production of fluorescence with 4′-aminoflavone, some of the amine was dissolved in specially prepared pure ether[1] (alcohol and water free), with the surprising result that no trace of fluorescence was apparent. However, when a drop of ethyl alcohol was added to this ether solution an intense blue fluorescence immediately appeared.

Likewise, when a drop of water was added to a solution of the amine in the pure ether, an intense blue fluorescence appeared—this makes it seem that the hydroxyl group of water as well as that from an alcohol will cause the fluorescence.

The failure of solvents like ligroin, benzene, etc., to produce fluorescence with the amine seems anomalous at first, in view of the fact that these solvents contain some water. But the following experiment seems to show that a rather high concentration of hydroxyl radical is necessary to produce the fluorescence. To 5 cc. of hot benzene was added an excess of 4′-aminoflavone. To this hot mixture was added, drop by drop, isoamylalcohol; when a drop of the alcohol came in contact with the surface of the benzene solution, an intense blue fluorescence was formed at that place, but on shaking the mixture the fluorescence disappeared. It was only when 0.5 cc. of the alcohol had been added that the fluorescence be-

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[1] The authors are indebted to Professor J. M. Nelson, from whom this ether was obtained. It was used by Professor Nelson in his work on "Electromotive Force in Non-Aqueous Solvents." (THIS JOURNAL, **39**, 82 (1917).)

came permanent. The failure, then, of solvents like ligroin, benzene, etc., to produce fluorescence with the amine, may be due to their not containing *enough* water.

No fluorescence is observed with the 4′-aminoflavone in water, presumably because the amine is insoluble in this solvent, cold or hot. The amine does not fluoresce in glacial acetic acid, or in glacial acetic acid to which has been added water (not enough to cause the amine to precipitate), most likely because of the action of the acetic acid in neutralizing the amino group, the presence of which in the free condition, only, causes the fluorescence. The presence of fluorescence in a pyridine solution of the amine is doubtless due to the water present in this solvent.

Another peculiar property of this amine is that it dissolves in some solvents with the formation of yellow solutions and in others forming colorless solutions; yellow in ethyl alcohol, methyl alcohol, ethyl acetate or glacial acetic acid; colorless in benzene, toluene, xylene, ligroin (100–110°), chloroform, carbon tetrachloride, isoamyl alcohol or amyl acetate.

Light yellow colors on wool and silk were obtained by impregnating these fibres with a hot solution of the 4′-aminoflavone hydrochloride in the presence of an excess of hydrochloric acid, and then developing the color in dil. sodium carbonate solution.

3′-Aminoflavone.—This substance was obtained pure by recrystallization from pyridine of the yellow product that was precipitated by neutralization of the filtrate from the precipitate of 4′-aminoflavone (above). 12 g. of the crude amine (m. p. 144–149.5°) was recrystallized twice from pyridine and then once from xylene, giving lemon-yellow straight needles. It melted 156–157° (corr.) to a yellow liquid. Yield, 8 g.

Subs., 0.2410: CO_2, 0.7068; H_2O, 0.0997.
Calc. for $C_{15}H_{11}O_2N$: C, 79.9; H, 4.6. Found: C, 80.0; H, 4.6.
Subs., 0.3101: N, 16.8 cc. at 20°, 749 mm.
Calc. for $C_{15}H_{11}O_2N$: N, 5.9. Found: 6.1.

The position of the amino group of this compound was determined as with 2′-aminoflavone.

Its solubilities are similar to those of the 2′-amine except that it is easily soluble in cold acetone.

Light yellow colors were obtained from this amine on wool and silk, by using a similar procedure to that outlined above for 4′-aminoflavone.

2′-Diacetylaminoflavone.—Small shining white oblong prisms (from alcohol), m. p. 186.5–187.5° (corr.). Yield, 0.9 g.

Subs., 0.2411: N, 9.5 cc. at 18°, 756 mm.
Calc. for $C_{19}H_{15}O_4N$: N, 4.4. Found: 4.5.

The compound is readily soluble in hot acetone, chloroform, glacial acetic acid or acetic anhydride; moderately soluble in hot ethyl alcohol or benzene; slightly soluble in hot ether, and insoluble in hot petroleum ether, carbon disulfide, carbon tetrachloride or ligroin (100–110°); and dissolves in conc. sulfuric acid, forming a colorless solution.

3′-Diacetylaminoflavone.—Delicate, small, hair-like, white needles (from acetone), m. p. 231–232° (corr.). Yield, 0.8 g.

Subs., 0.2612: N, 10.3 cc. at 17°, 768 mm.
Calc. for $C_{19}H_{15}O_4N$: N, 4.4. Found: 4.6.

The compound is easily soluble in hot ethyl alcohol or glacial acetic acid; moderately soluble in hot benzene, toluene, or ethyl acetate; and dissolves in cold conc. sulfuric acid, forming a colorless solution.

4′-Diacetylaminoflavone.—Small hair-like white needles (from alcohol). M. p. 246–248° (corr.). Yield, 0.65 g.

