CHEMISTRY OF THE $\gamma$-PYRONE GROUP

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HISTORICAL.

The study of the Benzo-γ-pyrone or flavone group was originated by Piccard (Ber., 1973, 5, 884; 1874, 7, 888; 1877, 10, 176), who isolated a yellow pigment, Chrysin, from the leaf buds of the poplar (Populus pyramidalis, Salisb., P. nigra, Linn., P. monilifera Ait.), which contained chrysin to the extent of 0.5 percent, crystallising in colourless leaflets, m.p. 275°C. Analysis of chrysin and its derivatives led to the composition, C\(_{15}\)H\(_{10}\)O\(_{4}\), for chrysin, and it was hence considered to be a homologue of alizarin, C\(_{14}\)H\(_{8}\)O\(_{4}\). The suggestion was, however, soon abandoned, as no anthracene derivative was obtained on distilling chrysin with zinc dust in a stream of hydrogen. On digestion with boiling concentrated aqueous caustic potash, it gave phloroglucinol, benzoic acid, acetic acid and in very small quantities acetophenone; and as a result Piccard indicated that chrysin was a derivative of phloroglucinol, in which one hydroxyl was benzoylated, another acetylated and the third eliminated in some way as water. Acetophenone was regarded as a secondary product of degradation.

V. Kostanecki (Ber., 1893, 26, 2901) observed that chrysin on acetylation gave a diacetyl derivative, C\(_{15}\)H\(_{18}\)O\(_{4}\) (C\(_{2}\)H\(_{3}\)O)\(_{2}\), colourless needles, m.p. 185°C, but on methylation with methyl iodide in the usual manner gave a monomethyl ether C\(_{15}\)H\(_{18}\)O\(_{3}\) (C\(_{2}\)H\(_{3}\)O), colourless needles, m.p. 149°C, which with
alcoholic sodium hydroxide gave a bright yellow sodium salt decomposable with water. Chrysain was, therefore, a dihydroxy compound and its properties and degradation products were best explained by a benzo-γ-pyrone structure. The constitution of 3:7-dihydroxy-3-phenylbenzo-γ-pyrone (I) was thus assigned to chrysain; and its degradation into phloroglucinol, benzoic acid, acetic acid and acetophenone took place according to the following scheme:

\[
\text{HO} \quad \text{C} \quad \text{HO} \quad \text{COOH} \\
\text{C} \quad \text{COH} \\
(I)
\]

\[
\text{HO} \quad \text{C} \quad \text{HO} \quad \text{COOH} + \text{PhCOOH} \\
\text{C} \quad \text{COH} \
\]

v. Kostanecki and his co-workers carried out the synthesis of chrysain by the following two methods and confirmed the constitution (I).

(a) By the condensation of phloracetophenone trimethyl ether (II) with ethyl benzoate in presence of metallic sodium, 2:4:6-trimethoxy-benzyolacetophenone (III) was formed; on digestion with hydriodic acid demethylation and ring closure occurred with the formation of chrysain (I)

(Emilewicz, Kostanecki and Tambor, Ber., 1899, 32, 244)
(b) Phloracetophenone dimethyl ether (IV) on condensation with benzaldehyde in presence of caustic potash resulted in 5:7-dimethoxyflavanone (V), which on bromination gave 2:6:8-tribromo-dimethoxy-flavanone (VI). On boiling it with caustic potash 6:8-dibromo 5:7-dimethoxyflavone (VII) was obtained, which, on demethylation with hydriodic acid in the usual way gave chrysin (I) (Kostanecki and Lampe, Ber., 1904, 37, 3167).

\[
\begin{align*}
\text{(V)} & \quad \text{H}_2\text{CO} \quad \text{C}^\text{\scriptsize{CH}_3} \\
\text{(VI)} & \quad \text{H}_2\text{CO} \quad \text{C}^\text{\scriptsize{CH}_3} \\
\text{(VII)} & \quad \text{H}_2\text{CO} \quad \text{C}^\text{\scriptsize{CH}_3} \\
\text{(IX)} & \quad \text{H}_2\text{CO} \quad \text{C}^\text{\scriptsize{CH}_3} \\
\end{align*}
\]

The parent substance 2-phenylbenzo-γ-pyrone or flavone (VIII) has been found to occur free in nature as the meal or farina of the leaves, stalks and seed capsules of varieties of Primula e.g. P. pulverulenta; P. japonica (Muller, J.C.S., 1915, 107, 375). The synthesis of flavone had been accomplished earlier by Feuerstein and Kostanecki (Ber., 1898, 31, 1757). In the synthesis, o-hydroxyacetophenone was condensed with benzaldehyde in presence of alkali to give 2-hydroxyphenyl-styrylketone, the acetyl derivative of which on bromination gave 2-acetoxyphenylstyryl ketone dibromide (IX). The hydrolysis of (IX) with alcoholic caustic potash resulted in the formation of flavone (VIII).
In a similar manner Emilewicz, Kostanecki and Tambor (Ber., 1899, 31, 703) by using monomethyl resacetophenone in place of o-hydroxy acetophenone prepared 7-methoxy flavone, which on dimethylation gave 7-hydroxyflavone (X).

![Chemical Structures](image)

This synthesis of flavone could not be extended because when veratraldehyde or piperonal was substituted for benzaldehyde (Kostanecki and Rosyoki, Ber., 1899, 32, 2257), Emilewicz and Kostanecki, (ibid., 309), the products were not flavones but coumaranones. Recently Hutchins and Wheeler (Current Sci., 1938, 6, 605) have shown that o-hydroxy styryl ketone dibromides in general give flavones when they are heated above the melting point, or treated with alcoholic potassium cyanide.

By the action of caustic alkali flavone (VIII) and hydroxyflavones undergo hydrolysis according to the following scheme:

The first product of the reaction owing to the disruption of the pyrone ring (VIII) is the diketone (XI), which then decomposes in one of two ways according to experimental conditions yielding (a) benzoic acid and o-hydroxy acetophenone or (b) salicylic acid and acetophenone.
The reverse of both of these reactions were carried out by Kostanecki and Tambor (Ber., 1900, 33, 330); when (a) 0-ethoxy acetophenone was condensed with ethyl benzoate and (b) ethyl-o-ethoxybenzoate was condensed with acetophenone, in presence of metallic sodium, both resulted in the formation of o-ethoxy-benzoyl-acetophenone (XII), which on digestion with hydriodic acid gave (VIII)

\[
\text{(a)} \quad \text{ON} \quad \text{COCH}_3 \quad + \quad \text{C}_2\text{H}_5\text{COOH}
\]

\[
\text{(XII)} \quad \text{ON} \quad \text{COCH}_3 \quad + \quad \text{COCH}_3
\]

Although this method has been successfully utilised in synthesising a number of flavones, e.g. apigenin (XIII) (Czajkowski, Kostanecki and Tambor, Ber., 1900, 33, 3410), and scutellarein (XIV) (Bargollini, Gazetta, 1913, 45, 169), yet it suffers from several disadvantages, notably at the hydriodic acid treatment stage, where in certain cases it gives a very poor yield of demethylated flavone or the final product is very difficult to purify.
The synthesis of partially methylated flavones like tricin (XV), wogonin (XVI), diosmetin (XVII), acacetin (XVIII), genkwanin (XIX) and oroxylin (XX) is obviously not possible by this method.

This brief review of the flavone group may be followed by a reference to 3-hydroxyflavones or flavonols, which form an important group in themselves.

Flavonols differ chiefly from flavones in that they dye deeper than flavones, but the shades given by the flavonols are not so fast. Flavonols are decomposed when air is blown through their alkaline solution, while flavones are unaffected by this treatment. Most of the flavonols yield well characterised crystalline compounds with mineral acids, which are readily prepared by adding mineral acids to the boiling solutions of the flavonols in acetic acid (Perkin and Pate, J.C.S., 1895, 87, 647). They also form yellow crystalline compounds with potassium acetate (Perkin, J.C.S., 1899, 75, 438; Perkin and Wilson, J.C.S., 1903, 83, 136).

The first member of the flavonol group to be investigated was fisetin, the colouring matter from the
stem and branches of Rhus cotinus (Linn.) Herzig (Monatsh. 1991, 12, 172) showed that fisetin had the molecular formula \( C_{13}H_{10}O_6 \), contained four hydroxyl groups; on passing air through an alkaline solution, fisetin underwent degradation and yielded resorcinol and protocatechelic acid. Fisetin tetra-ethyl ether on hydrolysis with alcoholic caustic potash gave fisetol diethyl ether which was shown to be identical with diethyl ether of -hydroxy-resacetophenone (XXI). Based on these facts and the close similarity of fisetin to known flavones, Herzig gave it the constitution of a trihydroxy flavonol (XXII). The suggestion was correct and was proved by the synthesis of fisetin by Kostanecki, Lempa and Laskor (Ber., 1904, 37, 784).

A mixture of 2-hydroxy-4-ethoxy acetophenone and veratraldehyde in presence of alkali gave 2-hydroxy-4-ethoxyphenyl-3,4-dimethoxy styryl ketone (XXIII). This on boiling with mineral acids in alcoholic solution underwent isomeric ring closure to give 7-ethoxy-3'4'-dimethoxy flavanone (XXIV).

\[
\begin{align*}
(XIV) & \quad (XVIII) & \quad (XIX) & \quad (XX) \\
& \quad & \quad & \quad \\
\text{The flavanone on treatment with amyl nitrite and hydrochloric acid gave the isonitroso derivative (XXV)}
\end{align*}
\]
which on boiling with glacial acetic acid containing 10 per cent sulphuric acid gave 7-ethoxy-3':4'-dimethoxy flavonol (XXVI).

Demethylation of XXVI with hydriodic acid yielded fisetin (XXII).

On similar lines quercetin (XXVII) (Kostanecki, Lampe and Tambor, Ber., 1904, 37, 1403), galangin (XXVIII) (Kostanecki and Tambor, Ber., 1904, 37, 2803), kaempferol (XXIX) (Kostanecki, Lampe and Tambor, ibid., 2096) and morin (XXX) (Kostanecki, Lampe and Tambor, Ber., 1908, 30, 525) were synthesised without much difficulty.

Although the method appears to be quite simple and straightforward, yet in some cases difficulties arose, e.g. the flavanone (XXXI) did not form the isonitroso derivative and hence myricetin (XXXII) could not be prepared by this method (Dean and Nicrenstein, J. Amer. Chem. Soc., 1935, 47, 1876); and in the case of morin (XXX) and datisacetin (XXXIII) the yields were extremely poor.
Tahara (Ber., 1892, 25, 302) and also Nagai (ibid., 1897) observed that when resacetophenone was refluxed for a long time with sodium acetate and acetic anhydride, it resulted in 2-methyl-3-acetyl-7-hydroxy-chromone. The observation remained unnoticed till 1924 when Robinson and his collaborators, in view of the various difficulties encountered in Kostanecki's method for synthesising flavon and its derivatives, utilised this method for the synthesis of chromones and chromonols (Crabtree and Robinson, J.C.S., 1913, 115, 859; Allen and Robinson, J.C.S., 1924, 125, 2193). Similarly by heating an intimate mixture of 7-methoxy phloracetophenone, benzoic anhydride and sodium benzoate at 185°C for 8 hours and hydrolysing the product with alkali, Kalfi and Robinson (J.C.S., 1925, 127, 161) prepared a monomethyl ether of galangin (XXXII), a colouring matter isolated from galanga root (Testoni, Gazetta, 1900, 30, 11, 327) and to which the constitution shown had been assigned by Perkin and Allison (J.C.S., 1902, 31, 472). Demethylation of the product gave them galangin identical with the specimen obtained from the natural source and with the synthetical product of Kostanecki and Tembor (loc.cit).
On similar lines myricetin (XXXII) and dactiscetin (XXXIII) were also synthesised by using appropriate ketones, acid anhydrides and sodium salts of the acids.

This method, however, presented another difficulty that the final product of reaction was a 3-methyl ether of the flavonol, demethylation of which, of course, removed the alkyl group present on any other hydroxyls, This difficulty was partially overcome by using -benzoyloxy instead of -methoxy-ketones (Heap and Robinson, J.C.S., 1926, 122, 2336), and the synthesis of kaempferide (XXXIV) and resokaempferide (XXXV) were thus accomplished.

Following this method of making flavonols, a number of naturally occurring flavonol derivatives have been synthesised: e.g. myricetin (XXXII) (Kalff and Robinson, J.C.S., 1925, 181) galangin (XXVIII) (Kalff and Robinson, loc. cit., c.f. Charen and Robinson, J.C.S., 1933, 363), fisetin (XXII), quercetin (XXVII) (Allen and Robinson, J.C.S., 1926, 2334), gossypetin (XXXVI), quercetagetin (XXXVII) (Baker, Jaduz and Robinson, J.C.S., 1929, 74), robinetin (XXVIII).
(Charlesworth and Robinson, J.C.S., 1933, 288), morin
(XXX) (Robinson and Venkataraman, J.C.S., 1929, 61),

(isorhamnetin (XXXI) (Heap and Robinson, J.C.S., 1936, 2336), kaempferol (XXIX) (Robinson and Shinoda, J.C.S., 1925, 1973), tangeretin (XL) (Goldsworthy and Robinson, J.C.S., 1937, 738), herbacitin (XLII) (Goldsworthy and Robinson, J.C.S., 1938, 50) and izalpinin (XLII)

The new method of flavonol synthesis by direct
acylation of derivatives of o-hydroxy acetophenone was
further utilised by Allen and Robinson (J.C.S., 1924, 2192) in the synthesis of flavone and its derivatives unsubstituted in the 3-position. Robinson and Venkata-
raman (J.C.S., 1926, 2334), during the course of their
study of conditions under which the best yields of
flavone and its derivatives unsubstituted in the 3'-position
could be obtained by this method, found that more acid
anhydride and longer heating were required than was the case with earlier preparations of flavonol derivatives. Thus by condensing with benzoic anhydride and sodium benzoate and with anisic anhydride and sodium anisate respectively, 7-hydroxyflavone (X) and 7-hydroxy-4'-methoxyflavone (XLVIII) were obtained. Similarly by using phloracetophenone instead of resacetophenone in the above experiments chrysin (I) and acacetin (XVIII) were also obtained by the same authors.

The following are a few more examples in which Robinson's new general method for synthesising flavone and flavonol derivatives has been successfully utilised:


During the study of the possibility of the preparation of various types of substituted \( \gamma \)-pyrones by the Robinson reaction, several chromones have been prepared by this method, e.g. chromones derived from resacetophenone, phloracetophenone, \(-\)methoxy resacetophenone, 2:5-dihydroxy acetophenone, 2:4:5-trihydroxy acetophenone, and \(-\)hydroxyphenyl benzyl ketone of the benzene series (Robinson and Venkataraman, *J.C.S.*, 1926, 129, 2344; Venkataraman, *J.C.S.*, 1929, 2219; Badhwar, Kang and Venkataraman, *J.C.S.*, 1932, 1107; Chadda and Venkataraman, *J.C.S.*, 1933, 1073; and Chadda, Mahal and Venkataraman, *J.C.S.*, 1933, 1459); and others derived from 2-acetyl-1-naphthol, 2-phenyl-propionyl-1-naphthol and 1-phenyl-acetyl-2-naphthol of the
naphthalene series have also been studied by Bhuller and Venkataraman (J.C.S., 1931, 1165), Menon and Venkataraman (J.C.S., 1939, 2591), Cheema and Venkataraman (J.C.S., 1932, 918) and Mahal, Chadd and Venkataraman (J.C.S., 1933, 1459).

The yields of flavones in the Robinson condensation are usually good in the case of co-substituted ketones, the reaction goes quite smoothly and the product requires hardly any purification, but in certain cases the yield is extremely poor, e.g. when o-hydroxyacetophenone was condensed with benzoic anhydride or trimethyl gallic anhydride, very poor yields of the respective flavones were obtained (Chadda and Venkataraman, loc. cit. c.f. Bachwaw and Venkataraman, loc. cit.), and in the case of gallacetophenone and anisic anhydride or varatataric anhydride or trimethyl gallic anhydride (Badhwar, Kang and Venkataraman, loc. cit.) the yields were poorer still.

Secondly, as already mentioned, the preparation of 3-hydroxy flavone derivatives usually involved demethylation with hydriodic acid, and hence the synthesis of partially methylated flavones was not possible by the original method. This difficulty was however overcome (Heap and Robinson, loc. cit.) by using -benzoyl-oxy-acetophenone derivatives instead of -methoxy acetophenone derivatives, but the preparation of the former presented
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its own difficulties. It has been observed by Mahal and Venkataraman that the demethylation of 3-methoxy flavone can be effected by aluminium chloride (c.f. Gulati and Venkataraman, J.C.S., 1936, 267), and this may prove a useful method for the synthesis of partially methylated flavonols. Thus the following scheme should be available for the synthesis of rhamnetin (LIII) and rhamnazin (LIV) (Allison and Perkin, J.C.S., 1902, 469).

\[ \text{HCO} + \text{RCO}_2\text{Na} \rightarrow \text{HCO} + \text{RCO}_2\text{Na} \]

Lastly, the synthesis of flavones by the Robinson reaction sometimes led to 3-acylation; it was first observed by Allan and Robinson (J.C.S., 1924, 2192) that when resacetophenone was benzoylated, it gave 7-hydroxy flavone (X) and also a crystalline product which they believed to be 7-hydroxy-3-benzoylflavone (LV). Later Shullar and Venkataraman (J.C.S., 1931, 1165) also recorded a similar observation when the reaction was carried out on 2-acetyl-1-naphthol with benzoic anhydride or anisic anhydride, the corresponding naphthaflavonones along with 3-acylated derivatives being obtained. The acyl group in the 3-acylated chromones has been shown to be easily removed by boiling them for one hour with 2 N caustic soda solution (Allan and
Robinson, *loc. cit*), but Bhullar and Venkataraman (*loc. cit.*.) could not accomplish it with any of their 3-acylated naphthapyrones; either their substances remained unaffected or with increased concentration of alkali and time of heating, the pyrone ring was broken down.

In view of these difficulties in carrying out the Robinson reaction in a few cases, attempts have been mad from time to time to devise a new method which would preclude 3-acylation and would yield a pure product of unambiguous structure.

Chadde and Venkataraman (*J.C.S.*, 1933, 1073), following the commonly assumed mechanism of the Robinson reaction (see also Wittig, Baagert and Richter, Annalen, 1925, 446, 155), as shown in the following scheme,

\[
\text{HO-CON} + (RCO)_2O \rightarrow \text{HCOCOON} \rightarrow \text{HCOCOON} \rightarrow \text{RCO-O-CO-R} \]

made many unsuccessful attempts to close round the ring by elimination of a molecule of water in acyl derivatives of -naphthol ketones by using a variety of dehydrating agents, such as phosphorus pentoxide, acetic anhydride, phosphorus oxychloride and zinc chloride under varied
experimental conditions. The second stage of the assumed mechanism, the direct dehydration of an o-scyloxy-phenyl methyl ketone, could not be achieved with the reagents mentioned (contrast Simonis, *Z. Anorg. Chem.*, 1926, 30, 1461). However, further attempts in this direction to effect the dehydration were made by Mahal and Venkataraman (Current Sci., 1933, 2, 214) who, instead of acidic or kationic type of dehydrating agents, made use of anionic reagents such as sodamide; while this work on sodamide as a reagent for the present purpose was still in its initial stages, Baker (J. Org. Chem., 1933, 142, 1381) achieved the transformation of o-scyloxy acetophenones to the corresponding dibenzoyl methanes by means of potassium carbonate in toluene by heating at the temperature of the water bath for a few hours; Baker also advanced a theory of the mechanism of the Robinson reaction which, without doubt, is correct and offers a feasible explanation of the formation of 3-acylated flavones (c.f. Schneider and Kuman, *Ber.*, 1921, 54, 2302; also Wittig, Annalen, 1925, 445, 159).
Mahal and Venkataraman (J.C.S., 1934, 1769) were able to prepare \( \alpha \)-naphthaflavones from 1-acyloxy-2-acetonaphthones in ether solution with the help of sodamide at room temperature. This synthesis of flavones at ordinary temperature might be of phytochemical significance. Further work (Vivkar and Wheeler, Current Sci., 1938, 7, 107, ibid., 1938, 7, 280) on the conversion of \( \alpha \)-acyloxy or acyloxyacetophenones into corresponding aryl or acyl \( \alpha \)-hydroxy benzoyl methane has shown, that the conversion can be brought about with sodium in ether or toluene, and even more readily by sodium ethoxide in ethyl alcohol.

