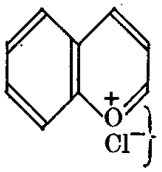
CHAPTER XV

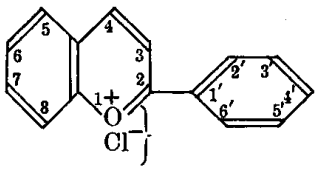
ANTHOCYANINS

§1. Introduction. Anthocyanins are natural plant pigments; they are glycosides and their aglycons, *i.e.*, the sugar-free pigments, are known as the *anthocyanidins*. The anthocyanins, which are water-soluble pigments, generally occur in the aqueous cell-sap, and are responsible for the large variety of colours in flowers; red—violet—blue. Willstätter *et al.* (1913–) showed that the various shades of colour exhibited by all flowers are due to a very small number of different compounds. Furthermore, these different compounds were shown to contain the same carbon skeleton, and differed only in the nature of the substituent groups. The anthocyanin pigments are amphoteric; their acid salts are usually red, their metallic salts usually blue and in neutral solution the anthocyanins are violet (see also §5).

§2. General nature of the anthocyanins. The fundamental nucleus in anthocyanidins is benzopyrylium chloride, but the parent compound is 2-phenylbenzopyrylium chloride or **flavylium chloride.** (The formulæ are now usually written with the oxygen atom at the top, *i.e.*, the formulæ



benzopyrylium chloride



flavylium chloride

shown are turned upside down; there is no change in numbering.) All anthocyanidins are derivatives of 3 : 5 : 7-trihydroxyflavylium chloride. The following table on page 546 shows some common anthocyanidins (as chlorides).

Various sugars have been found in anthocyanins; the most common are glucose, galactose and rhamnose, and the most important of these is glucose, which occurs as the diglucoside. Some pigments, as well as being glycosides, are also acylated derivatives, two common acids being *p*-hydroxybenzoic acid and malonic acid. The acid radical may be attached either to a phenolic hydroxyl group in the flavylium nucleus or to a hydroxyl group in the sugar residue.

A number of qualitative tests have been introduced to identify the various anthocyanins without actually isolating them (Robinson *et al.*, 1931–1933, 1938); *e.g.*,

(i) The pigment is extracted with amyl (pentyl) alcohol in the presence of sodium acetate containing a trace of ferric chloride; cyanidin gives a blue colour, delphinidin a less intense blue colour, and the others still less colour or no colour at all.

(ii) A dilute sodium hydroxide solution of the pigment is shaken with air; delphinidin (and petunidin) is decolorised and the others are not.

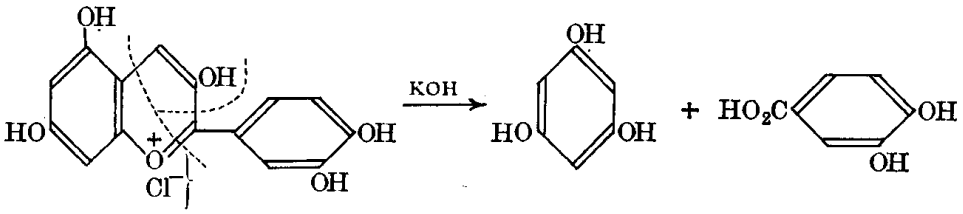
(iii) More recently chromatographic analysis has been used to identify anthocyanins (see also §5).

(iv) The spectra of the anthocyanins in the region 5000–5500 A are similar, but Geissman *et al.* (1953) have shown that the addition of aluminium chloride to solutions of certain anthocyanins shifts the absorption maximum. Only