Subs., 0.2112: N, 8.4 cc. at 15°, 751 mm.
Calc. for $C_{19}H_{15}O_4N$: N, 4.4. Found: 4.6.

The compound is readily soluble in cold ethyl alcohol or glacial acetic acid; moderately soluble in hot benzene, toluene, xylene or ethyl acetate; and dissolves in cold conc. sulfuric acid, forming a colorless solution.

2′-Hydroxyflavone.—This substance was synthesized by the decomposition, in water solution, of the diazonium salt derived from 2′-aminoflavone, and is the sixth of the 8 possible monohydroxyflavones to be isolated, the other 5 having first[1] been synthesized by Kostanecki.[2]

3.5 g. of 2′-aminoflavone was heated with 20 cc. of conc. hydrochloric acid in 150 cc. of water. To the mixture at 5° was added 8.4 cc. of sodium nitrite solution containing 1 g. of sodium nitrite (calculated amount). After stirring for one-half hour the amine hydrochloride had entirely dissolved. After boiling the solution for 10 minutes (the diazo salt decomposes slowly below the boiling point), nitrogen ceased to be evolved. The solution was then cooled and filtered, and the slightly colored flocculent precipitate washed with water. On stirring in 200 cc. of 1% aqueous sodium hydroxide solution, the precipitate dissolved, leaving a small amount of a brown solid which was removed by filtration. The yellow filtrate on acidification with dil. hydrochloric acid gave a white flocculent precipitate. This was washed with water and recrystallized thrice from alcohol. Shining white plates were obtained, m. p. 249–250° (corr.). Yield, 2.2 g.

Subs., 0.2101: CO_2, 0.5828; H_2O, 0.0816.
Calc. for $C_{15}H_{10}O_3$: C, 75.6; H, 4.2. Found: C, 75.7; H, 4.3.

Subsequent conversion of this hydroxyflavone into salicylic acid and *o*-hydroxyacetophenone (*q. v.*), proved the hydroxyl group to occupy the 2′-position in the flavone nucleus.

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[1] Two of these 5 have been also synthesized in this work (*q. v.*) by a different method than that used by S. v. Kostanecki.

[2] *Ber.*, **31**, 703 (1898); **32**, 331 (1899); **33**, 2516 (1900); **34**, 1692 (1901); **37**, 2820 (1904).

The compound dissolves slowly in cold conc. sulfuric acid forming a greenish yellow solution with a slight green fluorescence. It is soluble in cold dilute or hot conc. aqueous sodium hydroxide. From the latter solution, on cooling, small yellow needles are deposited.

It is moderately soluble in the common organic solvents when hot, and slightly so in hot ether or benzene.

3'-Hydroxyflavone.[1]—This substance was prepared in similar manner to 2'-hydroxyflavone. The crude hydroxyflavone was recrystallized twice from ethyl alcohol. From 4 g. of 3'-aminoflavone was obtained 2.5 g. of shining white narrow plates, m. p. 207–208° (corr.). St. v. Kostanecki gives 208°.

Subs., 0.1762: CO_2, 0.4894; H_2O, 0.0650.
Calc. for $C_{15}H_{10}O_3$: C, 75.6; H, 4.2. Found: C, 75.8; H, 4.1.

Subsequent conversion of this hydroxyflavone (*q. v.*) to *m*-hydroxybenzoic acid and *o*-hydroxyacetophenone, confirmed the position of the hydroxyl group in the flavone nucleus as assigned to it above.

The compound is soluble in cold dil. or hot conc. aqueous sodium hydroxide. From the latter solution, on cooling, yellow needles are deposited.

4'-Hydroxyflavone[1] was prepared in similar manner to 2'- and 3'-hydroxyflavones. The crude hydroxyflavone was recrystallized thrice from a mixture of pyridine and alcohol. Small white needles were obtained, m. p. 269–270° (corr.). St. v. Kostanecki gives 268°. Yield, 2.1 g. from 4 g. of 4'-aminoflavone.

Subs., 0.1523: CO_2, 0.4212; H, 0.0594.
Calc. for $C_{15}H_{10}O_3$: C, 75.6; H, 4.2. Found: C, 75.5; H, 4.4.

The compound dissolves in cold conc. sulfuric acid, forming a yellow solution with a green fluorescence which, on long standing of the solution, changes to a bluish fluorescence.

Subsequent conversion of this hydroxyflavone into *p*-hydroxybenzoic acid and *o*-hydroxyacetophenone (*q. v.*) confirmed the position of the hydroxyl group on the flavone nucleus as assigned to it above.

2'-Acetoxyflavone.—Long thin white needles (from dilute alcohol), m. p. 88.5–89° (corr.). Yield, 0.4 g.

Subs., 0.2131; CO_2, 0.5703; H_2O, 0.0838.
Calc. for $C_{17}H_{12}O_4$: C, 72.9; H, 4.3. Found: C, 73.0; H, 4.4.

The compound is soluble in cold glacial acetic acid, ethyl acetate, benzene or acetic anhydride; slightly soluble in hot ligroin (100–110°).