Baker (J.C.S., 1939, 1922) with the help of sodamide as the reagent has affected the synthesis of \( 5 \)-hydroxy-8-methoxy flavone primetin monomethyl ether (L) and has thus established the constitution of primetin (XLIX) as \( 5:8 \) dihydroxyflavone. Demethylation of \( 5 \)-hydroxy-8-methoxy flavone causes rearrangement to \( 5:6 \)-dihydroxy flavone.

Selenium dioxide is a specific oxidising agent for the conversion of \( \text{CH}_2\text{-to-CO-} \) (Muller, Ber., 1933, 66, 1688; Evans, Ridges and Simonon, J.C.S., 1934, 137; Chakravarti and Swaminathan, J. Indian Chem. Soc., 1934, 2, 715) but it was observed (Mahal, Rai and Venkataraman, J.C.S., 1935, 383) that when \( 2:3 \)-dihydro-
-naphthaflavone (LI) was heated in xylene solution with selenium dioxide, it gave \( \alpha \)-naphthaflavone and not the \( \alpha \)-naphthaflavonol (LII). Similarly \( \omega \)-hydroxy chalcones were smoothly converted into flavones by means of selenium dioxide. Algar and Flyn (Proc. Royal Irish Acad., 1934, Ser. B. 42, separate issue; also Gysmada, J. Chem. Soc., Japan, 1934, 55, 1256) have shown that flavonols are produced by the oxidation of 2-hydroxy chalcones with alkaline hydrogen peroxide.

Since the conversion of flavanone to the flavone is a process of dehydrogenation of a hydroaromatic to an aromatic system, it has been used in the preparation of naphthalene from tetrahydro-naphthalene (Mabai, Kai and Venkataraman, loc. cit.), the latter being an intermediate stage in the synthesis of naphthalenes by usual succinic anhydride method.

Finally referring to Kostanecki’s first method for the synthesis of flavones involving treatment of \( \alpha \)-acetoxy chalcone dibromides with alcoholic caustic potash (loc. cit.) the method as already stated has
hitherto not been applicable to the synthesis of numerous natural flavones, containing the phloroglucinol nucleus, since the corresponding chalcone dibromides give benzylidene coumaranones only. Hutchins and Wheeler (Current Sc., 1938, 6, 605, J.C.S., 1939, 91) observed that o-hydroxy chalcone dibromides in general give flavones when heated above their melting points or treated with alcoholic potassium cyanide. Chrysin (I), apigenin (XIII) and luteolin (LVI) have thus been synthesized.

\[ \text{(LVI)} \quad \text{(LIX)} \]

**2-Styryl Chromones:** The possible occurrence of 2-styryl chromone derivatives in nature has been indicated by Robinson and Shinoda (J.C.S., 1925, 127, 1973); it was thus suggested that fukugetin, C_{10}H_{14}O_{3} (Perkin and Phipps, J.C.S., 1904, 85, 58), the essential constituent of the Japanese dyestuff fukugi, may be a tetrahydroxy styryl chromone, analogous to luteolin, and pratensol, C_{17}H_{12}O_{5} (Power and Salway, J.C.S., 1910, 97), found in common red clover, may be similar to apigenin. It was regarded as significant.
that pratensol was found among the constituent of Trifolium pratense together with undoubted flavone derivatives such as quercetin and rhamnatin. Fukugetin, however, has been shown by Shinoda (J. Pharm. Soc. Japan, 1936, 535, 736) not to be a styrylchromone. Catalytic reduction with hydrogen in presence of palladium to a dihydro derivative did not take place, while styrylchromones are readily reduced to 2-β-phenyl ethyl chromone (LVII). Fukugetin (Kurkami and Irie, Proc. Imp. Acad., Tokyo, 1934, 10, 563) is now considered to be C24H16O9, heating with 50% caustic potash it gives garcinol (LVIIa) (Shinoda and Ueda, J. Pharm. Soc. Japan, 1933, 53, 921), garcinol contains three phenolic hydroxyl groups, a double bond and a lactone ring.

Styryl compounds are usually more intensely coloured than the corresponding flavones and as mordent dyestuffs, they are characterised by much greater tinctorial power.

As a contribution to the subject, Robinson and Shinoda synthesised several 2-styryl-3-hydroxy-chromones by the action of cinnamic (or substituted cinnamic) anhydride and the appropriate sodium salt on -methoxy-resacetophenone or -methoxy-phloracetophenone; these styryl derivatives were related more to flavonols than to flavones. The synthesis on similar lines of
styrlychromones with no methoxyl or hydroxyl group in the 3-position was found to be inapplicable. The interaction of phloracetophenone, cinnamic anhydride and sodium cinnamate and alkaline hydrolysis of the product gave, on saturation with carbon dioxide, uncrystallisable material from which no pure styrlychromone could be isolated; with resacetophenone and 2-acetyl-1-naphthol also no crystalline material was separated, but the introduction of an \( \omega \)-substituent into the ketone altered the results, the styrlychromones formation proceeding quite smoothly (c.f. also Baker and Robinson, J.C.S., 1925, 127, 1931). Thus, the action of cinnamic anhydride and p-methoxy cinnamic anhydride on respropiophenone readily led to the corresponding styrlychromones.

Although both the synthetic and the naturally occurring flavones are of no practical utility as dyestuffs, yet the discovery of numerous representatives of the flavone group from the roots, stems, barks, fruits, flowers and leaves of various plants clearly indicates their wide occurrence in nature, and has therefore attracted the attention of the organic chemist. As to their origin in plants, it is not known with certainty; they may originate at the point of vegetation, but are more frequently formed
in the older tissues and their occurrence and definite localisation in plants often clearly indicates the relationship of plants in particular families, genera and species (Klein and Wörner, *Z. Physiol. Chem.*, 1925, 143, 9). Their role in the plant cell too is not known with certainty, but they are important in the process of assimilation in that they absorb oxygen and transport it away from the cell (Rouge, *Bull. Soc. Bot. Geneva*, 1921, 13, 16; *Botan. Abstracts*, 12, 366).

On account of the discovery each year of new benzo-γ-pyrone derivatives from natural sources and also due to their occurrence in some medicinal plants, e.g., calycopterin in *Calycopteris floribunda* (Rothangirishwaran, Sahra and Venkataraman, *Biochem. J.*, 1934, 28, 1934; Nadkarni, *Indian Materia Medica*, p.233), gardenin, the first discovered representative of hexahydroxy flavone (Bose and Nath, *J. Indian Chem. Soc.*, 1938, 15, 139), obtainable from dikkamaligum, the resinous exudation of the leaf bud of *Gardenia ambigua*, to which has been assigned the constitution (LVIII) or (LVIIIa), colouring matter of the bark of *Croxyllum indicum*, vent, which has a definite therapeutic action in case of acute rheumatism and has also been found specific in case of ring worm in cattle consists of mixture of three hydroxy flavones (Bose and Bhattacharya, *J. Indian Chem. Soc.*, 1938, 15, 311), baikalein (LIX), 6-methyl baikalein and chrysin,
from the mixture of flavones, baicalin and chrysin have been isolated and identified, but 6-methyl baicalin could not be freed from chrysin, tambulin the active constituent of tambul (*xanthoxylum aphantherum D.C.*), used in indigenous medicines has also been found (Bose and Bose, *J. Indian Chem. Soc.*, 1939, 16, 183) to belong to flavone group, the flavonol glucoside of *Houttuynia cordata Thunb*, the Japanese drug (Nakamura, Octo and Fukwah, *J. Pharm. Soc. Japan*, 1936, 56, 98), nobiletin from *Citrus nobilis, Lour.*, the active constituent of the Chinese drug cheupi (Kwong, Fong. Tseng, *J.C.Si*, 1938, 1003), iso-quercitrin in *Folium urae* and *Folium vaccinium*, the Japanese diuretic drug (Hankuiti, Nakamura, Tato and Genitra Hukuti, *J. Pharm. Soc. Japan*, 1935, 55, 300, Abstracts in English, 1935, 158), further interest has been created in this group of naturally occurring pigments. The systematic study of the pharmacological action of flavones was first made by Koike (*Folia Pharmaceutical Japan*, 1931, 12, No. 1, 39, Breviaria, 6) who observed that myricetin, morin and kaempferol showed diuresis in normal rabbits and the diuretic action was greater with the flavone having a greater number of hydroxyl groups. Mahal (*Proc. Indian Acad. Sc.*, 1937, 5B, 184) tried the effect of 7-hydroxy flavone, genkwanin and 4-methyl-umbelliferon on rabbits isolated gut and uterine, in concentration
1,140,000 of the compounds, stopped the movements of the gut and uterus. 100 mg. of genkwanin clearly produced depression in the blood pressure and contraction in the uterus, similar results were recorded with 7-hydroxy flavone on the blood pressure and respiration of dog. He also found that 4-methylumbelliferon in concentration 1-1,000 has appriciable antiseptic properties.

It will be of great interest to note that the chemical and clinical observations of Rusznýa'k and Georgyi (Nature, 1936, 138, 298) have led them to believe that this great group of vegetable dyes, the flavones and flavonols, play an important role in animal life and that the dyes are of vitamin nature. Thus, vitamin P, (Lajoz and Gerendas, Biochem. Z., 1937, 291, 229), citrin, obtained from lemon juice is shown to belong to this group and its absorption spectra is made up of two flavone glucosides, hesperidin and eriodictyol.
Part I.

2-Styrylchromones.
2-Styrylchromones derivatives unsubstituted in the 3-position, as already mentioned, could not be synthesised by the Robinson condensation. Attention was, therefore, directed to other possible methods for the synthesis of 2-styryl chromones unsubstituted in the 3-position. As might be expected, ethyl cinnamate and sodium did not react with resacetophenone-4-methyl ether or with 2-acetyl-1-naphthol. The condensation of o-hydroxy acetophenone, gallacetophenone-3:4-dimethyl ether and 2-acetyl-1-naphthol respectively with cinnamic aldehyde in presence of alkali, led to the corresponding dicinnamylidene ketones (I), (II) and (III). None of these could be converted to 2-styrylchromones by the usual methods, i.e. treatment with boiling alcoholic sulfuric acid or prolonged contact with alkali, it was

![Chemical structures](image)

was hoped that the action of phosphorus pentachloride would yield 2-styrylchromones from the corresponding chromonones.

Heilbron, Barnes and Marton (J.C.S., 1923, 123, 2559) showed that in 2:3-dimethyl chromone (IV), the
methyl group attached to the 2-carbon atom is situated at the end of a conjugated system CːC⋅CMːC⋅CH₃ and so a tendency for more even distribution of valency forces will exist in the molecule.

\[
\text{C}_2\text{H}_5
\]

(IV)

In (IV a) the activated phase of the molecule is indicated, resulting in induced alternate polarities (Lapworth, J.C.S., 1922, 121, 416; Kermack and Robinson, ibid., 427). The activity of the 2-methyl group was confirmed, since the substance condensed readily in presence of alcoholic sodium ethoxide with aromatic aldehydes to yield 2-styryl derivatives of the type (V). When however, the 7-position was occupied, the condensation did not proceed. While studying the properties of 2-methyl-3-phenyl-1:4- naphthapyrone, and 2 methyl-3-benzyl-1:4- naphthapyrone, it was found that both the substances readily condensed with benzaldehyde, o-methoxybenzaldehyde, anisaldehyde and veratraldehyde, under the conditions described by Heilbron, Barnes and Marton (loc. cit.). A series of 2-styryl-1:4- naphthapyrones were thus prepared.
In 2-methyl-naphthapyrone the 7-position of the chromone is obviously occupied. It seemed, therefore, that the reaction of Heilbron, Barnes and Marton was more generally applicable than they considered.

Although all the 2-methyl chromones mentioned above carry a substituent in the 3-position, yet it is not necessary. It was shown that 2-methyl-1:4- \( \text{naphthapyrone} \) and 7:8-dimethoxy-2-methyl chromone also undergo condensation with aldehydes. The former was condensed with benzaldehyde, o-methoxybenzaldehyde, anisaldehyde and veratraldehyde, leading to the formation of 2-styryl naphthapyrones (VIII), (IX), (X) and (XI);

and the latter with benzaldehyde and anisaldehyde, leading to 7:3, dimethoxy-2-styrylchromone (XII) and 7:3:4'-trimethoxy-2-styrylchromone (XIII). Finally
2-methylchromone was treated with benzaldehyde and yielded 2-styrylchromone (XIV), the parent member of the whole series, with anisaldehyde and veratraldehyde respectively 4'-methoxy-2-styrylchromone (XV) and 3':4'-dimethoxy 2-styrylchromone (XVI) were obtained.

While this work was nearing completion, it was shown by Chakravarti (J. Indian Chem. Soc., 1931, 9, 129; see also Cantor, Curd and Robertson, J. Chem. Soc., 1931, 290, 1255) that the method by which Heilbron, Barnes and Marton (loc. cit.) prepared 7-methoxy-2:3-dimethylchromone really gave the isomeric coumarin and that the authentic 7-methoxy-2:3-dimethylchromone, readily reacted with aldehydes to form corresponding styrylchromones.

The three chromones, 2:3-dimethylchromone, 8-ethoxychromone, 2:3-dimethylchromone and 8-methoxy-2:3-dimethyl
chromones in which Heilbron and his coworkers
(loc.cit.) found the 2-methyl group to be reactive
were all prepared by them by the Simonis method
(Bsr., 1914, 47, 223). In view of the work of
Chakravarti and of Cantor, Curd and Robertson, the
probability that these three substances were
coumarins, becomes apparent; then contrary to the
suggestion of Chakravarti (loc.cit.), 4-methyl
coumarins would appear to react with aldehydes just
as readily as 2-methyl chromones. Dey and Rao
(J. Indian Chem. Soc., 1924, 4, 107) have already shown
the extreme reactivity of coumarin-4-acetic acids
towards aromatic aldehydes. A re-examination of
some of the compounds described by Heilbron and
his coworkers and a study of the reactivity of the
4-methyl group in 4-methyl coumarin were undertaken
in this laboratory by Mahal and Vankataraman (J.C.S.,
1933, 616).

In order to utilise the reaction of Heilbron,
Barnes and Martin for the synthesis of polyhydroxy-
2-styrylchromones the need for avoiding demethylation
was clear at the outset. The action of benzyl chloride
on resacetophenone led to the 4-benzyl ether; and
partial benzylation was of value for the preparation
of chalcones and isoflavones in this laboratory,
involving the use of ketones in which the o-hydroxyl alone is unprotected, the 4-benzyl ether being more accessible than the methyl and easier to dealkylate. From resacetophenone-4-benzyl ether, through the usual stages of Kostanecki's reaction and final debenzylstion with hydrobromic acid, 7-hydroxy-2-styrylchromone (XVII) and 7:4'-dihydroxy-2-styrylchromone (XVIII), were prepared.

Benzylation of phloracetophenone yielded a dibenzyl derivative, which was formulated as (XIX), since it did not undergo smooth chalcone or diketone condensation. The action of benzyl chloride on 5:7-dihydroxy-2-methylchromone under all conditions gave the 7-benzyl ether, which did not react with benzaldehyde, and neither its 5-0-acetyl derivative nor 5:7-diacetoxy-2-methylchromone underwent the styrylchromone condensation. Methylation gave (XX), from which the corresponding 2-styryl chromone could not be prepared. The project was to demethylate the latter with aluminium chloride (c.f. Bhardwaj and Venkataraman, Current Sci., 1933, 2, 50).
Contrary to the observation of Sen and Ghosh (J.C.S., 1920, 117, 61) no phloracetophenone was isolated from the products of the action of acetic acid and zinc chloride on phloroglucinol. The addition of acetic anhydride to the Nencki mixture (Badhwar and Venkataraman, 'Organic Synthesis', 14, 40) did not alter the result.

**EXPERIMENTAL.**

*5:7-Dicinnamolox-2-styrylchromone.*

Chloracetophenone (4.0 g.), cinnamic anhydride (45 g.) and sodium cinnamate (6 g.) were ground together and then heated at 160-185° with stirring for 8 hours. The powdered product was boiled with 50% alcoholic caustic potash (200 c.c.s.) for one hour, the solution poured into dilute aqueous sodium carbonate and the undissolved portion (14 g.), crystallised from glacial acetic acid (200 c.c.s.). The crystals (1.2 g.) were twice crystallised from acetic acid and separated in yellow needles m.p. 235° (Found: C, 77.5%; H, 4.1%. C_{35}H_{24}O_{6} requires carbon, 77.8%; H, 4.4%). The red solution in sulfuric acid exhibited very weak green fluorescence. The substance was boiled for half an hour with alcoholic caustic potash (10%), diluted with water and subsequently saturated with carbon dioxide, an amorphous material separated which defied all attempts on crystallisation.
5:7-Di-p-methoxy cinnamoyloxy-4'-methoxy-2-styryl chromone:-

was similarly prepared from phloracetophenone (5.5 g.), p-methoxy cinnamic anhydride (60 g.) and sodium p-methoxy cinnamate (8 g.). The product was dissolved in alcohol (200 c.c.s.), caustic potash (30 g.) in water (20 c.c.) was added slowly and boiling continued for further 30 minutes, most of the alcohol was removed under diminished pressure and the residue diluted with water. The precipitate crystallised from glacial acetic acid in small yellow needles (1.2 g.) m.p. 240-241\(^\circ\) (sintering at 230\(^\circ\); Found: C, 71.1; H, 4.9. C\(_{38}\)H\(_{30}\)O\(_9\) requires C, 71.2; H, 4.7%).
The solution of the substance in sulfuric acid was red.

7-hydroxy-2-styryl-3-methylchromone:- Nesperopio-phenone (3.7 g.) cinnamic anhydride (19 g.) and potassium cinnamate (8.3 g.) were heated together at 185-190\(^\circ\) for six hours, the powdered yellow mass was refluxed with 10% alcoholic caustic potash (120 c.c.s.), the solution poured into water (2 litres) and the filtered liquid which had a brilliant green fluorescence was saturated with carbon dioxide. The granular
precipitate crystallised from glacial acetic acid in cream coloured, stout, rectangular needles (2.1 g.) m.p. 307°C (Found: C, 77.4; H 5.1. C_{18}H_{14}O_{3} requires C, 77.7; H, 5.0%). The substance dissolves in sulfuric acid with a yellow colour and a bright green fluorescence. The alcoholic solution gives no coloration with ferric chloride, the substance is practically devoid of dyeing properties on wool mordanted with aluminium chromium, iron and tin.