Aglycon		Occurrence
Trivial name	Chemical name	
Pelargonidin .	3 : 4′ : 5 : 7-Tetrahydroxyflavylium chloride	Present in orange-red to scarlet flowers, *e.g.*, scarlet *Pelargonium*, orange-red dahlia.
Cyanidin . .	3 : 3′ : 4′ : 5 : 7-Pentahydroxyflavylium chloride	Present in crimson to bluish-red flowers, *e.g.*, deep red dahlia, red roses, blue cornflower.
Delphinidin .	3 : 3′ : 4 : 5 : 5′ : 7-Hexahydroxyflavylium chloride	Present in violet to blue flowers, *e.g.*, Delphinium.
Peonidin . .	3 : 4′ : 5 : 7-Tetrahydroxy-3′-methoxyflavylium chloride	Present in flowers less blue than the Cyanidin group, *e.g.*, red peony.
Malvidin (Syringidin)	3 : 4′ : 5 : 7-Tetrahydroxy-3′ : 5′-dimethoxyflavylium chloride	Present in flowers less blue than the Delphinidin group, *e.g.*, *Primula viscosa*.
Hirsutidin . .	3 : 4′ : 5-Trihydroxy-3′ : 5′ : 7-trimethoxyflavylium chloride	Present in *Primula hirsuta*.

anthocyanins with the 3′ : 4′-dihydroxyl groups *free* show this shift, and so this observation may offer a method for analysing anthocyanin mixtures.

§3. **Structure of the anthocyanidins.** The anthocyanin is first hydrolysed with hydrochloric acid and the anthocyanidin is then isolated as the chloride. The usual analytical methods are applied to determine the number of hydroxyl and methoxyl groups present in the molecule. The structure of the anthocyanidin is ascertained by the nature of the products obtained by fusing the anthocyanidin with potassium hydroxide (Willstätter *et al.*, 1915); phloroglucinol or a methylated phloroglucinol and a phenolic acid are always obtained, *e.g.*, cyanidin chloride gives phloroglucinol and protocatechuic acid.

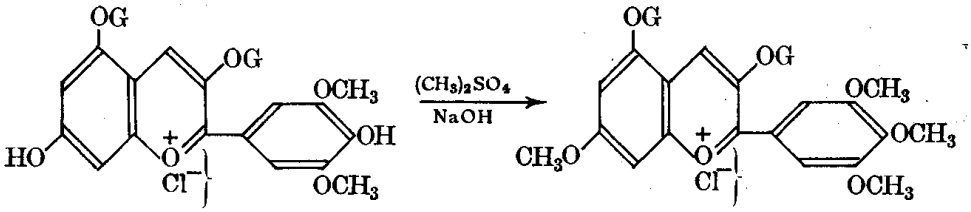


cyanidin chloride

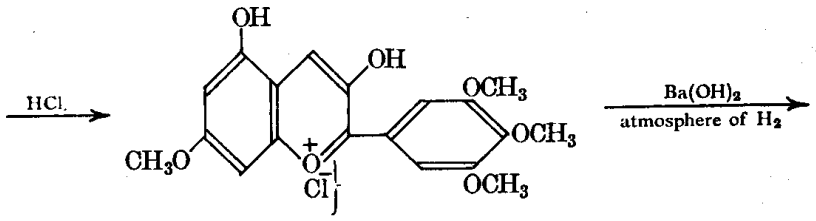
This method suffers from the disadvantage that the fusion (or boiling with concentrated potassium hydroxide solution) not only degrades the anthocyanidin, but also often demethylates it at the same time. Thus the positions of the methoxyl groups in the original compound are now rendered uncertain. This difficulty was overcome by Karrer *et al.* (1927), who degraded the anthocyanidin with a 10 per cent. solution of barium hydroxide or sodium hydroxide in an atmosphere of hydrogen; in this way, the methoxyl groups are left intact.

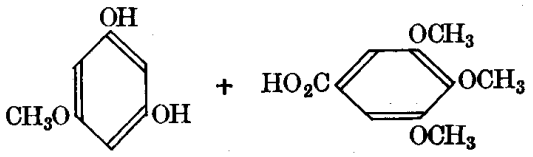
The next problem is to ascertain the positions of the sugar residues.