3'-Acetoxyflavone.—Long colorless needles (from dilute alcohol),

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[1] These hydroxyflavones were first synthesized by St. v. Kostanecki by another method than the one used here (*Ber.*, **31**, 703 (1898); **32**, 331 (1899); **33**, 2516 (1900); **34**, 1692 (1901); **37**, 2820 (1904).

m. p. 97–98° (corr.). St. v. Kostanecki gives 97°. 0.5 g. of the phenol gave 0.3 g. of the acetyl derivative.

Subs., 0.1857: CO_2, 0.4956; H_2O, 0.0747.
Calc. for $C_{17}H_{12}O_4$: C, 72.9; H, 4.3. Found: C, 72.8; H, 4.5.

4′-Acetoxyflavone.—White needles (from dilute alcohol), m. p. 136° (corr.). St. v. Kostanecki gives 137°. 0.5 g. of the phenol gave 0.35 g. of the acetyl derivative.

Subs., 0.1023: CO_2, 0.2738; H_2O, 0.0411.
Calc. for $C_{17}H_{12}O_4$: C, 72.9; H, 4.3. Found: C, 73.0; H, 4.5.

The Conversion of 2′-Hydroxyflavone into Salicylic Acid and *o*-Hydroxyacetophenone.—St. v. Kostanecki found that when a hydroxyflavone is heated with sodium ethoxide, the pyrone ring splits at the double bond and at the ether oxygen with the formation of an *o*-hydroxyacetophenone, and a benzoic acid derivative.[1]

When 2′-hydroxyflavone was treated with sodium ethoxide, it yielded salicylic acid and *o*-hydroxyacetophenone—thus proving that the hydroxyl group occupies the 2′-position in the flavone nucleus.

1.3 g. of 2′-hydroxyflavone was added to 2.3 g. of sodium dissolved in 40 cc. of ethyl alcohol, and the solution was boiled under a reflux condenser for two hours. The mixture was steam distilled to remove the alcohol. It was then acidified with a slight excess of hydrochloric acid and steam distilled again, until no more oil came over (which was the case after 10 minutes). 10 cc. of conc. hydrochloric acid was added to the hot solution (in the distilling flask) which, on cooling, deposited long white needles. After another crystallization from hot water these white needles melted at 156–157° (corr.). Yield, 0.5 g. This compound responded to the tests for salicylic acid with ferric chloride, bromine water, or methyl alcohol and conc. sulfuric acid.

The pale yellow oil present in the distillate (above) was extracted with ether, and freed of traces of salicylic acid by treatment with sodium carbonate solution. The ether after evaporation left a pale yellow oil of a characteristic aromatic odor which gave an intense violet color with ferric chloride. This oil was proven, by conversion to its phenylhydrazone, to be *o*-hydroxyacetophenone.

To a solution of the oil in 5 cc. of glacial acetic acid was added 0.7 g. of phenylhydrazine in 3 cc. of glacial acetic acid. The mixture was warmed for 10 minutes. On the addition of 5 cc. of water, a white precipitate came down. This was filtered and recrystallized once from dil. alcohol. Small, fine, shining white needles were obtained, m. p. 108–108.5° (corr.). Tahara[2] gives 108°.

Subs., 0.2512: N, 27.3 cc. at 17°, 754 mm.
Calc. for $C_{14}H_{14}ON_2$: N, 12.4. Found: 12.5.

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[1] *Ber.*, **31**, 702 (1898).

[2] *Ibid.*, **25**, 1309 (1892).

The Conversion of 3′-Hydroxyflavone into *m*-Hydroxybenzoic Acid and *o*-Hydroxyacetophenone.—This was accomplished with sodium ethoxide and ethyl alcohol (as above). The *m*-hydroxybenzoic acid formed melted at 199–200° (corr.). The *o*-hydroxacetophenone was identified by converting it to its phenylhydrazone, m. p. 108–108.5° (corr.).

The Conversion of 4′-Hydroxyflavone into *o*-Hydroxyacetophenone and *p*-Hydroxybenzoic Acid.—This was accomplished with sodium ethoxide and ethyl alcohol (as above). The *p*-hydroxybenzoic acid formed melted at 208–209° (corr.). The *o*-hydroxyacetophenone was identified by converting it to its phenylhydrazone, m. p. 108–108.5° (corr.).

Flavone (2′)-azo-β-naphthol.—1.5 g. of 2′-aminoflavone were heated for 10 minutes with 3 cc. of conc. hydrochloric acid in 50 cc. of water, in order to convert it to the hydrochloride. To this mixture at 0–5°, was added 3.6 cc. of sodium nitrite solution containing 0.45 g. of sodium nitrite (calculated amount). After stirring for one-half hour, the amine salt had completely dissolved. The resulting diazo salt solution was added to 0.9 g. (calculated amount) of β-naphthol dissolved in 25 cc. of 3 *N* aqueous sodium hydroxide solution, at 0–5°. The flocculent red precipitate which formed was filtered and well washed with water. The moist substance was crystallized once from glacial acetic acid, and tufts of hair-like red-orange needles were obtained which melted, with decomposition, at 265–266.5° (corr.) to a dark red liquid. Yield, 2.0 g.