**Acetyl derivative**, very long shining colourless needles from alcohol, m.p. 159°C (after shrinking at 152°C) (Found: C, 74.6; H, 5.1. C_{20}H_{16}O_{4} requires C, 75.0; H, 5.0%).

**7-Hydroxy-4′-methoxy-2-styryl-3-methylchromone.**

The reaction was carried out as in the previous case, resorcinol (2.5 g.), p-methoxy-cinnamic anhydride (15 g.) and sodium p-methoxycinnamate (5 g.) were heated together at 185 - 190°C for six hours. The brownish yellow reaction mixture was hydrolysed with 10% alcoholic caustic potash (30 c.c.), poured into water (2-litres), the filtrate was saturated with carbon dioxide. The granular precipitate was crystallised from alcohol acetic acid mixture in bright yellow needles (1.6 g.), m.p. 271-272°C (Found: C,
74.0; H. 5.4. C_{19}H_{16}O_{4} requires C, 74.0; H, 5.2%). The orange solution in sulfuric acid has a vivid green fluorescence the alcoholic solution is unchanged in colour by the addition of ferric chloride. The substance proved to be a very feeble dyestuff, dyeing pale shades on wool mordanted with aluminium chromium, iron and tin. The deepest shade was obtained in the last case.

**Acetyl derivative.** Very pale yellow silky needles from alcohol, m.p. 181°. (Found: C, 71.7; H, 5.3. C_{21}H_{18}O_{5} requires C, 72.0; H, 5.1%)

**2-styryl-3-methyl-1:4-α-naphthapyrone.** An intimate mixture of 2-propionyl-1-naphthol (3 g.), cinnamic anhydride (12 g.), and sodium cinnamate (5 g.) was heated at 180 - 190°C for six hours, treated with 10% alcoholic caustic potash (50 c.c.s.) and diluted with water. The precipitate was collected, crystallised from alcohol in long pale cream coloured needles (1.9 g.) m.p. 166°. (Found: C, 84.6; H, 5.0. C_{22}H_{18}O_{2} requires C, 84.6; H, 5.1%). The orange yellow solution in sulfuric acid exhibits green fluorescence.

**4'-methoxy-2-styryl-3-methyl-1:4-α-naphthapyrone:**

A mixture of 2-propionyl-1-naphthol (3 g.), p-methoxy-cinnamic anhydrid (13.5 g.) and sodium para-methoxy
cinnamate (4.5 g.) was heated for six hours at 180 - 190\(^\circ\). The reaction product was hydrolysed with 10% alcoholic caustic potash (70 c.c.) and diluted with water (2 litres). The precipitate collected and crystallised from alcohol acetic acid mixture in pale greenish yellow needles (2.3 g.) m.p. 169\(^\circ\). (Found, C, 80.8; H, 5.3 %. \(C_{23}H_{18}C_3\) requires C, 80.7; H, 5.2 %). The substance gives bright orange solution in sulfuric acid with green fluorescence.

2-cinnamylidene acetyl-1-naphthol: - To a solution and suspension of 2-cetyl 1-naphthol (3 g.) in alcohol (10 c.c.), cinnamic aldehyde (2.8 g.) and 10% caustic soda (12.5 c.c.) were added, the mixture was left over night. On pouring into water the precipitate was collected, washed and crystallised from alcohol. The brownish orange prisms (1.3 g.) melted at 134\(^\circ\). (Found: C, 34.1; H, 5.1. \(C_{12}H_{16}C_2\) requires C, 34.0; H, 5.3 %). The substance dissolves in sulfuric acid with an intense red colour, the alcoholic solution gives brownish orange coloration with ferric chloride, the substance has moderately strong dyeing properties, yielding different shades of yellowish brown on wool mordanted with aluminium, chromium, iron and tin.

2-Hydroxy-cinnamylidene acetophenone: - A solution of 2-hydroxy acetophenone
Ber., 1922, 55, 1748) (5.1 g.) in alcohol (30 c.c.) was treated with cinnamic aldehyde (5.0 g.) and 10% caustic soda solution (20 c.c.). After rigorous shaking and letting stand over night, water was added, the precipitate collected, crystallised from acetic acid and then from light petroleum containing a little ethyl acetate. The substance was obtained in small turmeric yellow prisms, m.p. 156 - 157° (1.2 g.) (Found: C, 31.8; H, 5.7. C₁₇H₁₄O₂ requires C, 31.6; H, 5.6%). The bright orange solution in sulfuric acid has no fluorescence. The alcoholic solution gives a dark brown coloration with ferric chloride. Alumimum, iron, chromium and tin mordants, give different shades of yellow, aluminium giving the weakest and iron the strongest.

2-hydroxy-3:4-dimethoxy-cinnamylidene acetophenone:—

The reaction was carried out as in the previous two cases with gallacetophenone dimethyl ether (Perkin and Weizmann, J.C.S., 1906, 82, 1654) (3.7 g.) alcohol (10 c.c.), cinnamic aldehyde (2.5 g.), and 10% caustic soda (10 c.c.). After two crystallisations from a mixture of acetic acid and alcohol the substance was obtained as deep yellow silky needles (1.3 g.), m.p. 141-143°, (Found: C, 73.4; H, 5.8. C₁₉H₁₈O₄ requires C, 73.5; H, 5.8%). The substance dissolves in sulfuric
acid with brilliant orange colour. The alcoholic solution gives with ferric chloride a very dark browned coloration. The dyeing properties were similar to those of the previous substances but the shades are throughout darker.

2-Styryl-3-phenyl-1:4-κ-naphthapyrone: To a solution and suspension of 2-methyl-3-phenyl-1:4-κ-naphthapyrone (Cheema and Venkataraman, J.C.S., 1932, 918) 1.0 g.) in absolute alcohol (75 c.c.), a solution of sodium (0.1 g.) in alcohol was added followed by benzaldehyde (0.5 g.). After shaking vigorously and standing over night the dark brown liquid was refluxed in water bath for 30 minutes and again left over night, he separated yellow solid was collected, washed with old alcohol and recrystallised from alcohol. The very pale cream coloured silky needles (0.5 g.) melted t 262-263°. (Found: C, 36.5; H, 4.9. C_{27}H_{18}C_{2} requires, C, 36.6; H, 4.2 %). The bright yellow solution in sulfuric acid has a green fluorescence. The substance readily decolorised alkaline potassium permanganate. The colourless solution in boiling glacial acetic acid turns bright yellow on addition of few drops of sulfuric acid and develops a green fluorescence. The alcoholic solution of the substance is unaffected by magnesium and hydrochloric acid and by sodium amalgam.
On dissolving the substance (0.5 g.) in carbon disulfide (50 c.c.) and adding a solution of bromine (0.2 g.) in carbon disulfide (5 c.c.) and evaporating off some of the carbon disulfide, after a few hours the dibromide was collected and crystallised from a mixture of alcohol and benzene. The colourless glistening rhombohedral prisms (0.5 g.) m.p. 198°. (Found: Br., 29.7% calculated for C_{27}H_{18}O_{2}Br_{2}, Br, 30.0%).

3-phenyl-2-o-methoxy styryl-1:4-α-naphthapyrone:

3-phenyl-2-methyl-1:4-α-naphthapyrone (1.5 g.) was dissolved in absolute alcohol (50 c.c.) sodium ethoxide from sodium (0.2 g.), and o-methoxy-benzaldehyde (0.6 g.) were added, reaction mixture was allowed to stand for 12 hours heated on water bath for 3 hours, and left over night. The precipitate was collected, crystallised from alcohol in bright yellow needles (0.7 g.) m.p. 231° (Found: C, 83.5; H, 4.9, C_{28}H_{20}O_{3} requires C, 83.1; H, 4.8%). The yellow solution in sulfuric acid has a green fluorescence.

3-Phenyl-2-p-methoxy styryl-1:4-α-naphthapyrone:

Was obtained when anisaldehyde was substituted for o-methoxy benzaldehyde in the above reaction. The substance crystallised from
alcohol in stout-deep yellow needles (0.6 g.)
m.p. 224-225° (Found: C, 82.8; H, 4.9. C_{28}H_{20}O_{3}
requires C, 83.2; H, 4.8%). The yellow solution
in sulfuric acid has a bright green fluorescence; the
crystals are coloured orange red by sulfuric acid.

3-phenyl-2-(3':4'-dimethoxy-styryl)-1:4-α-naph-
thapyrone:- 3-phenyl-2-methyl-1:4-α-naphthapyrone
(1.5 g.) was dissolved in absolute alcohol (75 c.c.), sodium
ethoxide (from sodium 0.2 g.) and veratraldehyde (1.0 g.)
were added, precipitate collected after allowing the
reaction mixture to stand over night. The substance
crystallised from alcohol in deep yellow stout
rectangular needles (1.0 g.) m.p. 215-216° (Found:
C, 79.8, H, 5.1. C_{29}H_{22}O_{4} require C, 80.2; H, 5.0%).
The substance is coloured deep red by sulfuric acid
and on shaking with more acid dissolves with a yellow
colour and a green fluorescence.

2-styryl-3-benzyl-1:4-α-naphthapyrone:- The
condensation was carried out
as in the previous cases with
2-methyl-3-benzyl-1:4-α-naphthapyrone (Cheem and Venkataraman,
loc. cit.) (0.6 g.), sodium (0.05 g.) and benzaldehyde
(0.3 g.). Crystallised from alcohol and acetic acid mixture, the colourless shining needles (0.3 g.), melted at 223° (Found: C, 86.4; H, 5.2. C_{28}H_{20}O_{2} requires C, 86.6; H, 5.1%). The yellow solution in sulfuric acid has a weak green fluorescence, the crystals being initially coloured orange. The dibromide crystallised from a mixture of alcohol and benzene in colourless shining leaflets, m.p. 167°. (Found: Br, 29.3. calculated for C_{28}H_{20}O_{2}Br_{2}, Br, 29.2%).

3-Benzyl-2-\alpha-methoxystyril-1:4-\alpha-naphthapyrone:-

The quantities used were the same as above, \alpha-methoxybenzaldehyde was substituted for benzaldehyde. The product crystallised from alcohol and acetic acid, in felted mass of long, glistening, yellow needles (0.4 g.) m.p. 200° (Found: C, 83.1; H, 5.1. C_{29}H_{22}O_{3} requires C, 83.3; H, 5.3%). The crystals are coloured bright orange by sulfuric acid and dissolve with a yellow colour and weak green fluorescence.

4'-methoxy-2-styril-3-benzyl-1:4-\alpha-naphthapyrone:-

The product was obtained from 2-methyl-3-benzyl naphthapyrone (1.4 g.), sodium (0.1 g.) and anisaldehyde (0.7 g.) crystallised from alcohol and acetic acid mixture in long glistening bright yellow needles (0.3 g.), m.p. 215°.
17°. (Found: C, 83.1; H, 5.5. C_{29}H_{22}O_{3} requires C, 83.3; H, 5.3%). The crystals are coloured intense orange with sulfuric acid and the yellow solution has a green fluorescence.

**3-Benzyl-2-(3'-4'-dimethoxystyril)-1:4-α-naphthapyrone:** Was obtained from 3-benzyl-2-methyl naphthapyrone (0.5 g.), sodium ethoxide from sodium (0.05 g.) and veratraldehyde (0.4 g.). The substance crystallised from alcohol acetic acid mixture in long yellow rectangular needles (0.2 g.) m.p. 215° (Found: C, 80.0; H, 5.3. C_{30}H_{24}O_{4} requires C, 80.4; H, 5.4%). The substance is coloured bright orange by sulfuric acid and the yellow solution in the acid has a weak green fluorescence.

**2:3-Dimethyl-1:4-α-naphthapyrone:** A mixture of 2-propionyl-1-naphthol (13 g.) fused sodium acetate (29 g.) and acetic anhydride (13 g.) was refluxed at 155-160° for 8 hours. The excess of acetic anhydride was removed by distillation. The residue treated with boiling 10% alcoholic caustic potash (400 c.c.) for one hour. The solution was poured into water and the long colour-less needles which separated were recrystallised from ligoroin (8 g.) m.p.
142° (Found: C, 80.2; H, 5.4. C₁₅H₁₂O₂ requires C, 80.4, H, 5.4%). The pale yellow solution in sulfuric acid has a brilliant deep blue fluorescence.

2-Styryl-3-methyl-1:4-α-naphthapyrone:— 2:3-Dimethylnaphthapyrone (1.5 g.) was condensed in the usual manner with benzaldehyde (0.8 g.) and sodium ethoxide from sodium (0.2 g.) in absolute alcohol. The pale yellow product after being washed with cold alcohol crystallised in long, pale cream coloured needles (0.7 g.) m.p. 136°. (Found: C, 84.3; H, 5.2. C₂₂H₁₆O₂ requires C, 84.6; H, 5.1%). The crystals are coloured yellowish orange by sulfuric acid, the solution has a green fluorescence.

2-p-Methoxystyryl-3-methyl-1:4-α-naphthapyrone:— Dimethyl-naphthapyrone (1.5 g.), sodium ethoxide from sodium (0.2 g.) and anisaldehyde (1.0 g.) were mixed together in absolute alcohol. The substance crystallised from alcohol in pale greenish yellow, long woolly needles (0.6 g.) m.p. 139° (Found: C, 80.4; H, 5.4. C₂₃H₁₈O₃ requires C, 80.7; H, 5.2%). The substance becomes deep orange in contact with
sulfuric acid and the orange solution in the acid has a deep green fluorescence.

\[ \text{2-(3':4'-Dimethoxy-styryl)-3-methyl-1:4-\(\alpha\)-naphthapyrone:} \] It was obtained as in the preceding reaction when veratraldehyde (1.2 g.) was substituted for anisaldehyde, the substance crystallised in large greenish yellow, rectangular plates (0.5 g.) m.p. 204° (Found: C, 77.0; H, 5.5. \(\text{C}_{24}\text{H}_{20}\text{O}_{4}\) requires C, 77.4; H, 5.4%). Sulfuric acid imparts an orange red colour to the crystals and the orange yellow solution has a dark green fluorescence.

\[ \text{2-Methyl-1:4-\(\alpha\)-naphthapyrone:} \] It was prepared as described by Wittig, Bangert and Richter, (Ann., 1925, 446, 155) but for the ring closure of 2-acetylacetoo-1-naphthol, it was found preferable to use 10% alcoholic sulfuric acid.

\[ \text{2-Styryl-1:4-\(\alpha\)-naphthapyrone:} \] 2-Methyl-naphthapyrone (1.7 g.) was dissolved in the minimum quantity of absolute alcohol and benzaldehyde (1.0 g.) was added,
followed by sodium ethoxide from sodium (0.2 g.) in absolute alcohol. The mixture was left over night and the crystalline product then twice crystallised from alcohol giving long, pale golden yellow needles (0.7 g.) m.p. 177°. (Found: C, 84.4; H, 4.7. C₂₁H₁₄O₂ requires C, 84.5; H, 4.7%). The bright yellow solution in sulfuric acid has a green fluorescence. The colourless solution in boiling glacial acetic acid assumes a bright yellow colour and a green fluorescence on addition of a drop of sulfuric acid. The colourless alcoholic solution is unaffected by sodium amalgam, but turns pale orange on treatment with magnesium and hydrochloric acid.

2-o-Methoxystyryl-1:4-α-naphthapyrone: It was prepared from 2-methyl-naphthapyrone (1.4 g.) o-methoxy benzaldehyde (0.9 g.) and sodium ethoxide from sodium (0.15 g.). The product was crystallised from alcohol acetic acid mixture, it formed silky yellow needles (0.3 g.) m.p. 169° (Found: C, 80.3; H, 5.0. C₂₇H₁₆O₃ requires C, 80.5; H, 4.9%). The crystals are coloured orange red by sulfuric acid and the orange yellow solution has weak green fluorescence.
2-p-Methoxystyryl-1:4-α-naphthapyrone:— Was obtained from 2-methyl-naphthapyrone (1.0 g.), anisaldehyde (0.7 g.) and sodium ethoxide from sodium (0.1 g.). The pale green solution was poured into water, the precipitate produced was collected and crystallised from alcohol containing few drops of acetic acid in long brilliant golden yellow needles (0.3 g.) m.p. 207°C (Found; C, 80.1; H, 4.8. C_{22}H_{16}C_{3} requires C, 80.5; H, 4.9%). The substance is coloured deep orange red in contact with sulfuric acid, on addition of more acid, the crystals dissolve, giving a bright orange yellow solution with green fluorescence.

2-(3':4'-dimethoxystyryl)-1:4-α-naphthapyrone:— Was prepared from 2-methyl-naphthapyrone (1.4 g.) veronaldehyde (1.1 g.) and sodium ethoxide from sodium (0.2 g.). The crude product was dark green but after two crystallisations from alcohol acetic acid mixture and treatment with norit charcoal, it formed dark yellow irregular plates (0.2 g.) m.p. 211 - 212°C (Found; C, 77.2; H, 5.1. C_{23}H_{18}O_{4} requires C, 77.1; H, 5.0%). The substance is coloured blood red by sulfuric acid and the pale brown solution exhibits dark green fluorescence.
7:8-Dimethoxy-2-methylchromone:— (Compare Blumberg and Kostanecki, Ber., 1903, 36, 2192). To a solution of gallacetophenone dimethyl ether (8.5 g.) in warm ethyl acetate (15 g.), finely divided sodium (4 g.) was added, when the reaction had moderated the mixture was heated on water bath for four hours, left stand over night and was then poured into ice cold dilute acetic acid, the precipitate was collected, treated with boiling 20% alcoholic sulfuric acid (50 c.c.) for 2 hours and poured into water, after concentration to a small bulk and cooling, the chromone crystallised out. It was recrystallised from hot water, it formed colourless needles m.p. 85-86° and 102° after drying at 115° (yield 2.2 g.) (Blumberg and Kostanecki give m.p. 102°).

7:8-Dimethoxy-2-styrylchromone:— 7:8-Dimethoxy-2-methylchromone (1 g.) was dissolved in the minimum quantity of absolute alcohol, benzaldehyde (0.5 g.) and sodium ethoxide from sodium (0.16 g.) was added, the mixture left over night. A yellow crystalline precipitate was collected and recrystallised from alcohol acetic acid mixture, it formed pale yellow wooly
needles (0.4 g.) m.p. 171° (Found: C, 74.1; H, 5.3. C₁₉H₁₆O₄ requires C, 74.0; H, 5.2 %).

7:8:4'-Trimethoxy-2-styrylchromone:— In the above experiment anisaldehyde (0.6 g.) was substituted for benzaldehyde, the collected solid was crystallised from alcohol containing few drops of acetic acid; it formed silky cluster of long greenish yellow needles (0.4 g.) m.p. 178° (Found: C, 71.2; H, 5.4. C₂₀H₁₈O₅ requires C, 71.0, H, 5.3 %).

Sulfuric acid imparts an orange colour to the crystals of these two flavones and gives bright yellow and orange solutions with green fluorescence.

2-Methylchromone (compare Wittig & Others, loc.cit.)