(i) Karrer *et al.* (1927) methylated the anthocyanin, then removed the sugar residues by hydrolysis (hydrochloric acid), and finally hydrolysed with barium hydroxide solution in an atmosphere of hydrogen; the positions of the *free* hydroxyl indicate the points of attachment of the sugar residues. In some cases, however, interpretation of the results is uncertain, *e.g.* (G represents a sugar residue):



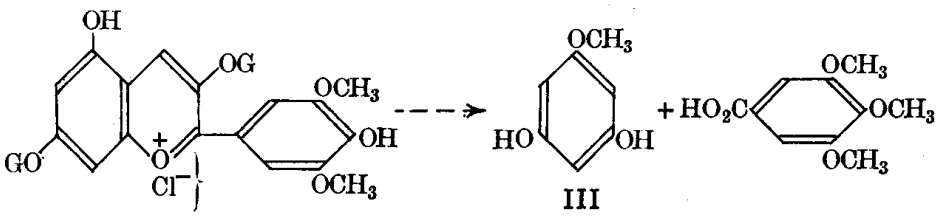
I II





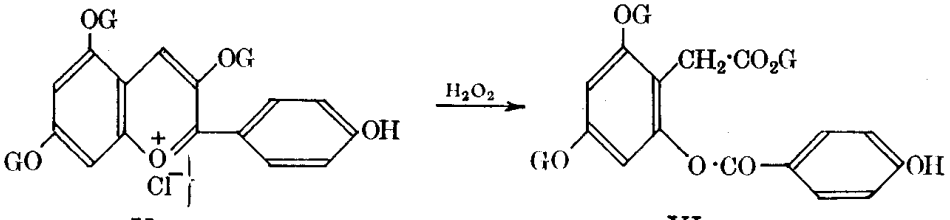
III

The problem is: Which of the two hydroxyl groups in monomethylphloroglucinol was originally attached to G? The above results do not lead to a definite answer, since had the structure of the anthocyanin been IV instead of I, III would still have been obtained:



IV

(ii) Hydrogen peroxide (15 per cent.) attacks anthocyanins as follows (Karrer *et al.*, 1927):



V VI

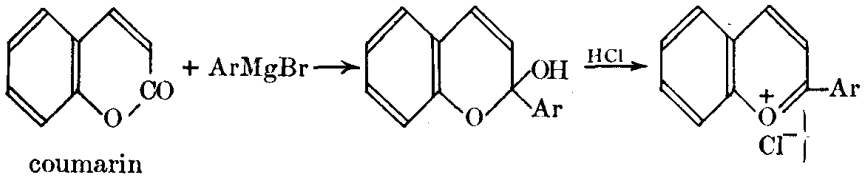
If the anthocyanin, V, has a glucose residue in the 3-position, then *this* glucose residue in VI is readily hydrolysed by dilute ammonia. If the glucose residue in V is in either the 5- or 7-position, then this glucose residue in VI is removed only by heating with dilute hydrochloric acid. Thus position 3 can be distinguished from positions 5 or 7, but the latter two cannot be distinguished from each other.

(iii) Anthocyanins with a free hydroxyl group in the 3-position are very readily oxidised by ferric chloride; the anthocyanins are rapidly decolorised in this oxidation (Robinson *et al.*, 1931).

Conclusive evidence for the positions of the sugar residues is afforded by the synthesis of the anthocyanins (see, *e.g.*, cyanin, §5). In general, it has been found that glucose residues are linked at positions 3 or 3 : 5.

§4. General methods of synthesising the anthocyanidins.

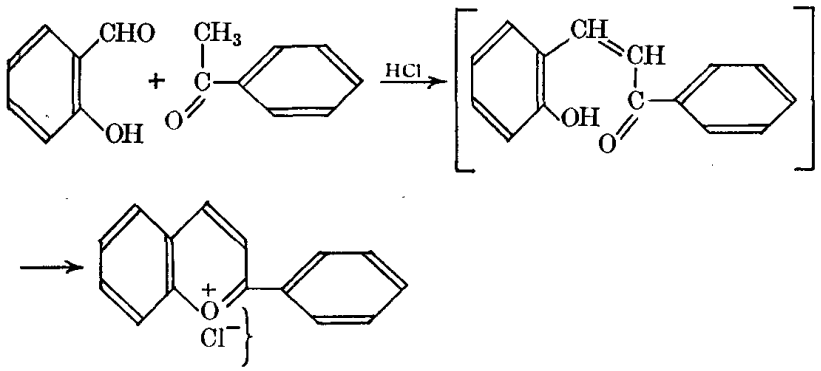
(i) Willstätter (1914) synthesised anthocyanidins starting from coumarin.