Subs., 0.3101: N, 19.6 cc. at 18°, 761 mm.
Calc. for $C_{25}H_{16}O_3N_2$: N, 7.1. Found: 7.3.

The compound dissolves in cold conc. sulfuric acid, forming a reddish purple solution. It is insoluble in aqueous sodium hydroxide solution, easily soluble in hot chloroform, moderately so in hot alcohol, benzene or glacial acetic acid, and insoluble in water, cold or hot.

It is assumed to possess the usual orthoquinoneimide configuration (with the nitrogen attached to the naphthalene ring in the α-1-position) which results on coupling a diazonium salt with β-naphthol. The two isomers of this compound, which are described below, are assumed to have similar configurations.

Flavone (3′)-azo-β-naphthol.—1.5 g. of 3′-aminoflavone were carried through a procedure similar to that described in the previous experiment. The flocculent red precipitate resulting was crystallized once from glacial acetic acid. Small, flat, shining crimson prisms were obtained. The compound assumed a metallic lustre at 253° and melted, with decomposition at 257° (corr.) to a dark red liquid. Yield, 2.1 g.

Subs., 0.2781: N, 17.6 cc. at 19°, 755 mm.
Calc. for $C_{25}H_{16}O_3N_2$: N, 7.1. Found: 7.2.

The compound dissolves in cold conc. sulfuric acid, forming a deep wine-red solution. Its other solubilities are similar to those of its 2′-

isomer except that it is only slightly soluble in hot chloroform, alcohol, or benzene.

Flavone (4′)-azo-β-naphthol.—Proceeding as above, 1.5 g. of 4′-aminoflavone gave a dark red flocculent precipitate which was crystallized once from glacial acetic acid. Radiating masses of small dark red needles were obtained which melted, with decomposition, at 274–275° (corr.) to a dark red liquid. Yield, 2.0 g.

Subs., 0.3112: N, 19.4 cc. at 17°, 765 mm.
Calc. for $C_{25}H_{16}O_3N_2$: N, 7.1. Found: 7.2.

The compound dissolves in cold conc. sulfuric acid, forming a deep purple solution. Its other solubilities are similar to those of its 2′-isomer except that it is only slightly soluble in hot alcohol.

Application of the Flavone-azo-β-naphthol Dyes to Silk, Wool and Cotton.—Silk, wool and cotton skeins were dyed by developing the colors directly on the fiber. Good results were obtained with silk and wool, but the cotton, even when previously impregnated with turkey-red oil, in all cases took the dyes unevenly.

Inferior shades were obtained by passing the skeins first through a solution of the diazo salt and then through an alkaline β-naphthol bath. But when the order was reversed and the goods impregnated first with the alkaline β-naphthol solution and then passed through the diazo salt bath in which the hydrogen-ion concentration from the excess of hydrochloric acid had been reduced by the addition of sodium acetate, good dyeings were obtained.

From flavone-(2′)-azo-β-naphthol, a bright orange color was obtained on silk, and a duller shade of orange on wool. Similar colors on silk and wool were obtained with flavone (3′)-azo-β-naphthol. With flavone (4′)-azo-β-naphthol, however, a bright red color was formed on silk and a less bright red shade on wool.

The fastness to light of the dyed materials was determined by exposing them in the north window of the laboratory. After a month's exposure (up to the time of this writing), a comparison with some of the unexposed dyed materials showed that no change in shade had been effected in any case.

The dyed silk and wool samples were found to be very resistant to the action of the alkali, the shades not being affected by hot soap solution or 3% aqueous sodium carbonate. In all cases, however, a 2% acetic acid solution caused a dulling in the shades.

III.

Methyl-β-bromocinnamate, $C_6H_5CHBr.CH_2.COOCH_3$.—This ester, which has not been prepared before, was synthesized for use in a reaction carried out in connection with the synthesis of β-phenoxyhydrocinnamic acid (*q. v.*). It was obtained by the esterification, with dry hydrogen bromide and methyl alcohol, of β-bromohydrocinnamic acid.

50 g. of β-bromohydrocinnamic acid was dissolved in 125 cc. of methyl alcohol, and the resulting solution was saturated with dry hydrogen bromide at room temperature. After standing overnight, the mixture was poured into ice water. The faint yellow oil that separated was extracted with petroleum ether and the ether layer was mixed with anhydrous calcium chloride and calcium carbonate and allowed to stand overnight. After filtering, half of the petroleum ether was evaporated, and the remaining solution, after standing in the ice box for a few hours, deposited large colorless thick prisms, m. p. 37.5–38.5° (corr.). Yield, 33 g.

Subs., 0.3114: AgBr, 0.2399.
Calc. for $C_{10}H_{11}O_2Br$: Br, 32.9. Found: 32.8.

The compound is moderately soluble in cold petroleum ether, ethyl ether, or ligroin (100–110°), and easily soluble in the cold in the other common organic solvents.

β-Phenoxyhydrocinnamic Acid, $C_6H_5CH(OC_6H_5).CH_2.COOH$.—This substance was synthesized by the action of phenol on β-bromohydrocinnamic acid.