α-Hydroxy acetophenone (20 g.) ethyl acetate (52 g.) and finely divided sodium (14 g.) were mixed. When the reaction had slackened, the mixture was heated on water bath for 4 hours, left over night and poured into ice cold dilute acetic acid; the oily mass was collected, boiled with 20% alcoholic sulfuric acid for two hours and then poured into water. The aqueous solution was extracted with benzene; benzene extract was concentrated by distilling off some of the benzene the concentrate was diluted with petroleum ether.
and cooled. 2-methylchromone (yield 4.6 g.) m.p. 68 -
69° (Wittig and others, 70-71°).

2-Styrylchromone:— The condensation was carried
out with 2-methylchromone
(1.5 g., benzaldehyde (1 g.)
and sodium ethoxide from sodium (0.22 g.). After
12 hours the dark green alcoholic solution was poured
into water, the precipitate was collected, dissolved
in aqueous alcoholic acetic acid mixture, treated
with charcoal and after few hours the liquid was
filtered; on slow evaporation of the filtrate, there
were deposited long yellow needles (0.4 g.) m.p. 131°.
(Found: C, 82.3; H, 4.5. C_{17}H_{12}O_2 requires C, 82.2;
H, 4.8%). The substance is coloured intensely red
by sulfuric acid and the pale brownish yellow solution
exhibits a distinct green fluorescence. The almost
colourless solution in boiling glacial acetic acid
becomes bright orange yellow on addition of drop of
mineral acid. The almost colourless solution in
alcohol turns pale orange on addition of magnesium
and hydrochloric acid; with sodium amalgam, the
colour first becomes pale orange and then rapidly
bright red. When dry hydrogen chloride is passed into
a solution of the substance in chloroform bright orange
red coloration is obtained and deep orange-coloured
crystals of the hydro-chloride are soon deposited;
on exposure to air the colour is rapidly bleached. The substance is insoluble in water, moderately easily soluble in cold ethyl and methyl alcohol and very readily in the boiling solvents; it is readily soluble in ethyl acetate, chloroform, benzene, and glacial acetic acid and moderately readily in light petroleurn.

4'-Methoxy-2-styrylchromone: 2-Methylchromone

\[
\begin{align*}
\text{O} & \quad \text{O} \\
\text{CO} & \quad \text{CO} \\
\text{C}_8 & \quad \text{C}_8 \\
\end{align*}
\]

(1.4 g.) was dissolved in minimum quantity of absolute alcohol, anisaldehyde (1.3 g.) and sodium ethoxide from sodium (0.2 g.) were added. The substance was isolated as in the previous experiment; it formed bright yellow long silky needles (0.5 g.) m.p. 140° (Found: C, 77.6; H, 5.0. \( \text{C}_{18}\text{H}_{14}\text{O}_3 \) requires C, 77.7; H, 5.0 %). The crystals are coloured bright orange red by sulfuric acid and the yellow solution has vivid green fluorescence.

3',4'-Dimethoxy-2-styrylchromone: Was obtained from 2-methylchromone (1.5 g.) veratraldehyde (1.6 g.) and sodium ethoxide from sodium (0.25 g.) The mixture was left over night, the yellow crystalline solid which separated was recrystallised from alcohol, giving pale,
green, long, wooly needles (0.3 g.) m.p. 185° (Found: C, 74.2; H, 5.2. \( \text{C}_{19}\text{H}_{16}\text{O}_4 \) requires C, 74.0; H, 5.2%). The substance is coloured bright orange by sulfuric acid and the yellow solution has scarcely perceptible green fluorescence.

7-Methoxy-2-ethyl chromone:

1. Resacatophenone-4-methyl ether: A mixture of resacatophenone (25 g.), caustic potash (5 g.), methyl alcohol (100 c.) and methyl iodide (20 g.) was heated for six hours on the water bath. Methyl alcohol was distilled off and the residue taken up in ether, the ether extract was shaken up with sodium carbonate and then with caustic soda solution. The sodium hydroxide extract was acidified and the mixture was steam distilled. The oil in the distillate was extracted with benzene, the benzene extract dried over magnesium sulfate, the benzene removed and the residue distilled in vacuo. Resacatophenone-mono-methyl ether (4.2 g.), boils at 270-280°/4 mm.

Improved yields were obtained by the following metho (Adams, J. Amer. Chem. Soc., 1919, 41, 280).

2. Resacatophenone (100 g.) was dissolved in just enough of a cold solution of 1.5% sodium hydroxide and dimethyl-sulfate (23 g.) was added, it was heated to about 90° and a small amount
of alkali was added. The heating was repeated. The mixture was acidified with hydrochloric acid, extracted with benzene, the benzene extract dried over anhydrous magnesium sulfate and the benzene removed. The residual oil was distilled in vacuo. Rosacetophenone monomethyl ether (27 g.) came over at 270-280°/4 mm. and solidified on cooling to a mass of transparent crystals m.p. 80°.

2-Methoxy-2-methyl chromone: - Rosacetophenone monomethyl ether (27 g.), dry ethyl acetate (27 g.) and finely divided sodium (7 g.) were heated on water bath for four hours and left over night. The mixture was poured into ice cold dilute acetic acid, the solid filtered and boiled with 20% alcoholic sulfuric acid for one hour. On pouring the solution into water the product was collected and crystallised from alcohol (5 g.) m.p. 113°.

7-Methoxy-2-styrylchromone: - A solution of 7-methoxy-2-methyl chromone (1 g.) in the minimum amount of absolute alcohol, added sodium ethoxide from (0.8 g., sodium and benzaldehyde (0.4 g.) was added. The mixture was kept over night. The crystalline material which had separated was crystallised from alcohol. The practically colourless prisms (0.6 g.)
melted at 180-190°C. (Found: C, 77.7; H, 5.2. C₁₈H₁₄O₃ requires C, 77.7; H, 5.2 %). The crystals are coloured orange with concentrated sulfuric acid and the pale orange solution has a pale green fluorescence. The yellow solution in boiling acetic acid does not change colour on the addition of drop of sulfuric acid. The colourless solution in alcohol turns bright yellow on the addition of magnesium powder and hydrochloric acid while it is unaffected by sodium amalgam. When dry hydrogen chloride is passed through the solution of the substance in chloroform, the solution is coloured bright yellow.

7,4'-Dimethoxy-2-styrylchromone: 7,4'-Dimethoxy-2-
\[\begin{array}{c}
    \text{H}_2\text{C} \\
    \text{OCH}_3 \\
    \text{C}_6\text{H}_5 \\
    \text{OCH}_3 \\
\end{array}\]
methylchromone (1.6 g.), anisaldehyde (0.4 g.) and sodium ethoxide from sodium (0.8 g.) in absolute alcohol were left over night. The solid separated was filtered and crystallised from alcohol. The small yellow needles, m.p. 144°C. (Found: C, 78.9; H, 5.5. C₁₉H₁₈O₄ requires C, 74.0; H, 5.2 %); were coloured orange with concentrated sulfuric acid and the yellow solution has a green fluorescence.

Acetophenone-4-benzyl ether: Acetophenone
\[\begin{array}{c}
    \text{C}_6\text{H}_5\text{COCH}_3 \\
\end{array}\]
(1.0 g.) was mixed with anhydrous potassium carbonate (1.8 g.), benzyl chloride (3.3 g.) and acetone (10 g.,
the mixture was refluxed for 8 hours. It was poured into water and the product crystallised from alcohol. The aminating colourless leaflets melted at 109°.  
(Found: C, 74.3; H, 5.6. C₁₅H₁₄O₃ requires C, 74.4; H, 5.9%). The alcoholic solution is coloured deep brown by ferric chloride.

The experiment was repeated with resacetophenone (20 g.), benzyl chloride (33 g.), potassium carbonate (36 g.) and acetone (200 c.c.). The product after pouring into water and crystallisation from alcohol gave resacetophenone monobenzyl ether, (9 g.).

7-benzyl oxy-4-methylchromone: - resacetophenone-4 benzyl ether (9 g.) was dissolved in dry ethyl acetate (15 g.) and the whole mass was added to finely divided sodium (3.5 g.). The mixture was heated on water bath for 4 hours and left over night. On pouring into excess of dilute ice cold acetic acid, the solid was collected and treated with boiling 30% alcoholic sulfuric acid for one hour. The solution was poured into water and the solid separated, which was filtered and crystallised from alcohol. The colourless almost needle-like (3.5 g.) melted at 137° (Found: C, 76.3; H, 5.3. C₁₇H₁₄O₃ requires C, 76.3; H, 5.2%).
7-Benzylxy-2-styrylchromone:—7-Benzylxy-2-methylchromone (4.0 g.) was dissolved in the minimum amount of absolute alcohol. Sodium ethoxide from sodium (0.4 g.) and benzaldehyde (1.6 g.) were added, and the mixture was kept over night. The solid which separated after 24 hours, was crystallised from a mixture of alcohol and acetic acid. The pale yellow flat prisms (2.0 g.) melted at 161° (Found: C, 80.9; H, 5.1. C_{24}H_{18}O_5 requires C, 81.6; H, 5.1%). The crystals are coloured orange with concentrated salicylic acid and the pale yellow solution had a green fluorescence.

7-Hydroxy-2-styrylchromone:—7-Benzylxy-2-styrylchromone was not de-benzylated when a solution of the substance in glacial acetic acid was treated with concentrated hydrochloric acid, even prolonged boiling left the benzyl ether unaffected. The de-benzylisation was finally brought about by boiling the substance (0.05 g.) in glacial acetic acid (4 c.c. with hydrobromic acid saturated at 0°) (2 c.c.) for one hour. Hot water 15 c.c. was added and on cooling a solid separated which melted at 310° - 315°.
The debenzylation was repeated with (1.4 g.) of the substance and it gave 7-hydroxy-2-styrylchromone (0.5 g.). Crystallization from alcohol gave glistening pale yellow needles m.p. 241-242°C. (Found: C, 77.3; H, 4.2. C_{17}H_{12}O_{3} requires C, 77.4; H, 4.7%). The crystals are coloured orange with concentrated sulfuric acid and the pale yellow solution exhibits a bluish green fluorescence. The pale yellow solution in boiling acetic acid does not change colour on the addition of a drop of concentrated sulfuric acid. The colourless solution in alcohol turns bright yellow on the addition of magnesium powder and hydrochloric acid, while it is unaffected by sodium amalgam. When dry hydrogen chloride is passed through the solution of the substance in chloroform, the solution is coloured bright yellow. The alcoholic solution is turned brown by ferric chloride.

7-p-Methoxy-1-p-benzyl-2-styrylchromone:— 7-methoxy.

7-p-Methoxy-1-p-benzyl-2-styrylchromone (6.0 g.) was dissolved in minimum quantity of absolute alcohol, sodium ethoxide from sodium (0.5 g.) and p-methoxy benzaldehyde (Mossbauer, Ber., 1911, 43, 1030) (4.6 g.) were
mixed together and allowed to stand over night. The yellow coloured solid was filtered off and crystallised from mixture of alcohol and acetic acid. The pale yellow prisms, (3.7 g.) melted at 175°, (Found: C, 80.7; H, 3.2. C₂₁H₂₄O₄ requires C, 80.2, H, 3.2 %).

\[ \text{7:4'-Dihydroxy-3'-styrilchromene = 7:4'-libersyloxy-3'-styrilchromene} \]

(5 g.) was dissolved in acetic acid (40 c.c.) and hydrochloric acid saturated at 0° (30 c.c.) was added. The mixture was boiled for one hour, after which hot water (100 c.c.) was added. The solid which separated was crystallised from acetic acid: alcohol mixture in long yellow silky needles (5.4 g.), melted at 332°. (Found: C, 73.3; H, 4.1. C₁₇H₁₂O₄ requires C, 72.8, H, 4.8 %). The substance is coloured orange by concentrated sulfuric acid and the yellow solution was bright green fluorescence. The alcoholic solution does not give any colouration with ferric chloride.

The dicycanyl derivative crystallised from alcohol in colourless needles m.p. 183° (Found: C, 69.2; H, 4.4. C₂₁H₁₆O₂ requires C, 69.2; H, 4.4 %).

\[ \text{Chloracetylenone:} \]

Chlorogluconol (31 g.) was dried and dissolved
in dry ether (100 c.c.), anhydrous zinc chloride (1.5 g.) and acetonitrile (9 g.) were added. The mixture was well cooled in ice and salt and dry hydrogen chloride was passed in for 8 hours. The mixture was allowed to stand for three days; the pale red solid was filtered, washed with dry ether (21 c.c.), dissolved in hot water 150 c.c.s. and heated on water bath for one hour.

The ketone was precipitated on cooling, the product was filtered and crystallised from water and a small amount of alcohol. The nearly colourless needles (21 g.) melted at 215°. (The substance (1.20 g.) when heated at 120° for three hours, the loss in weight was, -0.1140 i.e. 9.5 %, C₅H₈C₄.
H₂O requires water 9.6 %. Found in the dried material: C, 57.3; H, 4.6. C₅H₈C₄ requires C, 57.1; H, 4.7 %).

The product obtained by the action of acetic acid and zinc chloride on phloroglucinol under various conditions including those described by Sen and Ghosh (J.C.S., 1920, 117, 61) crystallised from very dilute alcohol in yellow needles, melting and decomposing above 290°. (Found: C, 63.8; H, 4.2. C₁₆H₁₂O₆ requires C, 64.0; H, 4.0 %).

According to Sen and Ghosh, 5:7:2:4':6'-penta hydroxyl-2-phenyl-4-methylene benzpyran separates
from hydrochloric acid yellow needles with one molecule of water of crystallisation. The author was unable to prepare crystalline acetyl derivative. The product obtained by alkaline hydrolysis and subsequent acidification had the physical properties described by Sen and Ganguly; but it did not yield a dinitrophenyl hydrazone.

The acetyl derivative was prepared by Chatterjee's method, by dissolving phloracetophenone (2.2 g.) in 10% sodium hydroxide solution (40 c.c.) and adding acetic anhydride (15 c.c.) and aniline. The salts crystallised from alcohol in colourless elongated prisms m.p. 103° (compare Jenn em. Quire, Ber., 1881, 26, 1691). Found: C, 57.0; H, 4.2. C_{14}H_{14}N requires, C, 57.1; H, 4.8%.

Phloracetophenone-2:4-Dinitrophenyl hydrazone:—

The dinitrophenyl hydrazone (Bredt, Ber., 1931, 758) (1 g.) was dissolved in concentrated sulfuric acid (3 c.c.) and cooled. 15 c.c. water was added. Phenacetophenone (1/20 g.; 1 c.c.) was added in alcoholic solution to the freshly prepared reagent. The dinitrophenyl hydrazone crystallized out as crystals. It was collected and washed with cold alcohol and
crystallised from alcohol in bright red needles
m.p. 280° (decomposition) (Found: N, 15.3. C_{14}H_{12}O_{7}N_{4}
requires N, 16.1%).

C-benzyl-chloracetophenone-4-benzyl ether:

\[
\begin{align*}
\text{Phloracetophenone (2 g.)} & \\
\text{Benzyl chloride (9.5 g.)} & \\
\text{Potassium carbonate (5 g.)} & \\
\text{Acetone (50 c.c.)} & 
\end{align*}
\]

were refluxed on water bath for 8 hours. The mixture
was then poured into water. The oily product was
dissolved in ether, washed the ether extract with
10% hydrochloric acid solution and then with water, removed
ether and crystallised the product from alcohol.

Chloroform solution (0.8 g.) m.p. 141° (Found: C, 78.4; H, 5.8. C_{16}H_{14}N_{4} requires C, 78.6; H, 5.7%).
Chloroform solution of the substance gave deep red
colour with ferric chloride.

5,7-Dihydroxy-3-acetyl-2-methyl chromone:

\[
\begin{align*}
\text{Heated together on sand} & \\
\text{bath phloracetophenone} & \\
\text{(10 g.)}, \text{anhydrous sodium acetate (10 g.) and acetic} & \\
\text{anhydride (80 g.) for 8 hours. The reaction mixture} & \\
\text{was poured into water (8000 c.c.), the solid was} & \\
\text{collected, washed with water and crystallised from} & \\
\text{alcohol. After two crystallisations from alcohol} & \\
\text{a substance (A) was obtained in colourless needles} & \\
\text{(5.1 g.) m.p. 131°. (Found: C, 60.4; H, 4.7. C_{16}H_{14}O_{7}} & \\
\text{requires C, 60.3; H, 4.4%).}
\end{align*}
\]
The mother liquor was cooled after the separation of substance (A), it deposited a substance (1.1 g.) melting indefinitely above 110°, dilution with half the volume of water, gave a second impure product (3.5 g.) melting above 120° over a long range. After the removal of this substance, mother liquor was diluted with large quantity of water, kept for 12 hours, the solid was collected, crystallized from dilute alcohol in colourless needles (B) (0.5 g.), melting point of the substance was 252°.

The substance (B) was identified as 5:7-dihydroxy-3-acetyl-2-methyl chromone (F. um.: C, 61.4; H, 4.3. C_{12}H_{10}C_{5} requires C, 61.5; H, 4.3 %).

5:7-dihydroxy-3-acetyl-2-methyl chromone was acetylated by refluxing with acetic anhydride and a few drops of pyridine, the mixture was poured into water, the solid collected, and crystallized from aqueous alcohol in colourless needles. Melting point of the diacetyl derivative and the mixed melting point with substance (A) was 131°.

When substance (A) (3 g.) was boiled with concentrated hydrochloric acid and water (1:1) (40 c.c.) for 45 minutes and the product poured into water,
a precipitate was obtained, which after two crystallizations from aqueous alcohol, formed colourless needles (i.e., g.), melting point and mixed melting point with substance (8) was 252°.

5:7-Dihydroxy-2-methylchromone: 5:7-Dihydroxy-3-acetyl-2-methylchromone (5.5 g.) was added with 10 percent sodium carbonate solution (50 c.c.s.). The solution after two hours became quite clear, on cooling it was acidified with hydrochloric acid, the solid was collected and crystallized from alcohol in colourless needles m.p. 143°. m.p. 179° (J. chem. and pharma. soc., 1924, 32, 509) gave 252°. It was identified as 5:7-dihydroxy-2-methyl chromone (Found: C, 52.4; H, 4.4; C₁₅₂O₆ requires C, 52.5; H, 4.4.).

The acetylated derivative crystallizes from alcohol in colourless needles m.p. 148° (J. chem. and pharma. soc., 1924, 32, 509) gives m.p. 149°. (Found: C, 50.3; H, 4.4; C₁₅₂O₆ requires C, 50.3; H, 4.3.)

The preceding experimental results differ from those recorded by G.Netzer, Cord and Robertson (J.C.S., 1931, 1858; see also Minoda, J. pharm. soc. Japan, 1928, 49, 33).
5-Hydroxy-7-benzylxoy-2-methylchromone:

5:7-Dihydroxy-2-methylchromone (5 g.) benzyl chloride (12 g.), potassium carbonate (15 g.) and acetone 100 c.c.s. were refluxed together on water bath for 3 hours. The reaction mixture was poured into water, excess of benzyl chloride was removed by steam distillation. The solid crystallised out from alcohol in cream coloured needles (3.1 g.) m.p. 148°C. Found: C, 71.6; H, 5.3. \( \text{C}_{17}\text{H}_{14}\text{O}_4 \) requires C, 72.8; H, 4.9%. The solution of the substance in alcohol gave dirty brown colouration with ferric chloride.