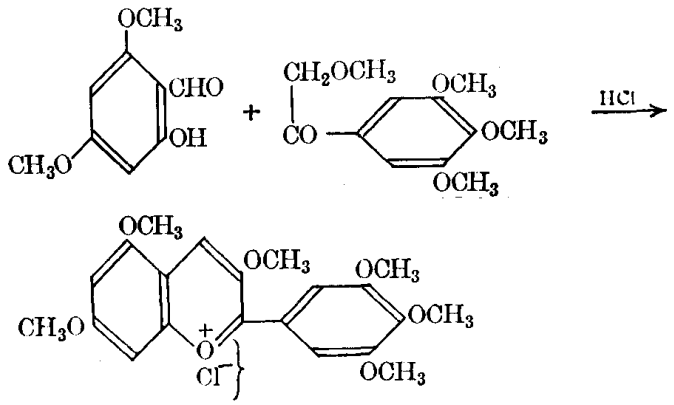
coumarin

This method has very limited application.

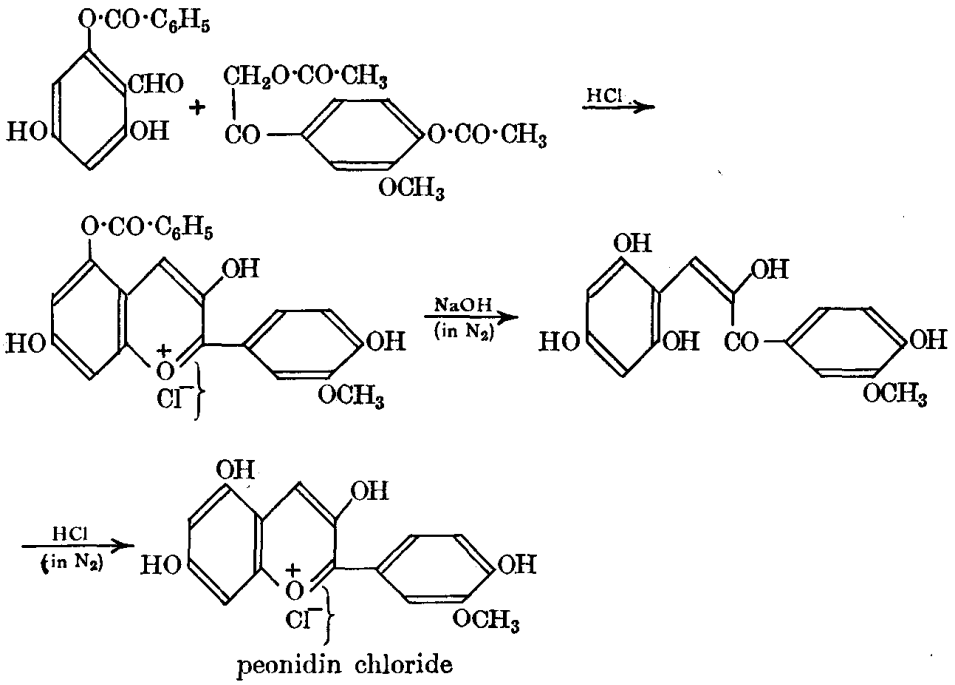
(ii) Robinson has introduced a number of methods whereby *all* anthocyanidins can be prepared. The basic reaction of these methods is the condensation between *o*-hydroxybenzaldehyde and acetophenone in ethyl acetate solution which is then saturated with hydrogen chloride.