Two other products, β-phenylhydrocoumarin and β-*p*-hydroxyphenylhydrocinnamic acid were also formed in this reaction. The latter two compounds have been previously synthesized by the reaction of phenol and allocinnamic acid.[1]

30 g. of β-bromohydrocinnamic acid was added to a solution of 13 g. dry phenol (calculated amount, 12.3 g.) in 50 cc. of dry benzene. The mixture was heated and the acid dissolved. The temperature of the solution was maintained at 85–90° for two hours until the evolution of hydrogen bromide had slackened. A small amount of water had collected below the cherry-red benzene layer. On cooling, the benzene solution deposited a white precipitate. This was filtered, washed twice with cold benzene and dried in the air. The product smelled strongly of phenol. It weighed 12 g. Two crystallizations from benzene gave 10.4 g. of matted, long, white silky needles, m. p. 150–151° (corr.). Yield, 33% of the amount calculated from the β-bromohydrocinnamic acid.

Subs., 0.1424: CO_2, 0.3880; H_2O, 0.0770.
Calc. for $C_{15}H_{14}O_3$: C, 74.4; H, 5.8. Found: C, 74.2; H, 6.0.

The compound is soluble in dil. sodium carbonate solution. It does not contain a double bond, a phenolic hydroxyl group, or bromine.

The empirical formula of the compound, its properties, and its method of formation prove it to be β-phenoxyhydrocinnamic acid.

Precipitates were formed on the addition of a solution of the ammonium salt of β-phenoxyhydrocinnamic acid to solutions of the nitrates of each

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[1] *Ber.*, 24, 2582 (1891).

of the following metals: cadmium, copper (cupric), lead and silver; but not with solutions of sodium, potassium, calcium, barium, bismuth, cobalt or iron (ferric salts).

The isolation of β-p-hydroxyphenylhydrocinnamic acid.—The benzene filtrate from the precipitate of β-phenoxyhydrocinnamic acid (above) was steam distilled. The phenol was isolated from the distillate by separating the benzene from the water layer, extracting the water layer with ether, extracting the benzene-ether solution with aqueous sodium carbonate (to remove some free acid), and evaporating off the ether and benzene. 1.5 g. of phenol, distilling at 185–187°, was thus obtained. This amount is 0.8 g. more than the excess of phenol which was used in the above reaction, thus showing that the reaction had not been complete with regard to the phenol.

The brown viscous oil in the distilling flask was dissolved in ether and extracted with dil. sodium carbonate until no more carbon dioxide was evolved. The water layer was separated and on acidification with dil. hydrochloric acid, a white precipitate came down.

Some of this white precipitate reduced sodium carbonate permanganate solution with the production of an odor of benzaldehyde, which indicated the presence of cinnamic acid (this was doubtless formed by decomposition of part of the β-bromohydrocinnamic acid into cinnamic acid and hydrogen bromide in the above phenol and β-bromohydrocinnamic reaction). The white precipitate however, contained another substance which was separated in pure form from the cinnamic acid by 4 recrystallizations from toluene. 1.4 g. of white needles was obtained, m. p. 151.5–152.5° (corr.). A mixture of the compound with β-phenoxyhydrocinnamic acid, melted at 117–126°, which proved that it was not β-phenoxyhydrocinnamic acid.

Subs., 0.2561: CO_2, 0.6975; H_2O, 0.1373.
Calc. for $C_{15}H_{14}O_3$: C, 74.4; H, 5.8. Found: C, 74.3; H, 6.0.

The compound is soluble in aqueous sodium carbonate. It responds to tests for the phenolic hydroxyl group with sulfuric acid and sodium nitrite, and with titanium dioxide in conc. sulfuric acid. It contains no bromine.

The compound is believed to be identical with β-*p*-hydroxyphenylhydrocinnamic acid, which was previously isolated by Liebermann,[1] and with which it agrees in its empirical formula and properties.

A solution of the ammonium salt of β-*p*-hydroxyphenylhydrocinnamic acid, produced precipitates when added to solutions of the nitrates of each of the following metals: cadmium, cobalt, lead or silver; but not with solutions of sodium, potassium, calcium, barium, bismuth, copper (cupric) or iron (ferric salts).

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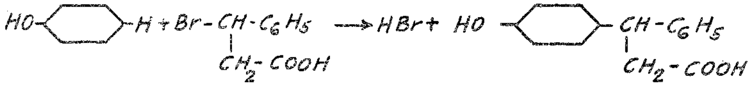
[1] *Ber.*, 24, 2582.

The formation in the above reaction, of β-*p*-hydroxyphenylhydrocinnamic acid, may be regarded as a simple metathesis between phenol and β-bromohydrocinnamic acid, through the para-hydrogen atom of phenol and the bromine atom of the acid (IX).



(IX)

Isolation of β-phenylhydrocoumarin.—The ether layer, from which the β-*p*-hydroxyphenylhydrocinnamic and cinnamic acids were extracted with sodium carbonate (above), was evaporated and a yellow oil remained which, on stirring, solidified to a crystalline mass (12 g.). Two crystallizations from alcohol gave thick, white, shining needles, m. p. 81.5–82° (corr.). Yield, 8.2 g.