5-Benzylxoy-7-benzylxoy-2-methylchromone:

Dimethyl sulphate (60 c.c.s.) and 20% of caustic soda solution (60 c.c.s.) were added alternately in small portions to a stirred solution of 5-hydroxy-7-benzylxoy-2-methyl chromone (4 g.) in acetone (100 c.c.), Dilution of the pale orange liquid gave a precipitate which on crystallisation from alcohol gave colourless needles (2.7 g. m.p. 153°C. Found: C, 72.8; H, 5.3. \( \text{C}_{18}\text{H}_{16}\text{O}_4 \) requires C, 72.9; H, 5.4%). The alcoholic solution of the substance develops no colouration with ferric chloride.
Interaction of 5-methoxy-7-benzylxy-2-methyl chromone (2 g.) and p-benzylxy-benzaldehyde (1.4 g.) and sodium ethoxide from sodium (0.2), gave a deep yellow solid which crystallized in stout bright yellow prisms from alcohol acetic acid mixture, m.p. 181°.

(Found: C, 82.9; H, 6.2. C₃₂H₂₆O₅ requires C, 78.4; H, 5.3 %).
Part II.

Synthesis of the Dye of Cascara Wood
(Scyfisatin) 3:7:3':4':5'-pentahydroxy flavone.
von Schmid and Rodros (Ber., 1932, 65, 1689) and Brass and Krantz (Ann. Chem., 1932, 492, 175) assigned the formula 3:7:3':4':5'-pentahydroxyflavone to the colouring matter of acacia wood.

![Chemical Structure Image]

(1)

This pentahydroxyflavone was synthesised by Suchower, Kang and Venkataraman (J.C.S., 1932, 141, 1107) by the condensation of \( \text{C}_6 \)-methoxyresacetophenone with trimethygallic anhydride and sodium trimethylgallate, and the treatment of the resulting 7-hydroxy-3:3':4':5'-tetramethoxyflavone with hydriodic acid gave the pentahydroxyflavone (1), m.p. 310-312\(^0\), Brass and Krantz pentahydroxyflavone melted at 310-312\(^0\), which according to them on repeated purification at 325-330\(^0\). The colour reactions of the synthetic flavone were found to be similar to those of the natural one as described by Brass and Krantz (loc. cit.), although there was a slight difference in the ferric chloride reaction due to differences in the concentration of the reagents.

A sample of the synthetic pentahydroxyflavone, its pentacetate and pentamethyl ether were sent to Prof. Brass, who on determination of melting points a mixed melting point
confirmed their identities.

Since the pentacetate of the natural compound according to Brass and Kranz melted at 224°, and according to Schmid and Tadros (loc. cit.) at 216°, and the pentacetate of Budhwar, Kang and Venkataraman (loc. cit.) melted at 175-176°, the latter work was repeated.

(I) was repeatedly crystallised; it decomposed and melted at 310-312°, but as it darkened above 300°, it was difficult to observe the exact melting point.

The pentacetate melted at 223-224° and after crystallisation from methanol at 225° (c.f. Brass and Kranz, loc. cit.); but on crystallisation from acetic acid, it shrunk at 195° and melted at 202-203°, and the substance obtained from mother liquor melted at 145-179°, and this on further recrystallisation from benzene gave a product m.p. 177-178° (c.f. Budhwar, Kang and Venkataraman loc. cit.). It is therefore concluded that the pentacetate exists in two dimorphic forms, although it has not yet been possible to precisely define the conditions of the respective conversion. Probably (I) also exists in two dimorphic forms of m.p. 310-312° and m.p. 325-330°; however, it has not been possible in this laboratory to isolate the latter. Such kind of dimorphism is not unknown in the case of...
flavone derivatives; e.g. lactoflavin trimethyl ether, quercetagetin hexamethyl ether, scutellarain 5:4'-dimethyl ether; and very recently it has been noticed in the case of 5:7:8-trihydroxyflavone (Shah, Mehta and Wheeler, *Current Sci.*, 1938, 6, 503).

The synthetic pentahydroxyflavone shows all the characteristic colour reactions described by Brass and Kranz, *(loc. cit.)*, and the same reactions are also given by myricetin (Perkin, *J.C.S.*, 1899, 75, 826) and gossypetin (Baker, Nodzu and Robinson, *J.C.S.*, 1926, 135, 30). The colour changes which the pentahydroxy compound undergoes with amonia or dilute alkali must therefore be due to the presence of hydroxyl groups in the 3:3':4':5'-positions and not merely in the 5':4':5'-positions (c.f. Anderson and Perkin, *J.C.S.*, 1931, 132, 2625).

**Experimental.**

3:7:3':4':5'-Pentahydroxyflavone:

![Chemical Structure](Image)

**Trimethylgallic acid:** (Organic syntheses, 6, 96). The process was modified slightly, being carried out in a current of coal gas and the mixture being mechanically stirred.

7-Hydroxy-3:3':4':5'-tetramethoxyflavone: (c.f. Budhwar, Kang and Venkataraman, *J.C.S.*, 1932, 141, 1107)
It was prepared by heating together an intimate mixture of \(-\text{methoxyresacetophenone}\) (Slater and Stephen, J.C.S., 1920, 117, 309) (6 g.), trimethylgallic anhydride (70 g.) and potassium trimethyl gallate (12 g.) on oil bath at 180-185\(^\circ\) for 6 hours. The reaction product was cooled, powdered, dissolved in alcohol (150 c.c.), refluxed on the water bath for 30 minutes during which a solution of caustic potash (17.5 g.) in 20 c.c. of water was gradually added; boiling was continued further for 1/2 hour, after which most of the alcohol was removed by distillation under reduced pressure, the residue diluted with water, filtered and the filtrate saturated with carbon dioxide. The precipitate collected, washed with water, dried in the oven, (4.8 g.). On crystallisation from alcohol it melted at 246\(^\circ\) (Budhwar and others 248\(^\circ\)).

Acetyl derivative: The crude product was acetylated, crystallised from methyl alcohol in long colourless wooly needles m.p. 144-145\(^\circ\) (Budhwar and others 146\(^\circ\)).

3;7;3';4';5'-Penta hydroxyflavone (Dye of Acacia wood): (c.f. Budhwar, Kang and Venkataraman, loc.cit.)

\[ \text{7-Acetoxy-3;3';4';5'} \text{-tetramethoxyflavone} \ (3\ g.) \]
which was purified by repeated crystallisations, from methanol was boiled with acetic anhydride (40 c.c.) and hydriodic acid (1.7; 40 c.c.) for two hours. The reaction mixture was allowed to cool and the dark orange coloured hydriodic acid which separated was collected on a cintered glass funnel and after suspension in boiling glacial acetic acid (40 c.c.) boiling water (40 c.c.s.) was added, whole refluxed for 5 minutes, treated with charcoal and filtered while hot. On cooling, it formed bright yellow needles (0.6 g.), m.p. 310-312°, whereas it darkened at 295-300°. Repeated crystallisation from dilute acetic acid did not raise the melting point any further.

The melting point 310-312° might not be the exact melting point as the substance darkened and it was not possible to judge the melting point accurately (compare Bock and Kranz; the substance melts at 310-315° and after number of crystallisations at 325-330°.)

The mother liquor from the hydriodic acid of the pentahydroxy flavone was poured into ice cold solution of sodium bisulfite, the yellow solid was
collected (0.2 g.) m.p. 310-312° after darkening at 293-302°. The substance was recrystallised from dilute acetic acid, but there was no change in the melting point. The solution of the substance with ferric chloride gives dirty deep brown colour.

3:7;3':4';5'-Pentacetoxyflavone: 3:7;3':4';5'-Pentahydroxyflavone (0.6 g.) was refluxed with acetic anhydride (10 c.c.s.) and pyridin (few drops) for two hours, the reaction mixture was poured into water, and the solid collected (0.95 g.) m.p. 223-224°. It crystallised from methyl alcohol in colourless needle; m.p. 225° (compare Brass and Kranz 224°; Schmid and Tadros 216°; Budhwar, Kang and Venkataraman 175-176°).

The penta acetate was crystallised from various solvents to find out, if it was possible to obtain the substance melting at 175-176°.

The substance after crystallisation from methyl alcohol, was recrystallised from acetic acid (50 %), m.p. 203-207° after shrinking at 195°. The mother liquor was poured into water and the solid collected m.p. 145-178° and this on further recrystallisation
from benzene gave a substance m.p. 177-178º, which was identical with the acetate of Budhwar, Kang and Venkataraman.

Substance m.p. 225º and m.p. 177-178º might be dimorphic, but the exact conditions to transform one into the other have not yet been thoroughly investigated.

Decacylation of the 3;7;3';4';5'-pentacetoxylflavone. Pentacetoxylflavone (0.2 g.) was refluxed with 50% acetic anhydride (10 c.c.) for one hour. It crystallised from alcohol in yellow needles (0.03 m.p. 150-153º after darkening at 305º, recrystallisation of the alcohol did not improve the melting point.

3;7;3';4';5'-pentamethoxylflavone. 3;7;3':4';5'-pentamethoxylflavone, m.p. 150º, 0.2 g. was admixed with sodium acetate (2 g.) and placed gently in water (10 c.c.) of 10% acetic acid. The mixture was then stirred vigorously, 3;7;3':4';5'-tetramethoxylflavone (0.5 g.) in acetone (10 c.c.) was added as a 10% solution, and the reaction was carried in course of 30 minutes and stirring continued for further thirty minutes, then refluxed on water bath for 15 minutes. The reaction mixture was then poured into water, precipitate collected, and crystallised from methyl alcohol.
in shining colourless needles, m.p. 148° (c.f. Brass and Kranz 148°).

The author is grateful to Professor Brass who compared the melting points and mixed melting points of the pentahydroxy flavone. Its pentacetate and pentamethyl ether with the corresponding oxyfiscetin and its derivatives and thus confirmed the identities of the compounds.
Part III.
The Synthesis of 'Tricin'
The Colouring Matter of 'Khapli' Wheat (Triticum Dicoccum).
Perkin and Anderson (J.C.S., 1931, 2624), who in the course of their investigation on the nature of rust in wheat examined the organic constituents of the resistant variety Khapli in the hope that amongst them a substance toxic to the fungus might be found, paid special attention to compounds possessing phenolic character; a flavone-like colouring matter was isolated in small quantity and given the name 'Tricin'.

They showed that it was a dimethyl ether of a penta-hydroxy flavone, tricitin (I), alkaline fusion of which led to phloroglucinol, and an acid resembling gallic acid. They reported that (I) did not have the obvious structure of 5:7:3':4':5'-penta-hydroxy flavone, as the synthesis of the latter disclosed differences in the properties of (I) and (II).

(II) was first synthesised by Bargellini and Monti (Gazzetta, 1915, 45, 65) and was described as decomposing above 270° and yielding an acetyl
derivative, m.p. 215-218°. Budhwar, Kang and Venkataraman (J.C.S., 1932, 141, 1107) prepared (II) by the Robinson reaction; they found that their product was similar to Bargellini and Monti's in its colour reactions, but they did not prepare the pentacetate (III).

Anderson (Canad. J. Res., 1932, 7, 285), repeated the synthesis of Budhwar and others (loc. cit.) and demonstrated the identities of (I) and (II) and also observed the m.p. of (III), 241-242°.

In view of the discrepancy between the melting points of the acetyl derivatives of Bargellini and Monti (215-218°) and Anderson (241-242°), the author undertook the re-examination of (I) and its derivatives and has confirmed Anderson's observations. The flavone itself, after repeated crystallisation, darkened and decomposed gradually above 310° as stated by Budhwar, Kang and Venkataraman (loc. cit.) (c.f. Anderson, loc. cit.)

If tricetin has the structure (II), it was thought that tricin (IV) must be 3':5'-dimethyl ether of (II). The wide occurrence of the syringic nucleus among anthocyanins and the probability of its recognition among natural flavone pigments have
been indicated earlier by Karrer and Widmer (Helv. Chem. Acta, 1927, 10, 5) and by Heap and Robinson, (J.C.S., 1929, 135, 63).

3'-5'-Dimethoxy-4':5:7-trihydroxyflavone (IV) has been synthesised by the method of Heap and Robinson (loc. cit.) for syringetin. Interaction of phloracetophenone with o-benzyl syringic anhydride and sodium o-benzyl syringate, followed by vigorous alkaline hydrolysis led to 5:7-dihydroxy-3':5'-dimethoxy-4'-benzyloxyflavone (V). Debenzylation of (V) with hydrochloric acid in acetic acid yielded

![Image](image)

The mixed melting point of (IV) with the natural specimen of tricin, supplied through the kindness of Dr. J.A. Anderson of the National Research Council of Canada, and examination of the colour reactions have confirmed the validity of the suggestion about the constitution of tricin.

**Experimental.**

5:7-Dihydroxy-3':4':5'-trimethoxyflavone:— (compare Budhwar, Kang and Venkataraman, J.C.S., 1932, 1107).
Phloracetophenone (4 g.), trimethylgallic anhydride (40 g.) and potassium trimethylgallate (8 g.) were mixed intimately and heated for six hours on oil bath at 180 - 185°. The mixture was ground finally, taken up in alcohol (80 c.c.), refluxed and to it was added caustic potash (10 g. in water 10 c.c.), continued refluxing for further half an hour, poured into water (1 litre), filtered and saturated the filtrate with carbondioxide, a brown precipitate was collected and crystallised from 50 % acetic acid containing few drops of sulfuric acid yield (2.5 g.) m.p. 264-265°.

5:7:3':4':5'-Pentahydroxyflavone: - 5:7-Dihydroxy-
110° 3':4':5'-trimethoxyflavone
(2 g.) was boiled with acetic anhydride (30 c.c.) and hydriodic acid (d, 1.7; 30 c.c.) for two hours; on cooling, hydriodicide separated out, which was collected, suspended in boiling acetic acid (30 c.c.) and hot water equal volume, refluxed for 10 minutes, treated with charcoal and filtered hot. The pentahydroxyflavone separated out from the filtrate in brownish yellow needles, yield (0.8 g.), m.p. 310° (d). The alcoholic solution of the substance gives greenish brown colour with ferric chloride.
5:7:3':4':5'-Pentacetoxylavone: - Pentahydroxy-
flavone (0.5 g.) was treated on sand bath with acetic
anhydride (5 c.c.) and pyridine few drops for two
hours. The reaction mixture was poured into water,
solid collected and crystallised twice from alcohol.
It gave colourless needles (0.3 g.), m.p. 241-242°,
a portion appeared to remain semi solid and complete
clarification took place at 246-248° (Found (micro
analysis by Dr. Schoeller): C, 59.2.; H, 4.1 C_{25}H_{20}O_{12}
requires C, 58.6.; H, 3.9 %).

The above melting point of the pentacetate
confirms Anderson's observation (compare Anderson,
whereas Bargellini and Monti (Gazzetta, 1915, 45, 84)
found the melting point of the 5:7:3':4':5'-pentacetoxylavone as 216-218°.

5:7-Dihydroxy-3':5'-dimethoxy-4'-benzyloxyflavone:

O-Benzylsyringic acid.

was prepared from
syringic acid (c.f.

5:7-Dihydroxy-3':5'-dimethoxy-4'-benzyloxyflavone:

A mixture of phloracetophenone (5 g.), O-benzylsyringic
anhydride (Heap and Robinson, J.C.S., 1929, 67)(35 g.)
and sodium C-benzylsyringate (6 g.) was heated at 180-185° for seven hours. The finely ground product was refluxed with 10% alcoholic caustic potash (140 c.c.) for 45 minutes and poured into water (1-litre), and the deep orange turbid solution saturated with carbon dioxide. A dark brown oil separated together with an orange solid, both were collected and boiled with 2.5% aqueous potassium hydroxide (100 c.c.) for 15 minutes, the liquid was filtered and again saturated with carbon dioxide; the deep orange powder that separated was crystallised from acetic acid and then from aqueous acetone forming pale orange stout, prismatic needles (0.4 g.) m.p. 234°. (Found (Micro): C, 68.6; H, 4.9. C_{24}H_{20}O_{7} requires C, 68.6; H, 4.8%). The substance dissolves in sulfuric acid with pale yellow colour and no fluorescence and in aqueous sodium hydroxide with a pale yellow colour. An alcoholic solution gives greenish brown colouration with ferric chloride.

**5:7:4'-Trihydroxy-3':5'-dimethoxyflavone:**

![5:7:4'-Trihydroxy-3':5'-dimethoxyflavone](image)

5:7-Dihydroxy-3':5'-dimethoxy-4'-benzylloxyflavone (0.2 g.) in acetic acid (15 c.c.), was heated on water bath, concentrated hydrochloric acid (1 c.c.)
was added drop by drop. The red mixture turned to a clear yellow solution. More acid (1 c.c.) was added and heating continued for 1/2 hour. The reaction mixture was diluted with water, a pale yellow precipitate was collected, crystallised twice from 70% alcohol. It formed pale old gold yellow needles which sintered at 278° and melted at 283-287° (tricin has a melting point 288°). Mixed melting point with natural tricin was 286-288°.

(Found (micro): C, 61.5; H, 4.2. C₁₇H₁₄O₇ requires, C, 61.3; H, 4.2 %).

The pale yellow solution of the substance in sulfuric acid exhibits no fluorescence. The solution of the substance in dilute alkali gives a yellow colour, the alcoholic solution of the substance, gives red brown colour with ferric chloride. Yellow precipitate is obtained on adding lead acetate solution to the solution of the substance in alcohol. Addition of a drop of concentrated sulfuric acid to the boiling solution of the substance in glacial acetic acid gives bright orange needles (compare, Anderson and Perkin, J. E. S., 1931, 2824).

**Triavetyl derivative:**- It crystallised from alcohol in colourless silky needles, m.p. 249-251°
(triacetyltricin 251-254°). (Found (micro); C, 60.5; H, 4.6. C\textsubscript{23}H\textsubscript{26}O\textsubscript{10} requires, C, 60.5; H, 4.5%).

Deacetylation with hot 50% hydrochloric acid and crystallisation of the product from alcohol gave pale yellow ¼ cm. long needles of tricin, m.p. 286-287°.

The author is greatly indebted to Dr. J.A. Anderson, of the National Research Council of Canada for the natural specimen of tricin.
Part IV.

Demethylation with Aluminium Chloride
and

a New Method of Oximation of Flavones.
The Friedel and Crafts reaction between phloroglucinol trimethyl ether and acetyl chloride at low temperature in the absence of a solvent leads to phloracetophenone trimethyl ether, when this is heated with aluminium chloride, the dimethyl ether is formed (Kostanecki and Tambor, Ber., 1899, 32, 2260). The same reaction in benzene or chlorobenzene solution leads, however, to phloracetophenone monomethyl ether (I) having the properties of one of the two compounds obtained by Sonn and Bülow (Ber., 1925, 58, 1691) by a Soeschen reaction between phloroglucinol monomethyl ether and acetonitrile; the constitution of (I) has now been confirmed by preparing its monobenzyl ether (II), since a hydroxyl in

\[
\begin{align*}
(I) & \quad \quad \quad \quad (II) \\
& \quad \quad \quad \quad (III)
\end{align*}
\]

the o-position to the ketonic group cannot be benzylated under the usual conditions (Gulati, Seth and Venkataraman, J.C.S., 1934, 1765); The monobenzyl ether condenses smoothly with aldehydes to form chalcones (see also Shinoda and Sato, J.Pharm.Soc. Japan, 1928, 48, 220).
Since the 5-hydroxyl in a flavone resembles the o-hydroxyl of an aromatic ketone in its resistance to facile methylation, it appears probable that the ease with which an o-methoxy ketone is demethylated would find a parallel in 5-methoxy flavone. This is proved to be the case, the action of aluminium chloride on chrysin dimethyl ether (III) in nitrobenzene solution, causing partial demethylation to techtochrysins (IV). Heating (III) with solid aluminium chloride leads to a mixture of (IV) and chrysin (V), but (III) is the only product of the action of aluminium chloride on 2:4:6-trimethoxy-benzoyl acetophenone (VI) in nitrobenzene and subsequent treatment with sulfuric acid. By the regulated action of hydriodic acid on (VI), (IV) or (V) or a mixture of both is obtained, but apparently (III) cannot be obtained (compare also Kizura and Hosi, J. Pharm. Soc. Japan, 1937, 57, 163).