The original method of Robinson (1924) resulted in the formation of a product in which the substituent groups were either all hydroxyl groups or all methoxyl groups, *e.g.*,



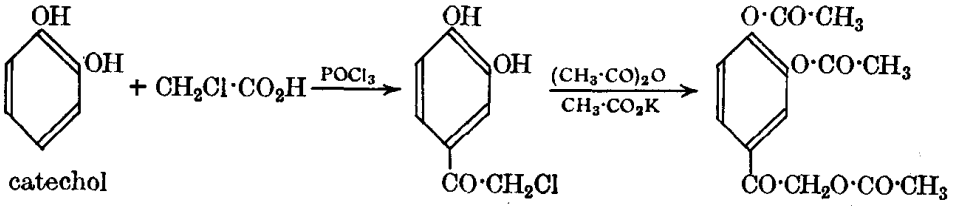
Robinson (1928, 1931) then modified this method so that the product could have both hydroxyl and methoxyl substituent groups, *e.g.*,



peonidin chloride

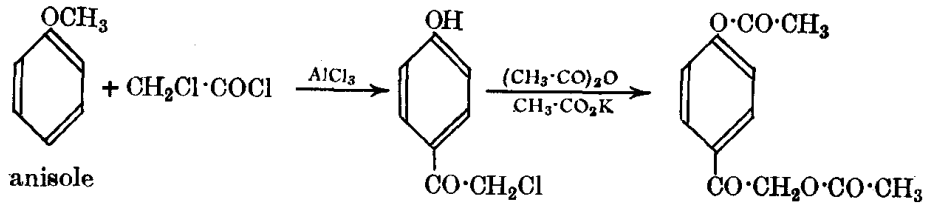
The following is a brief account of the methods used by Robinson and his co-workers for preparing the substituted acetophenones and substituted benzaldehydes.

ω : 3 : 4-Triacetoxyacetophenone.



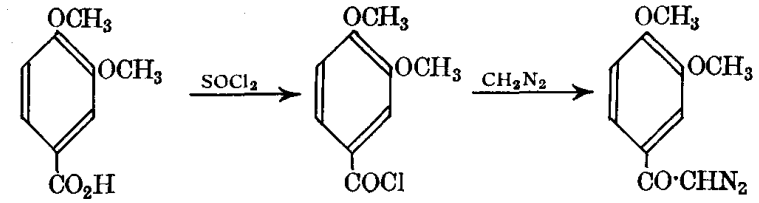
catechol

ω : 4-Diacetoxyacetophenone.

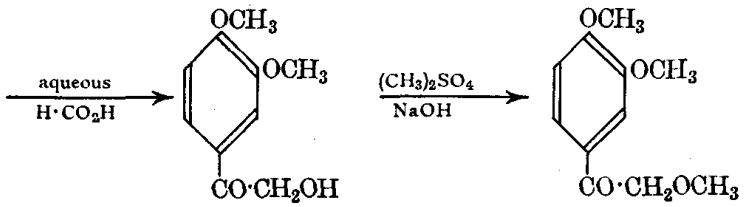


anisole

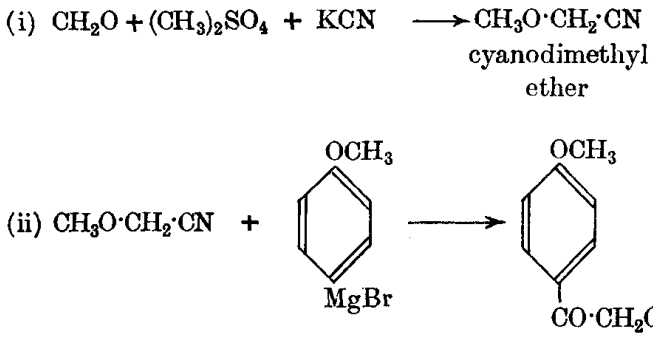
ω : 3 : 4-Trimethoxyacetophenone.