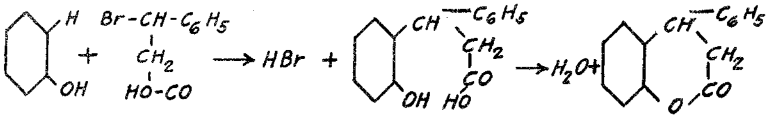
Subs., 0.1550: CO_2, 0.4642; H_2O, 0.0873.
Calc. for $C_{15}H_{12}O_2$: C, 81.6; H, 6.3. Found: C, 81.7; H, 6.3.

The compound is insoluble in cold aqueous sodium carbonate solution, and only partially so in the same boiling solvent. It is insoluble in cold, and easily soluble in hot dil. sodium hydroxide solution. On acidification of the sodium hydroxide solution, a white precipitate comes down. This white precipitate is soluble in cold sodium carbonate solution.

The compound distills at 243° (uncorr.) at 40 mm. pressure. Liebermann gives 237° (uncorr.) at 30 mm. The colorless oil that comes over quickly solidifies in the condenser tube as white needles, m. p. 81–81.5° (corr.).

The compound is believed to be identical with β-phenylhydrocoumarin, which was first isolated by Liebermann,[1] and with which it agrees in its empirical formula and properties.

The formation, in the above reaction, of β-phenylhydrocoumarin may be regarded as proceeding by the initial metathesis between phenol and β-bromonhydrocinnamic acid, through the ortho-hydrogen atom of phenol and the bromine atom of the acid, to form an intermediate compound, β-*o*-hydroxyphenylhydrocinnamic acid, which immediately condenses to form β-phenylhydrocoumarin with elimination of water (X). The observed formation of water in the above reaction is in accord with this explanation.



(X)

In an attempt to obtain a better yield of β-phenoxyhydrocinnamic acid, phenol was heated with methyl β-bromohydrocinnamate; but the

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[1] *Ber.*, 24, 2582 (1891).

greater part of the phenol was recovered unchanged, and most of the methylbromohydrocinnamate was found to have decomposed into methylcinnamate and hydrogen bromide. Only a small amount of β-phenoxyhydrocinnamic acid (isolated by the saponification of its methyl ester which was formed) was obtained.

β-Bromohydrocinnamic acid when treated with potassium phenolate gave only cinnamic acid and styrol.

The Barium Salt of a Disulfonic Acid of β-Phenoxyhydrocinnamic Acid, $[C_6H_3(SO_3)_2.CH(OC_6H_5).CH_2.COO]_2Ba_3.5.5H_2O$.—It was considered probable that β-phenoxyhydrocinnamic acid, by the dehydrating action of conc. sulfuric acid, would be converted into flavanone according to Equation VII on page 86. It was found, however, that a disulfonic acid derivative of β-phenoxyhydrocinnamic acid was formed instead. This disulfonic acid was isolated in the form of its hydrated barium salt.

6.7 g. of β-phenoxyhydrocinnamic acid was added to 60 g. of conc. sulfuric acid, heated to 130–135°, and immediately dissolved with the formation of a pale yellow solution. The mixture was maintained at the above temperature for one minute (no odor of sulfur dioxide was perceptible) and then poured into ice. 120 g. of solid barium carbonate was added (calculated amount for 60 g. of sulfuric acid), the neutral solution filtered, the filtrate evaporated to dryness, and the yellow solid residue extracted with hot alcohol. The alcohol dissolved the yellow impurity, leaving a white crystalline solid.

The alcohol solution was evaporated and a slight amount of a yellow oil was left. This oil was very soluble in water, gave an intense purple color with ferric chloride, reduced potassium permanganate in the cold, and gave a purple color in hot aqueous sodium hydroxide solution. Not enough of the oil was available for further investigation.

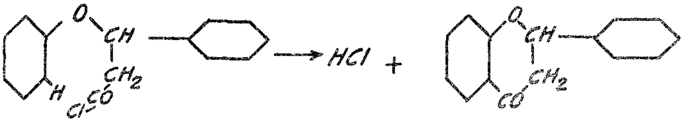
The white barium salt, after the above alcohol treatment, was recrystallized three times from water and ethyl alcohol. A white flocculent precipitate was obtained. Under the microscope this precipitate was seen to consist of thin broad irregular plates. The precipitate was filtered and dried over sulfuric acid. Yield, 4 g.

Subs., 0.4600: H_2O lost at 100–110°, 0.0352; $BaSO_4$, 0.2461.
Calc. for $C_{30}H_{22}O_{18}S_4Ba_3.5.5H_2O$: H_2O, 7.57. Found: 7.65.
Calc. for $C_{30}H_{22}O_{18}S_4Ba_3$: Ba, 34.00. Found: 34.04.

A solution of the barium salt produced precipitates when added to solutions of the nitrates of each of the following metals: bismuth, chromium, (chromic), cobalt, silver, or tin (stannic). No precipitates were formed with solutions of salts of sodium, potassium, calcium, barium, aluminum, cadmium, copper (cupric), iron (ferric), lead, magnesium, manganese, mercury (mercuric) nickel, or zinc.