The observation that the 5-methoxyl in a flavone
can be preferentially demethylated with aluminium chloride has been helpful in elucidating the constitution and effecting the synthesis of several natural flavones, e.g. genkwanin (Mahal and Venkataraman, J.C.S., 1936, 569); wogonin (Shah, Mehta and Wheeler, J.C.S., 1933, 1555); primetin (Nakazawa, J.Pharm.Soc. Japan, 1939, 59, 524). Baker (J.C.S., 1939, 1922) demethylated 5:8-dimethoxyflavone to 5-hydroxy-8-methoxyflavone (primetin monomethyl ether) and thus established the constitution of primetin as 5:8-dihydroxyflavone.

Since Tasaki (Act.Phytocim., 1923, 2, 118) gives 115-117° as the melting point of (III), whereas the author found it to be 143°, the author has confirmed the constitution of the compound by its synthesis from 2-benzoyloxy-4:8-dimethoxy acetophenone and sodamide (c.f. Mahal and Venkataraman, J.C.S., 1934, 1767; Shalla, Mahal and Venkataraman, J.C.S., 1935, 363). Although the action of benzoic anhydride on phloracetophenone leads ordinarily to chrysin (Robinson and Venkataraman, J.C.S., 1923, 2344), methylation of the product in one experiment gave in addition to (III) its 3-benzoyl derivative (VII).
Treatment of the former with aluminium chloride gave (IV). The possibility of 3-acylation during the Robinson reaction has already been indicated by Allan and Robinson (J.C.S., 1924, 2192), Bhullar and Venkataraman (J.C.S., 1931, 1165), Anderson (Canadian J.Res., 1932, 7, 285), and by Chadda and Venkataraman (J.C.S., 1933, 1074).

\[
\begin{align*}
\text{(VII)} & \\
\text{(VIII)} & \\
\text{(IX)} & \\
\text{(X)} & \\
\text{(XI)} & \\
\text{(XII)} &
\end{align*}
\]

Another by-product of the condensation of phloracetophenone and benzoic anhydride has been formulated as (VIII) (c.f. Baker, J.C.S., 1933, 1381).

The benzylolation of chrysin under various conditions gave only 5-hydroxy-7-benzyloxy-6-benzylflavone (IX) with the usual properties of a 5-hydroxy-flavone.

Oximation of flavones:—Haq, Hay and Malkana (J.C.S., 1934, 1328) showed that anthraquinone and buphazarin dimethyl ether readily gave oximes in pyridine solution. Cook, Hewett and Lawrence (J.C.S., 1936, 79) prepared the oximes of cis and trans
hexahydroanthrone by following an identical method, but made no reference to the work of Haq, Ray and Malkana (loc. cit.). They, however, admitted the usefulness of the method of oximation in difficult cases. This method is particularly suitable for the preparation of those oximes which are formed with great difficulty.

\[ (X) \quad (XI) \]

It has now been found that the method is applicable to flavone derivatives. Oximes of flavone and 1:4-α-naphthoflavone have thus been prepared.

**Experimental.**

**Phloroglucinol trimethyl ether:** Phloroglucinol \( (15 \text{ g.}) \) was boiled for five hours with methyl alcohol \( (88 \text{ g.}) \) and sulfuric acid \( (15 \text{ g.}) \), to it water \( (75 \text{ c.c.}) \) was added, removed most of the methyl alcohol by distillation, ether extracted, distilled off ether and treated the residue with 40% caustic soda \( (75 \text{ g.}) \) and added dimethylsulfate \( (45 \text{ g.}) \) drop by drop to the stirred mixture, steam distilled the reaction.
product, extracted the distillate with ether, dried
the ether extract, removed ether and crystallised
the residue from light petroleum (40-60°), cooled
in ice, trimethyl ether (8.5 g.) m.p. 52°.

2:4:6-Trimethoxyacetophenone:— In place of
\[ \text{FeCl}_3 \text{CCH}_3 \text{OCCH}_3 \]
\[ \text{COCCH}_3 \]
ferric chloride Kostanecki
and Tamber (Ber., 1899
32, 2260) anhydrous aluminium chloride was used.
Phloroglucinoltrimethyl ether (25 g.) was taken
in a flask fitted with calcium chloride tube,
added acetyl chloride (26 g.), cooled the flask
in mixture of ice and salt, when the temperature
had fallen to -5 to -10 C, added aluminium chloride
(13 g.) in course of 3 hours, let stand the
mixture for further three hours, added crushed
ice, crystalline solid separated, which crystal-
llised from dilute alcohol in colourless needles
(19 g.) m.p. 110°.

2:4-Dihydroxy-6-methoxyacetophenone:— Mixture
\[ \text{HO} \text{CCH}_3 \text{OCCH}_3 \]
\[ \text{COCCH}_3 \]
\[ \text{HO} \text{CCH}_3 \text{OCCH}_3 \]
of 2:4:6-Trimethoxy
acetophenone (1 g.),
aduminium chloride (1 g.) and chlorobenzene (10 c.c.),
was refluxed for 1 hour, chlorobenzene was removed
by steam distillation, on cooling the residue solid
separated, which crystallised from alcohol in cream
coloured needles (0.3 g.) m.p. 203°. (compare Sonn and Bullow, Ber., 1925, 58, 169, 205-207°)
(Found: C, 59.2; H, 5.5. C_{9}H_{10}O_{4} requires, C, 59.3; H, 5.3 %). The alcoholic solution of the
substance gave deep red coloration with ferric chloride.

2-Hydroxy-4-benzylloxy-6-methoxyacetophenone: -

\[
\begin{align*}
    & \text{C}_{9}\text{H}_{5}\text{C} = \text{O} \quad \text{C}_{6}\text{H}_{4}\text{O} \quad \text{C}\text{O} \quad \text{CH}_{3}
    \end{align*}
\]

2:4-Di-hydroxy-6-methoxy-
acetophenone (1 g.)

was mixed with anhydrous potassium carbonate
(2 g.), benzyl chloride (3 g.) and acetone
(20 c.cs.). The mixture was heated on water
bath for 8 hours, poured into water, solid
collected. It crystallised from dilute alcohol
in colourless needles (0.4 g.) m.p. 72° (Found:
C, 70.5; H, 5.9. C_{16}H_{16}O_{4} requires C, 70.6;
H, 5.9 %).

Chrysin: - (Robinson Condensation)

\[
\text{Phloracetophenone}
\]

(5 g.), benzoic
anhydride (60 g.) and sodium benzoate (8 g.)
were mixed together intimately and heated on oil
bath at 185-190°C for 8 hours, the reaction
product was finely ground, treated with 10 %
alcoholic caustic potash (40 c.c.) in course of half an hour, and the mixture was refluxed for an hour more, recovered some of the alcohol by distillation under reduced pressure, poured the residue into water (1.5 l.), filtered and saturated the filtrate with carbon dioxide. Collected solid, crystallised from alcohol yield (2.2 g.) m.p. 276°.

\[
\text{Reduced the mother liquor to a small bulk, a solid separated, m.p. 156° (not sharp); further recrystallisation from alcohol gave cream coloured needles (0.5 g.) m.p. 157°. The alcoholic solution of the substance gave deep red colouration with ferric chloride.}
\]

The substance was identified as 2-hydroxy-4,6-dibenzoyloxy-o-benzoylacetophenone. (Found: C, 72.2; H, 4.4. C_{29}H_{20}O_{7} requires C, 72.5; H, 4.2 %). The substance was not affected when boiled with 50 % hydrochloric acid for 1 hour. When it was hydrolysed by boiling with alkali, the odour of acetophenone was perceptible. Dissolution of the substance in concentrated sulfuric acid and on pouring into ice, a solid separated, which from its melting point appeared to be a mixture. However, on boiling with
with 10% alcoholic caustic potash and then pouring into water saturation of the clear filtrate with carbon-dioxide gave precipitate, which crystallized from alcohol m.p. 275° (chrysain).

**Chrysindimethylether:** Chrysain (0.2 g.) was dissolved in acetone, 20% caustic soda (2.5 c.c.) and dimethyl sulfate (1 c.c.) were added, the reaction mixture was shaken and then heated on water bath for 30 minutes, poured into water, collected solids crystallized from dilute alcohol; it formed colorless needles (0.12 g.), m.p. 143° (Found: C, 72.1; H, 4.9. C_{17}H_{14}O requires C, 74.6; H, 4.7%);

**3-Benzyl-chrysindimethylether:** The same product (3 g.) in the experiment of the m-benzen reaction with chloracetophenone and benzoic anhydride obtained by precipitation with carbon dioxide was dissolved in acetone (2 c.c.), 10% caustic soda solution (50 c.c.) and dimethyl sulfate (85 g.) were added during two hours while the reaction mixture was mechanically stirred, the mixture was diluted with water, solid collected and after two crystallizations from acetone, it formed yellow needles (0.5 g.), m.p. 312° (Found: C, 74.6; H, 4.3. C_{24}H_{16}O_5 requires C, 74.6; H, 4.7%).
Evaporation of the mother liquor and crystallisation of the residue from alcohol gave chrysin-dimethylether (0.6 g.) m.p. 143°.

5-Hydroxy-7-benzylxyloxy-8-benzylflavone:

(a) Chrysirn (0.5 g.) was mixed with anhydrous potassium carbonate (4 g.), benzyl chloride (5 g.) and acetone (10 c.c.). The mixture was heated on water bath for 3 hours, diluted with water excess of benzyl chloride was removed by steam distillation, the solid formed was collected, crystallised from acetone; it formed yellow needles (0.2 g.) m.p. 205°. (Found: C, 80.3; H, 5.4. C_{29}H_{22}O_{4} requires C, 80.2; H, 5.1%).

(b) To a solution of caustic potash (0.25 g.) in alcohol added chrysin (0.5 g.) and benzyl bromide (0.4 g.), after shaking for few minutes, the mixture was heated on water bath for 30 minutes, the orange precipitate was collected suspended in water and acidified with dilute hydrochloric acid, collected the solid, crystallised from acetone, pale yellow needles (0.3 g.) m.p. 205°. The product was identical with the benzyl ether obtained in the previous experiment. The alcoholic
solution of the substance gives light green colouration with ferric chloride.

2-Hydroxy-4:6-dimethoxyacetophenone - 2:4:6-

\[
\begin{align*}
&\text{Trimethoxyacetophenone} \\
&\text{(6.5 g.) was heated at 113 - 115 with equal quantity of anhydrous aluminium chloride for half an hour, treated the reaction product with ice cold dilute hydrochloric acid, collected the solid, crystallised from 50 % alcohol, it formed cream coloured needles (1.7 g.) m.p. 80-81° C.}
\end{align*}
\]

The experiment was repeated with trimethoxyacetophenone (13 g.), yield of the substance was (3.7 g.).

2-Benzoyloxy-4:6-dimethoxyacetophenone -

\[
\begin{align*}
&\text{2-Hydroxy-4:6-dimethoxyacetophenone (1 g.)}
\end{align*}
\]

Benzoyl chloride (1 g.) and pyridin (2 gm.) were heated on water bath for 15 minutes, poured into dilute hydrochloric acid, an oil separated, took up the oil in ether, washed with dilute alkali and then with water, distilled off ether; an oil was left behind, took up the oil in alcohol, on standing, it formed colourless needles (0.65 g.)
m.p. 91° (Found: C, 68.1; H, 5.3. \( \text{C}_{17}\text{H}_{14}\text{O}_5 \) requires C, 68.0; H, 5.3 %).

**2-Hydroxy-4:6-dimethoxy-benzoylacatophenone**

and its conversion into chrysin dimethyl ether: -

The benzoate (1 g.) from the previous experiment, 
sodamide (1 g.) and dry ether (15 c.c.) were shaken 
together for 2 hours, the deep chocolate brown 
solid was collected, washed with ether and 
treated with ice and acetic acid, the diketone 
separated as an oil and was refluxed with 20% 
alcoholic sulfuric acid for two hours, poured 
into water, collected the solid, crystallised from 
dilute alcohol, it formed colourless needles 
(0.4 g.) m.p. 143°, mixed melting point with 
chrysin dimethyl ether prepared by the direct 
methylation of chrysin was not affected.

**2:4:6-Trimethoxy benzoyl acatophenone:**

\[
\text{H}_3\text{CO} \quad \text{CO} \quad \text{CO} \quad \text{CO} \\
\text{H}_3\text{CO} \quad \text{CO} \quad \text{CO} \quad \text{CO} \\
\text{H}_3\text{CO} \quad \text{CO} \quad \text{CO} \quad \text{CO}
\]

A mixture of 2:4:6-

trimethoxyacatophenone 
(3 g.) ethyl benzoate (15 g.) and finely divided 
sodium (0.5 g.) was heated at 120° for three hours. 
The semi solid mass was then poured into ice cold 
dilute acetic acid, extracted with ether, ether 
extract was twice shaken with 10% caustic soda 
solution, the alkali extract was saturated with
carbon dioxide, sticky solid separated, which was taken up in ether, dried the ethereal part, and distilled off ether. A shining crystalline brown solid separated, which crystallised from dilute alcohol in light brown needles (1.5 g.) m.p. 92.94°. The alcoholic solution of the substance had a deep red ferric chloride reaction.

Chrysin dimethyl ether:— To a solution of aluminium chloride (1.4 g.) in nitrobenzene (10 c.c.), 2:4:6-trimethoxyacetophenone (0.7 g.) was added. After 12 hours the mixture was treated with ice and the nitrobenzene was removed by steam distillation. The cooled residue was partly crystalline and contained 2-hydroxy-4:6-dimethoxy-dibenzoylethane as indicated by the ferric chloride colouration. It was collected, washed with dilute hydrochloric acid, boiled for two hours with 20% alcoholic sulfuric acid (20 c.c.) and poured into water, collected solid, crystallised from alcohol, it formed colourless needles (0.5 g.) m.p. 143°. Mixed melting point with chrysin dimethyl ether was not depressed and the substance gave no colouration with ferric chloride.

Techeochrysin:— A mixture of aluminium chloride (0.2 g.) in nitrobenzene (5 c.c.}
and dimethyl chrysin (0.2 g.) was heated on water bath for one hour, cooled and treated with ice cold dilute hydrochloric acid, nitrobenzene was removed by steam distillation, a solid residue was left behind, which was collected on crystallisation from alcohol; it gave colourless needles (0.12 g.), m.p. 165°. (Found: C, 71.5; H, 4.7. C_{16}H_{12}O_{4} requires, C, 71.6; H, 4.8%). The alcoholic solution of the substance gives deep red colouration with ferric chloride.

(b) Chrysindimethylether (0.5 g.) and aluminium chloride (0.5 g.) were mixed intimately and the mixture was heated on oil bath at 115° for 30 minutes, treated with dilute ice cold hydrochloric acid, a yellow solid separated, which on fractional crystallisation from aqueous alcohol gave techochrysin (0.08 g.), m.p. 165° and chrysin (0.18 g.) m.p. 275°.

(c) 2:4:8-Trimethoxybenzoylacetoephone (0.5 g.) was heated with hydriodic acid (d, 1.7; 5 c.c.) and acetic anhydride (5 c.c.) for five minutes and the product poured into sodium bisulfite solution; crystallisation of the product from alcohol gave techochrysin (0.2 g.) m.p. 165°.
In another experiment heating was prolonged to 20-minutes, a minute amount of technochrysin and (0.2 g.) of chrysin m.p. 275° were obtained on fractional crystallisation.

**Flavone oxime:** A mixture of flavone (0.1 g.) hydroxylamine hydrochloride (0.15 g.) in water (0.5 c.c.) and pyridin (1 c.c.) was refluxed on sand bath for 1 hour, and then poured into dilute acetic acid, the precipitated solid crystallised from hot dilute acetone in colourless needles, m.p. 237°, yield was almost quantitative, (Found: N, 9.95; C_{15}H_{11}C_{2}N requires N, 6.19 %).

1:4-α-naphthaflavone oxime:—was also prepared as in the above case except that α-naphthaflavone was substituted for flavone. It formed colourless needles on crystallisation from dilute acetone, m.p. 181°. (Found: N, 4.85; C_{19}H_{13}O_{2}N requires N, 4.8 %).
Part V.

Derivatives of 3:7:4'-Trihydroxyflavone.
Furukawa (Sci. Papers. Inst. Phys. Chem. Res. Tokyo, 1932, 19, 27) isolated from the leaves of *Ginkgo biloba* a colouring matter, $C_{16}H_{12}O_5$, to which he ascribed the structure of a trihydroxyflavone mono methyl ether. On demethylation and fusion with caustic potash the substance gave p-hydroxy benzoic acid. A comparison of the properties of its dimethyl ether with those of known trihydroxy flavones derived from anisic acid has shown that bilobetin (as the colouring matter may be named in accordance with usual practice) is not a methyl ether of apigenin, 6:7:4'-trihydroxyflavone or 7:8:4'-trihydroxyflavone. Considering the orientation of hydroxyl groups commonly encountered in naturally occurring flavones, it appeared probable that the demethylation product of bilobetin may be 3:7:4'-trihydroxyflavone. The methylation of 7-hydroxy-3:4'-dimethoxyflavone obtained by the interaction of $O$-methoxy resacetophenone and anisic anhydride led to 3:7:4'-trimethoxy flavone (I), crystallising in dimorphic forms, m.p. 152° and 225°, the latter identical with the melting point of bilobetin dimethyl ether.

A synthesis of the three monomethyl ethers
(II), (III) and (IV) of 3:7:4'-trihydroxy flavone was, therefore, necessary in order to see if one of them exhibited the properties of bilobatin. The Robinson reaction between 3-methoxy resacetophenone and p-benzxyloxybenzolic anhydride gave 3-methoxy-7-hydroxy-4':benzyloxyflavone (V),

![Chemical structure images](image)

VII)

(VIII)

treatment of which with hydrochloric acid in acetic acid led to (II). Similarly from 7-benzxyloxyresacetophenone (VI) and anisic anhydride and subsequent debenzylation of the resulting 7-hydroxy-3-benzxyloxy-4':methoxyflavone (VII), (III) was obtained; (III) has previously been described by Heap and Robinson (J.C.S., 1926, 2336),
who have prepared it from benzoyloxy resace-
tophenone. Neither (II) nor (III) resembled
bilobatin; the synthesis of (IV) is in hand.
The new ketone (VI) was prepared by carrying
out a Hoesch reaction between resorcinol and
benzoyloxyacetoneitrile (VIII) under carefully
prescribed conditions; (VIII) was obtained
by heating benzyl chlormethyl ether with cuprous
cyanide.