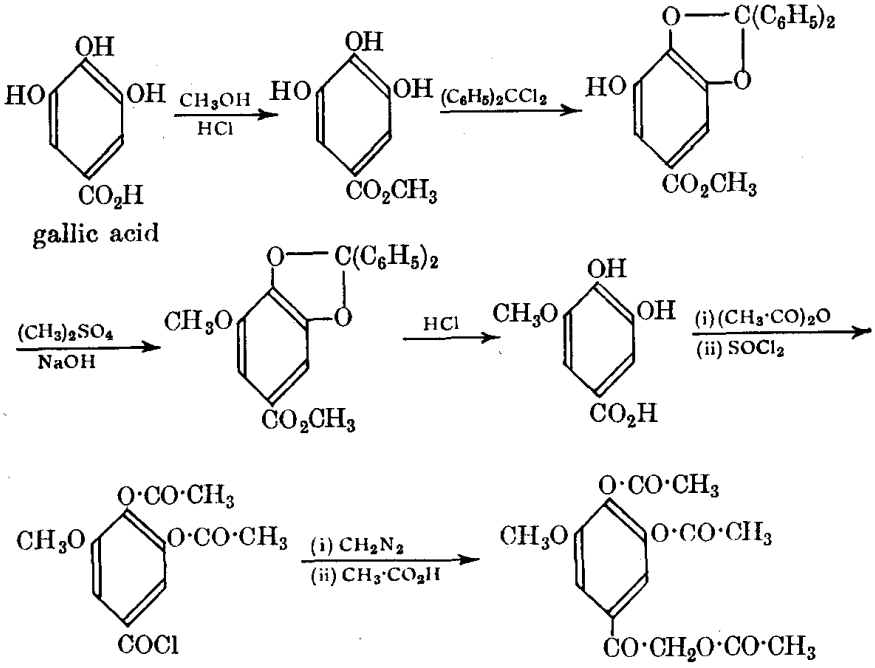
veratric acid diazoketone



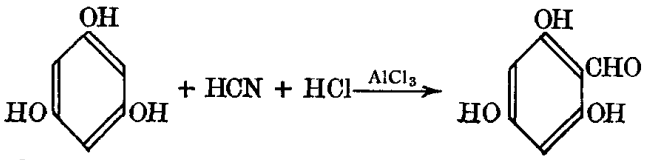
ω : 4-Dimethoxyacetophenone.



ω : 3 : 4-Triacetoxy-5-methoxyacetophenone.

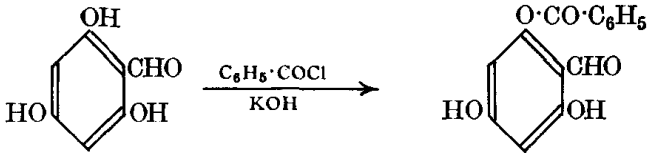


2 : 4 : 6-Trihydroxybenzaldehyde (phloroglucinaldehyde).



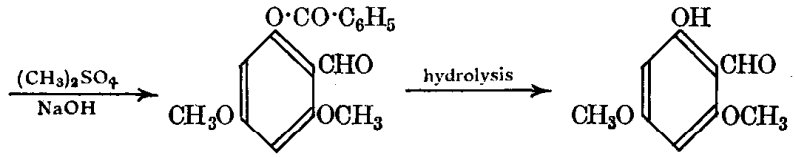
phloroglucinol

2-Hydroxy-4 : 6-dimethoxybenzaldehyde.



phloroglucinaldehyde

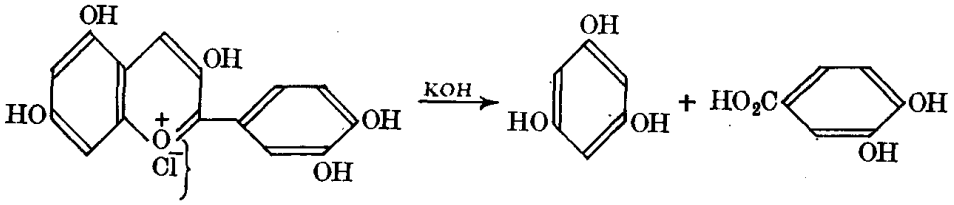
2-benzoylphloroglucinaldehyde-(2-benzoyloxy-4:6-dihydroxybenzaldehyde)



§5. Cyanidin chloride, $C_{15}H_{11}O_6Cl$. Cyanin chloride, on hydrolysis with hydrochloric acid, gives cyanidin chloride and two molecules of D-glucose.