The same sulfonic acid was formed when β-phenoxyhydrocinnamic acid, dissolved in cold conc. sulfuric acid, was allowed to stand for three days.

An attempt was made to convert the acid chloride of β-phenoxyhydrocinnamic acid into flavanone by treating it with anhydrous aluminum chloride, with the expectation of causing an internal condensation by the elimination of hydrogen chloride, according to the following Equation XI,



(XI)

in analogy to the formation of flavone from β-phenoxycinnamylchloride.[1]

β-Phenoxyhydrocinnamic acid in benzene, was easily converted to its acid chloride by phosphorus pentachloride. The phosphorus oxychloride was removed from the acid chloride by distillation *in vacuo*. The remaining acid chloride in benzene solution gave no reaction, at room temperature, on the addition of anhydrous aluminum chloride; but, on heating, a slow evolution of hydrogen chloride took place and a brown amorphous mass separated from the benzene. The brown mass was insoluble in water and in nearly all of the organic solvents. From hot chloroform it precipitated in an amorphous condition (m. p. 141–196°), and was found to contain aluminum from which it could not be separated.

Finally, attempts were made to effect the condensation of β-phenoxyhydrocinnamic acid to flavanone with other dehydrating agents.

Phosphorous pentoxide gave no reaction in the cold, and a charred mass when the temperature was raised. Fuming stannic chloride or anhydrous zinc chloride and acetic anhydride, even when heated for many hours with the acid, likewise were unsuccessful in bringing about the desired condensation.

2-Nitroflavanone.—This substance was synthesized directly by the action of *p*-nitrophenol on β-bromohydrocinnamic acid.

25 g. of β-bromohydrocinnamic acid and 15.5 g. of *p*-nitrophenol (calculated amount 15.1 g.) were mixed with 30 cc. of dry benzene in a flask with a reflux condenser, and heated at 80–85°. The solids dissolved, and a copious evolution of hydrogen bromide lasted for 15 minutes. The heating was continued for 30 minutes. The solution had become dark green and about one cc. of water had collected below the benzene layer. The benzene and water were removed by distillation *in vacuo*. Weight of the solid residue, 40 g. The crude product was added to 700 cc. water containing 12 g. of sodium hydroxide, and heated on the water bath. The greater part of the solid dissolved to a yellow solution, leaving a small amount of a heavy black oil which solidified in the cold. The black solid was separated by filtration, washed with water, and dried over

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[1] *Ber.*, 46, 2188 (1913).

sulfuric acid. Yield, 1.5 g. Three crystallizations from glacial acetic acid, in the presence of bone-black, gave long, thin, white silky needles, m. p. 144–144.5° (corr.). Yield, 0.57 g., or 2% of the calculated amount from the β-bromohydrocinnamic acid.

Subs., 0.0931: N, 4.48 cc. at 23°, 768 mm.
Calc. for $C_{15}H_{11}O_4N$: N, 5.2. Found: 5.4.

The compound is insoluble in aqueous sodium carbonate or sodium hydroxide solution. It does not reduce cold alkaline potassium permanganate solution, and even on boiling the permanganate solution is reduced slowly. This indicates the absence of a double bond or a phenolic hydroxyl group.

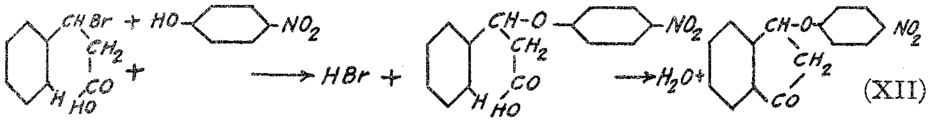
The compound is easily soluble in cold chloroform or conc. sulfuric acid (in which it forms a yellow solution), and in hot ethyl alcohol, and is insoluble in cold or hot water.

From its empirical formula, its properties and the method of its formation, the compound is believed to be 2-nitroflavanone. The course of its formation consists, most likely, of the initial metathesis between *p*-nitrophenol and β-bromohydrocinnamic acid to form an intermediate compound, β-*p*-nitrophenoxyhydrocinnamic acid, which immediately undergoes an internal condensation with the elimination of water. The observed formation of water is in accord with this explanation.

There are two compounds of the same empirical formula as 2-nitroflavanone, whose possible formation from *p*-nitrophenol and β-bromohydrocinnamic acid would also have resulted in the production of water.

(1). β-phenyl-5-nitrohydrocoumarin might have been formed in analogous manner to β-phenylhydrocoumarin from phenol and β-bromohydrocinnamic acid (*q. v.*). But this substance would be soluble in sodium hydroxide solution, which property the compound, actually obtained, does not possess.