**Experimental.**

3:4'-Dimethoxy-7-hydroxyflavone:

An intimate mixture

\[
\begin{array}{c}
\text{HO} \\
\text{C} \\
\text{C} \\
\text{C} \\
\text{C} \\
\text{C} \\
\text{C} \\
\text{C} \\
\text{C} \\
\text{C} \\
\text{C} \\
\text{C} \\
\text{C} \\
\text{C} \\
\text{C} \\
\text{C}
\end{array}
\]

of α-methoxyresaceeto-
phenone (2 g.), anisic anhydride (14 g.) and
sodium anisate (5 g.) was heated at 180-135° for
six hours. Hydrolysis with alcoholic caustic
potash, filtration and saturation of the filtrate
with carbon dioxide gave yellow flakes which
crystallised from alcohol in glistening pale
yellow needles (1.8 g.) m.p. 264° (Found: C,
68.4; H, 4.6. C\textsubscript{17}H\textsubscript{14}O\textsubscript{5} requires C, 68.4; H, 4.7 %).

The acetyl derivative crystallised from
alcohol in colourless needles, m.p. 130°. (Found:
C, 37.2; H, 4.4. C\textsubscript{19}H\textsubscript{18}O\textsubscript{6} requires, C, 67.0;
H, 4.7 %).
3:7:4'-Trimethoxyflavone: - To a solution of 3:4'-dimethoxy-7-ace-

toxyflavone (0.5 g.) in acetone (10 c.c.), 50 % caustic soda solution
(20 g.) and dimethylsulphate (13 g.) were alternately added in small portions, the mixture
was heated on water bath for an hour and poured into water. The precipitate was collected and
crystallised from alcohol. The colourless needles (0.3 g.) melted at 152° (Found: C, 69.1; H, 5.2.
C_{18}H_{16}O_5 requires C, 69.2; H, 5.1 %).

The substance was dissolved in minimum amount of boiling acetone, the substance which separated
on cooling to room temperature melted at 152°; the mother liquor was poured into water, the
precipitate was collected, crystallised from alcohol; it formed needles which were found to
melt at 225° (The substance was just enough for few melting points).

Benzylxyacetonitrile: - A mixture of benzyl-

cleormethyl ether

(C_{6}H_{5}CH_{2}CN)

(Hill and Keoch,
J. Am. Chem. Soc. 1926, 48, 259), dry cuprous cyanide
(15 g.) and toluene (20 c.c.) was refluxed on
sand bath for six hours. The toluene was removed
in an oil bath and the residue distilled in vacuo. The distillate was redistilled and fraction distilling at 105-120\(^{\circ}\) / 2 m.m. was collected. It was further refractionated and a fraction b.p. 180-110\(^{\circ}\) was obtained as colourless oil. (Found: N, 9.2. \(C_9H_8C\) N requires N, 9.5%).

\[\text{\(\alpha\)}-\text{benzyloxyresorcinophenone}\]: A rapid stream of dry hydrogen chloride was passed for two hours into a mixture of resorcinol (4 g.), benzyloxy acetonitrile (5 g.) and dry ether (25 c.c.), cooled in ice and salt. The colour of the solution changed to pale brown, blue, violet and finally dark brown; after standing in frigidair for five days, the separated crystalline product was collected, washed with dry ether and heated on water bath with alcohol (12 c.c.) and water (25 c.c.) for 12 hours. Water was added, till the solution became just turbid and on cooling, the oily precipitate which separated was collected and crystallised from 15% alcohol. The colourless shining irregular plates (1.2 g.) m.p. 142\(^{\circ}\). (Found: C, 69.6; H, 5.5. \(C_{15}H_{14}O_4\) requires C, 69.3; H, 5.4%).
The 2:4-dimetrophenylhydrazone crystallised from alcohol acetic acid in deep orange plates, m.p. 222°

(Found: C, 12.7. C₂₁H₁₉O₇N₄ requires N, 12.8 %).

Methyl-p-benzyloxy benzoate: - To a solution of ethyl-p-hydroxybenzoate (126 g.) and benzylchloride (100 c.) in methyl alcohol (200 c.c.), caustic potash (45 g.) in methyl alcohol (400 c.c.) was added. After refluxing for five hours, the boiling solution was filtered rapidly, the colourless elongated prisms (75 g.) which were insoluble in sodium carbonate solution, were recrystallised from methyl alcohol; it melted at 91°

(Found: C, 74.9; H, 4.1; C₁₉H₁₈O₃ requires C, 75.0; H, 4.1 %).

Hydrolysis of the ester with 10 % alcoholic caustic potash solution gave the known p-benzyloxybenzoic acid m.p. 192°.

p-Benzylloxybenzoyl chloride: - p-Benzylloxybenzoic acid (10 g.) was heated with
thionyl chloride (20 g.) on water bath for two hours, excess of thionyl chloride was removed under reduced pressure and the semi solid residue poured into light petroleum. The precipitate was collected and crystallised from a mixture of ethyl acetate and light petroleum; colourless needles (8 g.) melted at 110° (Found: Cl, 14.2. \( \text{C}_{14}\text{H}_{11}\text{O}_{2}\text{Cl} \) requires Cl, 14.4 %).

\[ \text{p-Benzylxoybenzoic anhydride:} \]  The chloride (8 g.) and acid (7 g.) were dissolved in dry chloroform (25 c.c.) and pyridin (5 g.) was added, left over night, after which the mixture was poured into alcohol (175 c.c.); after 30 minutes, the precipitate was collected, washed with sodium carbonate solution and crystallised from ethyl acetate and light petroleum. The colourless needles (9 g.) melt at 119°. (Found: C, 76.7; H, 5.1. \( \text{C}_{26}\text{H}_{22}\text{O}_{5} \) requires C, 76.7; H, 5.0 %).

\[ 3\text{-Methoxy-7-hydroxy-4'-benzylxoyflavone:} \]  The Robinson reaction was carried out in the usual manner with methylxoyresacetophenone (1.5 g
p-benzylxybenzoic anhydride (12 g.) and sodium p-benzylxy benzoate (4 g.). Hydrolysis with alcoholic potash, dilution with water, filtration to remove small amount of undissolved matter and saturation of the clear filtrate with carbondioxide gave reddish brown precipitate, which was found to be a mixture of required flavone and the sparingly soluble potassium salt of benzylxybenzoic acid; the product was collected, boiled with water, filtered and the residue crystallised from alcohol. The pale yellow prismatic needles (0.25) melted at 235° (Found: C, 73.6; H, 4.8. C_{23}H_{18}O_{5} requires, C, 73.8; H, 4.8 %).

3-Methoxy-7:4'-dihydroxyflavone:—3-Methoxy-7-
hydroxy-4'-benzylxy-
flavone (0.15 g.) was suspended in glacial acetic acid (10 c.c.) heated on water bath, concentrated hydrochloric acid (2 c.c.) was added drop by drop during fifteen minutes heating on the open flame, the solution was poured into water, the precipitate collected and crystallised from alcohol. The pale yellow needles (0.08 g.) m.p. 289°. (Found (micro): C, 37.7; H, 4.3. C_{18}H_{12}O_{5} requires, C, 67.6; H, 4.2 %).
The diacetyl derivative of the above flavone was prepared in the usual manner, it crystallised from alcohol in colourless needles m.p. 135°.

The substance was just enough for melting point, so the carbon and hydrogen determination could not be done.

**3-Benzylxoy-7-hydroxy-4'-methoxyflavone:**

![Chemical structure](image)

(0.8 g.), anisic anhydride (12 g.) and sodium anisate (3 g.) were mixed together intimately, heated at 180-190° for 6 hours, product worked up in the usual manner, it crystallised from dilute alcohol in glistening pale yellow needles (0.4 g.) m.p. 188°. (Found: C, 75.5; H, 4.7. C_{23}H_{18}O_{5} requires C, 73.8; H, 4.8 %).

**3:7-dihydroxy-4'-methoxyflavone:** Debenzylation of the 3-benzylxoy-7-hydroxy-4'-methoxyflavone as in the previous case and crystallisation from alcohol gave shining straw coloured needles, m.p. 236° (Heap and Robinson (loc. cit.) 233-234°)

(Found: C, 67.3; H, 4.2. C_{16}H_{12}O_{5} requires C, 67.6; H, 4.2. %).
The diacetyl derivative of the above was prepared in the usual manner by boiling the hydroxy compound with acetic anhydride and pyridin. Crystallisation of the product from alcohol gave pale grey needles m.p. 203° (Heap and Robinson, loc.cit. 197°) (Found: C, 35.3; H, 4.2. C₂₀H₁₆O₇ requires C, 35.2; H, 4.3 %).
SUPPLEMENT.
Part I.

Synthesis of 1-Alkyl-2-Naphthols.
Johnson and Lane (J. Amer. Chem. Soc., 1921, 43, 348) showed that the antiseptic properties of alkyl-resorcinols increased and the toxicity diminished with the length of the alkyl chain. The dihydroxy phenols were submitted to bacteriological examination for the determination of the phenol co-efficient by a modification of the Hideal-Walker method.

The "Phenol Co-efficients" of the substance examined are given in column 'A' of Table I, while in column 'B' are recorded more striking values obtained by arbitrarily placing the antiseptic value of resorcinol as equal to unity.

<table>
<thead>
<tr>
<th>Substances</th>
<th>A</th>
<th>B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resorcinol</td>
<td>0.3</td>
<td>1</td>
</tr>
<tr>
<td>Ethyl resorcinol</td>
<td>1.3</td>
<td>4.9</td>
</tr>
<tr>
<td>n-Propyl resorcinol</td>
<td>4.3</td>
<td>13.9</td>
</tr>
<tr>
<td>n-Butyl resorcinol</td>
<td>8.0</td>
<td>23.0</td>
</tr>
</tbody>
</table>

Proceed. Soc. Exper. Biol. and Med., 1931, 23, 1036; Lamson, Brown, Robbins and Ward, Amer. J. Hyg., 1931, 13, 303; Lamson, Cadwell, Brown and Ward, ibid., 1932, 15, 308), several investigations have been made on the preparation of alkyl derivatives of other phenols (Klarmann and Wowern, J. Amer. Chem. Soc., 1930, 52, 4866; Brester and Harris, ibid., 1930, 52, 4866; Cox, ibid., 1930, 52, 353; Lamson, Stoughton and Bass, J. Pharmacol., 1936, 56, 50; Stewart, Cornell, 1937, 27, 338; Miller, Hartung, Rock and Crossley, J. Am. Chem. Soc., 1938, 60, 7) Klarmann and his collaborators have reported on the antiseptic properties of polyhydroxy benzene monomethylethers, alkyl hydroquinones and alkyl phloroglucinols. Shone, 1932, U.S.P., 1558, 042, has prepared higher alkyl resorcinols such as octyl, nonyl etc. and has shown their low toxicity and better antiseptic and anthelmintic properties, Coulthard and Pymar (J. State Med., 1931, 39, 599; Brit. J. Exptl. Path., 1931, 12, 331), have shown that 4-amyI-m-cresol has a Rideal-Walker Co-efficient 200-250° and is less than half as toxic as hexylresorcinol. Examining the antiseptic properties of alkyl resorcinols, Brewer and Harris showed that the same halogenated
alkyl resorcinol was obtained whether the halogenated ketone was reduced or the ketone reduced before halogenation.


Acylated β-naphthols (I) were converted by means of anhydrous aluminium chloride into 1-acyl-2-naphthols (II); Clemmenson reduction of (II) led to the 1-alkyl-2-naphthols (III). 1-Methyl-2-naphthol (Pickart, Ber., 1906, 39, 441) and 1-ethyl-2-naphthol (Fries and Engel, Ann., 1924, 432, 233) have been prepared earlier; the 1-n-propyl, 1-n-butyl, 1-n-pentyl and 1-n-hexyl homologues have now been synthesised. Miller and others (loc.cit) have prepared alkyl catechols, catechol alkyl ketones were prepared by Fries rearrangement of appropriate ester of either catechol or guaiacol, in the latter case reaction was accompanied by simultaneous demethylation, catalytic reduction with palladium catalyst gave 4-alkyl catechols,
Clemmensen reduction gave less satisfactory results.

The constitution of the ketone (II) has been assumed on the basis of the fact that the Fries reaction on \( \text{napthyl acetate yields 1-acetyl-2-naphthol} \) (Fries, Ber., 1921, 54, 709). In the Fries reaction, the rearrangement of the phenolic esters to hydroxy aromatic ketones by means of anhydrous aluminium chloride, Fries, Witt and Auwers considered the reaction to be an intramolecular change. Skraup and Poller, however, prepared \( o\text{-acetyl-m-cresol} \) by the action of anhydrous zinc chloride on \( m\text{-tolyl acetate} \) and contended that the ester was first decomposed by zinc chloride into acyl chloride and \( m\text{-cresol} \) and the acid chloride then reacted with \( m\text{-cresol} \) to form the ketone. Rosenmund and Schnurr also disagree with the Auwers view of the intramolecular nature of the reaction. They have found that when a mixture of \( o\text{-chloro-p-tolyl acetate and p-tolyl benzoate} \) is acted upon by aluminium chloride, not only \( 2\text{-acetyl-6-chloro-p-cresol} \) and \( o\text{-benzoyl-p-cresol} \) are formed, but also \( 2\text{-benzoyl-6-chloro-p-cresol} \) and \( acetyl-p\text{-cresol} \) are obtained. They state that if this reaction were intramolecular, the latter two
compounds should not have been formed. These authors have also taken exception to Skraup's explanation of the reaction, for they were unable to distill out any free acid chloride, even working at reduced pressure and in a stream of hydrogen; they have interpreted the mechanism of the Fries' change, as one involving two molecules of esters and have compared the reaction to a Friedel and Crafts' reaction, where acetic anhydride is the acetylationating agent. The possibility of free radical exchange is also indicated.

In the present experiments the author has confirmed the ketonic structure of the product of the Fries reaction in each case by converting it by means of benzoic anhydride and sodium benzoate into the 2-alkyl-α-naphthaflavone (IV) (Compare Menon and Venkataraman, J.C.S., 1931, 139, 2591). Menon and Venkataraman showed that acetic anhydride and sodium acetate gave only 2-acetyl-3-methyl-1:4-β-naphthapyrone (V) and aromatic anhydrides gave naphthaflavones unsubstituted in the 2-position e.g. by heating 1-acetyl-2-naphthol with benzoic

\[ (IV) \]

\[ (V) \]

\[ (VI) \]

anhydride and sodium benzoate -naphthaflavone
The presence of an -alkyl substituent in 1-acetyl-2-naphthol greatly facilitated the chromosome condensation and naphthoflavones were formed in nearly quantitative yields (c.f. Cheema and Venkataraman, J.C.S., 1932, 121, 919).

In order to ensure that the n-valeric and n-caproic acid used for the preparation of 1-valeryl-2-naphthol and 1-capryl-2-naphthol were unmixed with isomers, they were synthesised by the malonic ester method.

**Experimental.**

1-Propionyl-2-naphthol: A solution of 1-naphthol propionate (Zinhorneud Hollandt, Ann., 1898, 301, 112) (50 g.) in carbon disulfide (100 c.c.) was heated with aluminium chloride (51 g.) for 1 hour. Carbon disulfide was then removed by distillation and the residue heated at 120° for 4 hours. The reddish brown mass was decomposed with hot water, dissolved in hot caustic soda solution, treated with charcoal for few minutes and filtered, acidification of the clear filtrate led to the required ketone, which was collected, washed, dried and crystallised from ligoroin. The long pale yellow needles (30 g.) melted at
70-71° (Found: C, 78.0; H, 6.1 C_{13}H_{12}O_2 requires C, 78.0; H, 6.0%). The alcoholic solution of this and the other 1-acyl-2-naphthols give an intense reddish violet colouration with ferric chloride.

2-Methylβ-naphthoflavone: An intimate mixture of 1-propionyl-2-naphthol (3 g.), benzoic anhydride (25 g.) and sodium benzoate (15 g.) was heated at 185-190° for six hours. Hydrolysis of the excess of anhydride was effected by means of boiling 10% alcoholic potash (130 c.c.) on pouring into water (1-litre), the precipitate was collected and crystallised from alcohol. The glistening, cream coloured leaflets melt at 110° (Found: C, 83.5; H, 4.8, C_{20}H_{14}O_2 requires C, 83.3; H, 4.8%). This substance and the other naphtha flavones described below, exhibit a bright greenish blue fluorescence in sulfuric acid solution.

1-Propyl-2-naphthol: A mixture of 1-propionyl-2-naphthol (20 g.), zinc amalgam (100 g.) and hydrochloric acid (equal part of concentrated hydrochloric acid and water, (130 c.c.), was kept at a gentle boiling on sand bath. Zinc amalgam
was prepared by allowing X gms. of commercial zinc to remain about an hour at ordinary temperature in contact with 2X c.c. of 5% aqueous solution of mercuric chloride. The supernatant liquid was poured off. A little concentrated hydrochloric acid was added from time to time and heating was continued until a test portion, carefully neutralised with very dilute caustic soda solution gave no colouisation with ferric chloride (35 hours). The mixture was repeatedly extracted with ether, the ether extract washed with water, dried, over magnesium sulfate and the ether removed. The residual oil was redistilled and fraction boiling at 143-145°/1-2 m.m. was collected. It is a pale brown oil (Found: C, 84.2; H, 7.6. C_{13}H_{14}O requires C, 83.9; H, 7.3%). The alcoholic solution of this and other alkyl-β-naphthols develop no colouration with ferric chloride.

β-Naphthol butyrate:- The chlorides of n-butyric acid, n-valeric acid and n-caproic acid were prepared by treatment of the respective acids with thionyl chloride on water bath and fractionation of the mixtures (c.f. Organic synthesis; 9, 32).
\( \beta \)-Naphthol (70 g.) was heated with butyryl chloride (80 g.) on oil bath at 120° for six hours, poured into water, oil was isolated by means of ether, the pale yellow ester has boiling point 134 - 135°/3 mm. (Found: C, 79.3; H, 6.3. \text{C}_{14}\text{H}_{14}\text{O}_2 \text{ requires C, 78.5; H, 6.5%}).
1-Butyryl-2-naphthol: A solution of \( \text{CO(OCH}_2)_2 \text{CH}_3 \) \( \beta \)-naphthol butyrate (50 g.) in carbon disulfide (100 c.c.) was heated with aluminium chloride (51 g.) on a water bath for one hour. Carbon disulfide was removed by distillation and the residue heated for four hours at 120\(^\circ\)C. The reddish brown mass was decomposed with ice cold water, dissolved in hot caustic soda solution, treated with charcoal for few minutes and filtered. The alkaline solution gave on cooling glistening golden yellow rectangular plates of the sodium salt of the ketone; this was collected, suspended in water and acidified. The oil was purified by distillation; b.p. 167-168\(^\circ\)/1-2 mm. yield (20 g.) (Found: C, 78.4; H, 6.5. \( \text{C}_{14} \text{H}_{14} \text{O}_2 \) requires C, 78.5; H, 6.5%).