(2). β-*p*-nitrophenoxyhydrindone might have been formed by internal condensation, through the hydrogen atom of the unnitrated phenyl nucleus and the carboxyl group, of β-*p*-nitrophenoxyhydrocinnamic acid (assumed as an intermediate product) (XII). The properties (*q. v.*) of the compound actually obtained, do not enable us to decide between the hydrindone or the flavanone structure; and lack of a sufficient quantity of the compound prevented further investigation to conclusively establish its configuration. The following considerations, however, point strongly to the compound being 2-nitroflavanone:



(XII)

β-Phenoxyhydrocinnamic acid, in the presence of dehydrating agents like hydrogen bromide or conc. sulfuric acid did not form either flavanone or hydrindone (*q. v.*). The reason for this is, very probably, that neither of the ortho-hydrogen atoms on the phenyl or phenoxy nuclei is labile enough to react with the carboxyl group to form water. However, in β-*p*-nitrophenoxyhydrocinnamic acid the presence of the nitro group would be expected to render more labile the hydrogen atom lying in the meta-position to it on the same benzene ring, and thus cause the flavanone condensation.

To assume the formation of nitrohydrindone would mean that the presence of the nitro group on the benzene ring of the phenoxy group renders the hydrogen atom of the far removed phenyl group more labile than the hydrogen atom lying with it (the nitro group) on the same benzene ring—which is not plausible.

The sodium hydroxide filtrate from 2-nitroflavanone was acidified with hydrochloric acid and the precipitate was found to consist of unchanged *p*-nitrophenol and cinnamic acid—thus indicating that, concurrent with the formation of 2-nitroflavanone, the greater part of the β-bromohydrocinnamic acid had decomposed into cinnamic acid and hydrogen bromide.

It was considered probable that the decomposition of β-bromohydrocinnamic acid would be minimized if the reaction between it and *p*-nitrophenol were carried out under pressure—with the consequence that more β-bromohydrocinnamic acid would be available for interaction with the *p*-nitrophenol. It was found, however, that no increased yield of 2-nitroflavanone resulted when the reaction was carried out in sealed tubes at temperatures which varied in different experiments from 80 to 125°.

The interaction of β-bromohydrocinnamic acid with the sodium or silver salt of *p*-nitrophenol gave styrol and cinnamic acid, and no β-*p*-nitrophenoxycinnamic acid or 2-nitroflavanone.

When 2,4-dinitrophenol and β-bromohydrocinnamic acid were suspended in xylene and heated at 120–125°, hydrogen bromide was evolved rather freely. Examination of the reaction mixture showed that it consisted of cinnamic acid and unchanged dinitrophenol. No 2,4-dinitroflavanone, as expected, or dinitrophenoxyhydrocinnamic acid was found to have been formed.

Summary.

1. 2′-Aminoflavone, 3′-aminoflavone, and 4′-aminoflavone have been synthesized. They all possess a yellow color, in contrast to the corresponding hydroxyflavones which are white, thus indicating the more powerful auxochromic effect of the amino group in comparison with that of the hydroxyl group on the flavone nucleus. Also, 4′-aminoflavone displays the remarkable property of fluorescing only in neutral solvents which contain the hydroxyl group.

2. A fast red dye, flavone-(4′)-azo-β-naphthol, and two fast orange dyes, flavone-(2′)-azo-β-naphthol, and flavone-(3′)-azo-β-naphthol have been synthesized.

3. 2-Nitroflavanone has been prepared by a rapid method, although in poor yield.

4. Other compounds which have been synthesized for the first time are: 2′-hydroxyflavone, 2′-acetoxyflavone; 2′-diacetylaminoflavone; 3′-diacetylaminoflavone; 4′-diacetylaminoflavone; β-phenoxyhydrocinnamic acid, the barium salt of a disulfo derivative of β-phenoxyhydrocinnamic acid; and methyl-β-bromohydrocinnamate.

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QUANTITATIVE DETERMINATION OF SOLUBLE STARCH IN THE PRESENCE OF STARCH AND ITS HYDROLYTIC CLEAVAGE PRODUCTS.

BY JAMES CRAIG SMALL

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Introduction.

Solutions of alcohol, barium hydroxide, ammoniacal lead acetate and ammonium sulfate have been employed in the fractioning of dextrins and the separation of soluble starch from the dextrins. These reagents precipitate not only soluble starch, but also some of the products of more advanced starch hydrolysis, the action in any case depending upon the concentration of the precipitant in the hydrolysis mixture. In effecting a quantitative precipitation of soluble starch, some of the higher dextrins are precipitated as well. Because of this fact, and because of the difficulty in handling such precipitates as well as their constant tendency to undergo further hydrolysis on manipulation, it has been difficult to obtain a precipitate of soluble starch sufficiently pure to warrant its quantitative determination.

Young[1] first called attention to the separation of soluble starch from the dextrins and lower carbohydrates by means of half-saturated ammonium sulfate. This reaction is slow and not dependable for quantitative results. The precipitate can be washed free from the lower carbohydrates only.

Our ignorance of the number and nature of the products of the hydrolysis of starch, adds to the difficulties encountered in a study of the soluble starch fraction of hydrolysis mixture. Much confusion exists in regard to the mode of progress of the hydrolysis reaction and as to the number and the properties of the products. If starch be regarded as a

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[1] *J. Physiol.*, **22**, 401 (1898).