2-Ethyl-\( \beta \)-naphtho-flavone: An intimate mixture of 1-butyryl-2-naphthol (2 g.), benzoic anhydride (15 g.) and sodium benzoate (4 g.) was heated at 130-135\(^\circ\) for six hours. Hydrolysis of excess of benzoic anhydride was effected by boiling with 10% alcoholic caustic potash (80 c.c.). On pouring into water, the precipitate was collected and crystallized from alcohol. The shining pale
1-Butyl-2-naphthol: - A mixture of 1-butyryl-2-naphthol (10 g.), zinc amalgam (111 g.), and hydrochloric acid (1:1. 177 c.c.) was kept at gentle boiling on sand bath, a little concentrated hydrochloric acid was added from time to time and boiling as in the previous case was continued for 35 hours. The mixture was repeatedly extracted with ether, the ether extract washed with water and dried over anhydrous magnesium sulfate and then the ether was removed. The residue was distilled in vacuo, the oil coming over at 130°/3 mm. solidified on standing and crystallized from light petroleum m.p. 80-81° (Found: C, 84.0; H, 8.1. C_{14}H_{16}O requires C, 84.0; H, 8.0 %). The yields of the two alkyl naphthols were poor (20 % of theory).

n-Valeric acid: - n-propyl alcohol (350 g.) was treated with sodium bromide (750 g.) and concentrated sulfuric acid (975 g.). The mixture was refluxed for 4 hours. The propyl bromide (309 g.), was distilled. n-Propyl bromide
(309 g.) gave on treatments with sodium (57 g.), absolute alcohol (1250 c.c.) and diethyl malonate (412 g.), n-propylmalonic ester (309 g.), n-propylmalonic ester (309 g.) was treated with caustic potash (332 g.) and acidification with sulfuric acid (530 g.) gave n-valeric acid (57 g.). The crude acid was mixed with an equal volume of benzene and fractionated. The portion coming at 86° was collected.

β-Naphthol valerate:—On heating β-naphthol
\[
\text{\text{C}}_{10}\text{H}_{8}\text{O}_2 \quad (38 \text{ g.}) \text{ with valeryl-chloride (51 g.) at 130°}
\]
for six hours and pouring into water, the oil was taken up in ether, the ether extract washed with 10% caustic soda solution then with water, dried and ether removed. The residue boiled at 168°/4 m.m. (Found: C, 79.0; H, 6.7 C_{13}H_{16}O_2 requires C, 78.8; H, 7.0%); yield 40 g.

1-Valeryl-2-naphthol-β-naphthol valerate

\[
\text{C}_9\text{H}_{12}\text{O}_2 \quad (38 \text{ g.}) \text{ in carbon}
\]
was heated with aluminium chloride (37 g.) on a water bath for 1 hour, carbon disulfide was
removed and the residue heated for 4 hours at 120°. The reddish brown mass was decomposed with ice cold water, dissolved in hot caustic soda solution, treated with charcoal and filtered. The flietening, golden yellow rectangular plates separated on cooling, these were separated, suspended in water and acidified, the oil was purified by distillation, b.p. 165-166 ° 1, m. m. (28 g.) (Found: C, 78.5; H, 6.7. C₁₅H₁₆O₂ requires C, 78.9. H, 7.0 %).

2-Propyl-α-naphthoflavone: The condensation was carried out in the usual manner with 1-valeryl-1-2-naphthol (2 g.), benzoic anhydride (15 g.) and sodium benzoate (4 g.). After boiling with 10% alcoholic caustic potash (80 c.c.) and pouring into water, the undissolved material was collected and crystallized from alcohol (0.6 g.), colourless needles m.p. 103° (Found: C, 84.4; H, 5.6. C₂₂H₁₈O₂ requires C, 84.1; H, 5.7 %).

1-Pentyl-2-naphthol: A mixture of 1-valeryl-
2-naphthol (5 g.), zinc amalgam (40 g.) and hydrochloric acid (40 c.c. 1:1) was boiled gently
on sand bath for 31 hours, a little concentrated hydrochloric acid was added now and then. At the end of the reaction liquid was decanted off from zinc and distilled with supper heated steam, the oily distillate solidified and was crystallised from ligoroin, the cream coloured needles (1 g.) m.p. 84° (Found: C, 83.0; H, 3.4. C₁₅H₁₈C requires C, 84.0; H, 8.4\%). When the reduction was carried out with larger amounts of ketone the yield of alkyl naphthol diminished.

n-Butyroic acid:— It was prepared from n-butyl alcohol just as n-valeric acid was obtained from n-propyl alcohol. n-butyl alcohol (122 g.) was used and butyl bromide (162 g.) was prepared. From butyl bromide (160 g.) n-butyl malonic ester (173 g.) was prepared. n-Butylmalonic ester (160 g.) gave n-caproic acid (42 g.). The acid was separated by automic separator (Organic Synthesis, 1, 68) and the crude acid was mixed with an equal volume of benzene and distilled. The acid came over at 205°.

α-Naphthol caproate:— Caproyl chloride (40 g.) was condensed with α-naphthol (32 g.) in the usual way. On pouring into water, the oil
was extracted with ether, the ether extract washed with 10% caustic soda solution, then with water, dried and ether removed. The residue on distillation in vacuo gave \( \beta \)-naphthol caproate (34 g.) which distilled over at 176-177\(^0\)/1-2 m.m. (Found: C, 79.1; H, 7.4. \( \text{C}_{16}\text{H}_{18}\text{O}_2 \) requires C, 79.3; H, 7.4\%).

\[ \text{1-Capryl-2-naphthol: \( \beta \)-Naphthol caproate} \]

heated with aluminum chloride (35 g.) on a water bath for 1 hour, and after the removal of carbon disulfide, at 180\(^0\) for 4 hours; the residue on decomposition with ice cold water and purification of the oil in the usual way gave 1-capryl-2-naphthol (28 g.). The ketone distilled over at 188-190\(^0\)/2 m.m. (Found: C, 78.9; H, 7.5. \( \text{C}_{16}\text{H}_{18}\text{O}_2 \) requires C, 79.3; H, 7.4\%).

\[ \text{2-Butyl-\( \beta \)-naphthothenone: 1-Capryl-2-naphthol} \]

(2 g.) benzoic anhydride (15 g.) and sodium benzoate (4 g.) were heated together for 8 hours and the product boiled with alcoholic caustic
potash; on pouring the solution into water the undissolved material was collected and crystallised from alcohol. The long shining straw coloured needles (0.6 g.) m.p. 103° (Found: C, 83.9; H, 6.1, C_{23}H_{20}O requires C, 84.1; H, 6.0%).

1-Hexyl-2-naphthol - 1-Capryl-2-naphthol (5 g.) zinc amalgam (40 g.) and hydrochloric acid (44 c.c. 1:1) were boiled gently for 25 hours. The reduction product was purified by means of superheated steam as in the case of 1-pentyl-2-naphthol. The oily distillate was extracted with ether, the ether extract washed with water and dried over magnesium sulfate, the ether was distilled off and the oil kept in contact with light petroleum (100-110°). The brown crystalline material which separated was crystallised from light petroleum. The nearly colourless shining rhombohedral plates melted at 123° (Found: C, 84.2; H, 3.9. C_{16}H_{20}O requires C, 84.2; H, 3.7%). The alkyl naphthols exhibit the reaction of 2-naphthol, when an aqueous alkaline solution is boiled with few drops of chloroform, a blue colour is
developed, which slowly vanishes on standing. An orange picrate is formed by adding a warm alcoholic solution of picric acid to an alcoholic solution of alkyl naphthol and cooling.
Part II.

Attempted synthesis of the Naphthalene \( \beta \)
Analogue of Thymol.
Thymol (I) is a powerful antiseptic (Faust, *J. Am. Med. Assoc.*, 1937, 103, 383) and is according to Lane (Lancet, 1928, 1, 1301) the best anthelmintic for hookworms. Caius and Mnaskar (Indi. J. Med. Res., 1919, 7, 433) have shown that 84-99 per cent of the hookworms are removed by thymol in doses of 30-60 grains. It, therefore, appeared probably that the naphthalene analogue (II) of thymol which is obviously also a naphthol derivative would have interesting properties as an anthelmintic and attempts towards its synthesis are now described. Thymol methyl ether condensed readily with succinic anhydride and aluminium chloride to give an acid to which the structure (III), rather than (IV), is assigned from general considerations of the relative orienting influence of methyl and methoxyl groups. Clemensen reduction of (III) gave the 1-phenyl butyric acid (V). Attempts to convert (V) into the ketotetrahydro naphthalene (VI) proved unsuccessful; among the methods tried were direct ring closure with sulphuric acid and a Friedel Crafts reaction on the acid chloride.
prepared by means of thionyl chloride. In an alternative route to the desired tetrahydronaphthalene (VII) by the method of Bogart (Bogart and Davidson, J. Amer. Chem. Soc., 1934, 56, 185; Bogart, Davidson, and Apfelbaum, ibid, 959), the ethyl ester of (V) was reduced to the alcohol (VIII) by the Bourseault-Blanc process using sodium and amyl alcohol; the alcohol (VIII) was not convertible to (VII), but failures in this direction would seem to be paralleled by the difficulties encountered by Adams (J. Amer. Chem. Soc., 1923, 45, 2439, 2455; 1924, 46, 1312) in cyclising the keto acid (IX) to the anthraquinone, the position meta to the methoxyl being deactivated.

**Experimental.**

2-Methyl-4-methoxy-5-isopropylbenzoylpropionic acid: (III): - Powdered aluminium chloride (6.3 g.) was slowly added to a solution of thymol methyl ether (5 g.)
and succinic anhydride (3 g.) in acetylene tetrachloride (50 c.c.). The mixture was maintained at 5-10° for an hour and the reaction completed by warming the deep red mass at 65° C. for 5 hours. Decomposed with ice and hydrochloric acid and washed repeatedly with dilute hydrochloric acid, the product was extracted with sodium carbonate solution, the acid recovered from the filtrate and crystallised from hot water. The colourless needles melted at 98° (Found: C, 67.9; H, 7.3. C₁₅H₂₀C₄ requires C, 65.1; H, 7.5 %).

\[ \text{1-2-Methyl-4-methoxy-5-isopropylphenylbutyric acid (V):} \]

A mixture of (III) (5 g.), zinc amalgam (25 g.) and hydrochloric acid (equal parts concentrated hydrochloric acid and water; 65 c.c.) was kept at a gentle boiling on the sand bath, a little concentrated hydrochloric acid being added from time to time, until a test portion, carefully neutralised with very dilute sodium hydroxide solution, gave no colouration with ferric chloride (35 hours). Crystallisation of the oily product
from water, gave colourless needles melting at 52°, but in another experiment it was found more convenient to extract the reaction mixture with carbon tetrachloride, dry over anhydrous sodium sulphate, remove the solvent and to distill the residual oil in vacuo. The fraction coming over at 212-215°/5-6 mm. was collected. The clear, pale yellow oil solidified when thoroughly stirred under water, (Found: C, 72.0; H, 3.6. \( \text{C}_{15}\text{H}_{22}\text{O}_3 \) requires C, 72.0; H, 3.3 %).

Ethyl-\( \text{Y}-2\)-methyl-4-methoxy-5-isopropylphenylbutyrate: - The oil, boiled at 179-180°/4-5 mm. (Found: C, 73.2; H, 9.1. \( \text{C}_{17}\text{H}_{23}\text{O}_3 \) requires C, 73.3; H, 9.4 %).

\( \text{Y}-2\)-Methyl-4-methoxy-5-isopropylphenylbutyl alcohol (VIII): - In a three necked flask were placed metallic sodium (10 g.) and dry toluene (50 c.c.s). It was fitted with a mechanical stirrer and a condenser and a separating funnel containing 2-methyl-4-methoxy-5-isopropylphenylbutyric acid (18 g.) in 40 c.c. of amyl alcohol. The flask was heated
on the oil bath until the sodium melted. The
stirrer started and when sodium got finely divided
it was cooled to 60°. The mixture of acid and
alcohol from the dropping funnel was allowed to
run in and then more of amyl alcohol (100 c.c.s.)
was added as rapidly as possible. When the
reaction had subsided the flask was heated on
the steam bath to dissolve sodium. The mixture
was steam distilled. The contents of the flask
were separated from water while hot and washed
with amyl alcohol (50 c.c.). then 2-methyl-4-methoxy-5-isopropylphenylbutyl alcohol was extracted
with ether, ether extract washed with water, then
with sodium carbonate solution and again water.
It was then dried over anhydrous magnesium sulphate.
Ether removed and residue was distilled under
vacuo. The product coming at 193-195°/2 mm. was
collected. (Found C, 76.4; H, 10.1. C_{15}H_{24}O_2
requires C, 76.3; H, 10.2%).

1-keto-5-isopropy-7-methoxy-8-methyl-1:2:3:4-
tetrahydronaphthalene: 2-methyl-4-methoxy-5-
isopropyl phenyl butyric acid (4.4 g.), 95% 
sulphuric acid (9 c.c.) were heated on the water bath
for 1/2 hour. An ethereal extract of the diluted
substance was washed with water and then with dilute aqueous ammonia, dried with potassium carbonate and free from the solvent. The residue was crystallised from light petroleum. Author got a very small amount of the substance which was insufficient for analysis.
**LIST OF THE NEW COMPOUNDS.**

1. 5:7-Dicinnamoyloxy-2-styrylchromone.
2. 5:7-di-p-methoxy-cinnamoyloxy-4'-methoxy-2-styrylchromone.
3. 7-Hydroxy-2-styryl-3-methyl chromone.
4. 7-Acetoxy-2-styryl-3-methylchromone.
5. 7-Hydroxy-4'-methoxy-2-styryl-3-methylchromone.
6. 7-Acetoxy-4'-methoxy-2-styryl-3-methylchromone.
7. 2-Styryl-3-Methyl-1:4-α-naphthapyrone.
8. 4'-methoxy-2-styryl-3-methyl-1:4-α-naphthapyrone.
9. 2-Cinnamylidene-acetyl-1-naphthol.
10. 2-Hydroxy-cinnamylidene-acetophenone.
11. 2-Hydroxy-3:4-dimethoxy-cinnamylidene-acetophenone.
12. 2-Styryl-3-phenyl-1:4-α-naphthapyrone.
13. 3-Phenyl-2-o-methoxy styryl-1:4-α-naphthapyrone.
14. 3-Phenyl-2-p-methoxy styryl-1:4-α-naphthapyrone.
15. 3-Phenyl-2-(3:4'-dimethoxy styryl)-1:4-α-naphthapyrone.
16. 2-Styryl-3-benzyl-1:4-α-naphthapyrone.
17. 3-Benzyl-2-o-methoxy styryl-1:4-α-naphthapyrone.
18. 4'-Methoxy-2-styryl-3-benzyl-1:4-α-naphthapyrone.
19. 3-Benzyl-2-(3:4'-dimethoxy styryl)-1:4-α-naphthapyrone.
20. 2:3-Dimethoxy-1:4-α-naphthapyrone.
21. 2-Styryl-3-methyl-1:4-α-naphthapyrone.
22. 2-(3:4'-dimethoxy styryl)-3-methyl-1:4-α-naphthapyrone.
23. 2-Styryl-1:4-α-naphthapyrone.
24. 2-o-Methoxy styryl-1:4-α-naphthapyrone.
25. 2-p-Methoxy styryl-1:4-α-naphthapyrone.
26. 2-(3:4'-dimethoxy styryl)-1:4-α-naphthapyrone.
27. 1:8-Dimethoxy-2-styrylchromone.
28. 1:8:4'-Trimethoxy-2-styrylchromone.
29. 2-Styrylchromone.
30. 1:4'-Methoxy-2-styrylchromone.
31. 3:4'-Dimethoxy-2-styrylchromone.
32. 7-Methoxy-2-styrylchromone.
33. 7:4'-Dimethoxy-2-styrylchromone.
34. 7-Benzoyloxy-2-methylchromone.
35. 7-Benzoyloxy-2-styrylchromone.
36. 7-Hydroxy-2-styrylchromone.
37. 7:4'-Dibenzoyloxy-2-styrylchromone.
38. 7:4'-Dihydroxy-2-styrylchromone.
40. Palmaracetonone-2:4-dinitrophenylhydrazone.
41. 2:4-Chloracetophenone-4-benzyl ether.
42. 5:7-Dihydroxy-3-acetyl-2-methylchromone.
43. 5-Hydroxy-7-benzoyloxy-2-styrylchromone.
44. 5:7:4'-Trimethoxy-2-styrylchromone.
45. 5-Methoxy-7-benzoyloxy-2-methylchromone.
46. 5:7:4'-Trimethoxy-2:5'-dimethoxyflavone.
47. 5:7-Dihydroxy-3:4'-dimethoxy-4-benzoyloxyflavone.
48. 5:7:4'-Trihydroxy-3:5'-dimethoxyflavone.
49. 5:7:4'-Acetoxy-2:5'-dimethoxyflavone.
50. 2:4-Dihydroxy-8-methoxyacetophenone.
51. 2-Hydroxy-4-benzyloxy-6-methoxyacetophenone.
52. 2-Hydroxy-4:6-dibenzoyloxy-α-benzylacetophenone.
53. 3-Benzoyl chrysin dimethyl ether.
54. 5-Hydroxy-7-benzyloxy-6-benzylflavone.
55. 2-Benzoyloxy-4:8-dimethoxyacetophenone.
56. Flavone oxime.
57. 1:4-α-naphthoquinone oxime.
58. 3:4'-Dimethoxy-7-hydroxyflavone.
59. 3:4'-Dimethoxy-7-acetoxyflavone.
60. 3:7:4'-Trimethoxyflavone.
61. Benzylxycetonitrile.
62. α-Benzylxoyresacetophenone.
63. 2:4-Dinitrophenylhydrazone of α-benzylxoyresacetophenone.
64. Methyl-p-benzyloxy benzoate.
65. p-Benzylxoybenzoyl chloride.
66. p-Benzylxoybenzoic anhydride.
67. 3-Methoxy-7-hydroxy-4'-benzylxyflavone.
68. 3-Methoxy-7:4'-(di)hydroxyflavone.
69. 3-Methoxy-7:4'-diasetoxyflavone.
70. 3-Benzylxoy-7-hydroxy-4'-methoxyflavone.
71. 1-Propionyl-2-naphthol.
72. 2-Methyl-α-naphthaflavone.
73. 1-Propyl-2-naphthol.
74. β-Naphthol butyrate.
75. 1-Butyryl-2-naphthol.
76. 2-Ethyl-α-naphthaflavone.
77. 1-Butyl-2-naphthol.
78. α-Naphthol valerate.
79. 1-Valeryl-2-naphthol.
80. 2-Propyl-α-naphthaflavone.
81. 1-Pentyl-2-naphthol.
82. α-Naphthol caproate.
83. 1-Capryl-2-naphthol.
84. 2-Butyl-α-naphthaflavone.
85. 1-Hexyl-2-naphthol.
86. 2-Methyl-4-methoxy-5-isopropylbenzoylpropionic acid.
87. 2-Methyl-4-methoxy-5-isopropylphenylbutyric acid.
88. Ethyl-2-methyl-4-methoxy-5-isopropylphenyl butyrate.
89. 2-Methyl-4-methoxy-5-isopropylphenylbutyl alcohol.
List of Publications.

1. 2-styrylchromones  

2. The colouring matter of 'Khapli' wheat  
   K.C.Gulati & K.Venkataraman.
   Current Science, 1935, 238.

3. Antiseptic, and Anthel- 
   mintics, Part I.  
   Journal fur prakt. Chemie, 1933, 47.

4. The Dye of Acacia Wood  
   K.C.Gulati & K.Venkataraman.

   K.C.Gulati & K. Venkataraman.

6. Synthesis of 7-hydroxy and Journal Chemical Society 
   5;7-dihydroxy-2-styryl- 1934, 1765.  
   Chromones

7. Phloracetophenone  
   Organic Synthesis, Vol.15

8. Demethylation with alu- 
   minium chloride  
   K.C.Gulati & K.Venkataraman.
   Journal of the Chemical Society, 1933, 267.

9. A new method of oximation  
   Current Science, 1936.
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