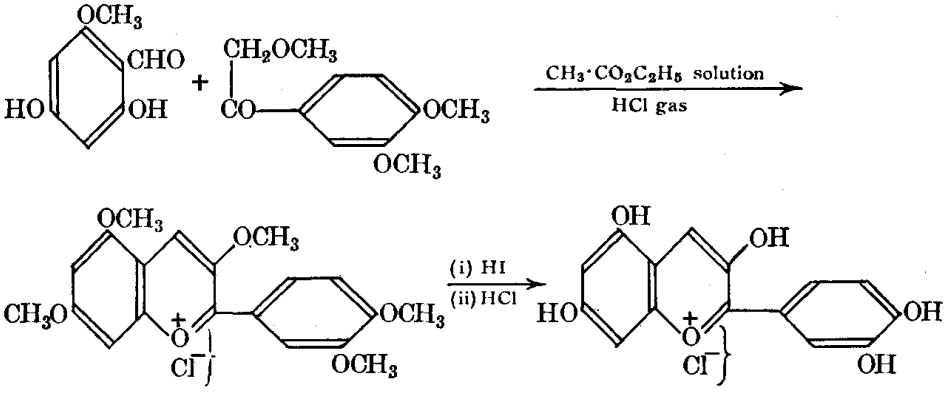
$$C_{27}H_{31}O_{16}Cl + 2H_2O \xrightarrow{HCl} C_{15}H_{11}O_6Cl + 2C_6H_{12}O_6$$

Since cyanidin chloride forms a penta-acetate, the molecule therefore contains five hydroxyl groups. No methoxyl groups are present, and so the potassium hydroxide fusion may be used to degrade this compound; this gives phloroglucinol and protocatechuic acid. Thus cyanidin chloride has the following structure:



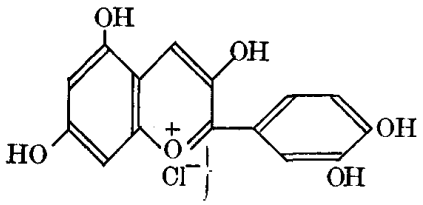
cyanidin chloride

This structure has been confirmed by synthesis (Robinson *et al.*, 1928):

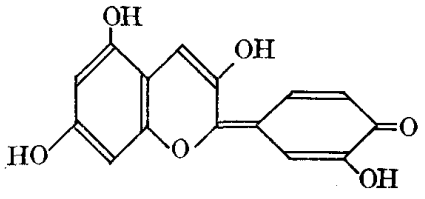


The formation of phloroglucinol and protocatechuic acid by the alkaline fusion of cyanidin chloride suggests a relationship to quercetin, since the latter also gives the same fusion products (see §14).

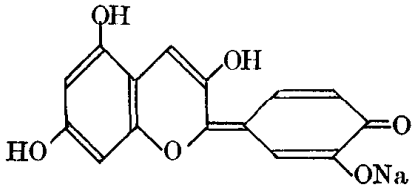
Cyanidin is insoluble in water, but is very soluble in ethanol. It is also soluble in aqueous sodium hydroxide, the solution being blue. The addition of hydrochloric acid changes the colour to purple when the solution is neutral, and when acid the solution becomes red. According to Everest (1914), the colours are due to the following structures (see also Ch. XXXI, Vol. I):



Oxonium salt
Red in acid solution



Colour base
Purple in neutral solution

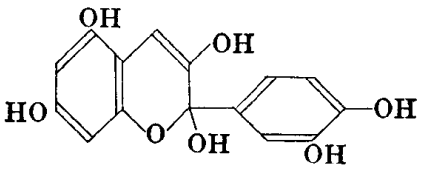


Salt of the colour base
Blue in alkaline solution

Thus a variation of the *p*H will produce a variation in the range of colour.

On the basis of these ionic structures (positive for oxonium salts and negative for salts of the colour bases), anthocyanins should migrate in an electric field. Markakis (1960) has shown that various anthocyanins, when placed within an electric field applied across filter paper, move to the anode or cathode according to the *p*H of the solution. The method of paper electrophoresis may prove to be a very good means of separating, purifying, characterising and preparing anthocyanins.

Markakis also showed that isoelectric point (§4c. XIII) and the *p*H of minimum colour display coincide. On the acidic side of the isoelectric point, the oxonium salt-form predominates; and when the *p*H is higher than that of the isoelectric point, the salt of the colour base predominates. Sondheimer (1953) proposed that a pseudo-base of the structure shown is also possible (this is formed by the addition of a molecule of water to the colour

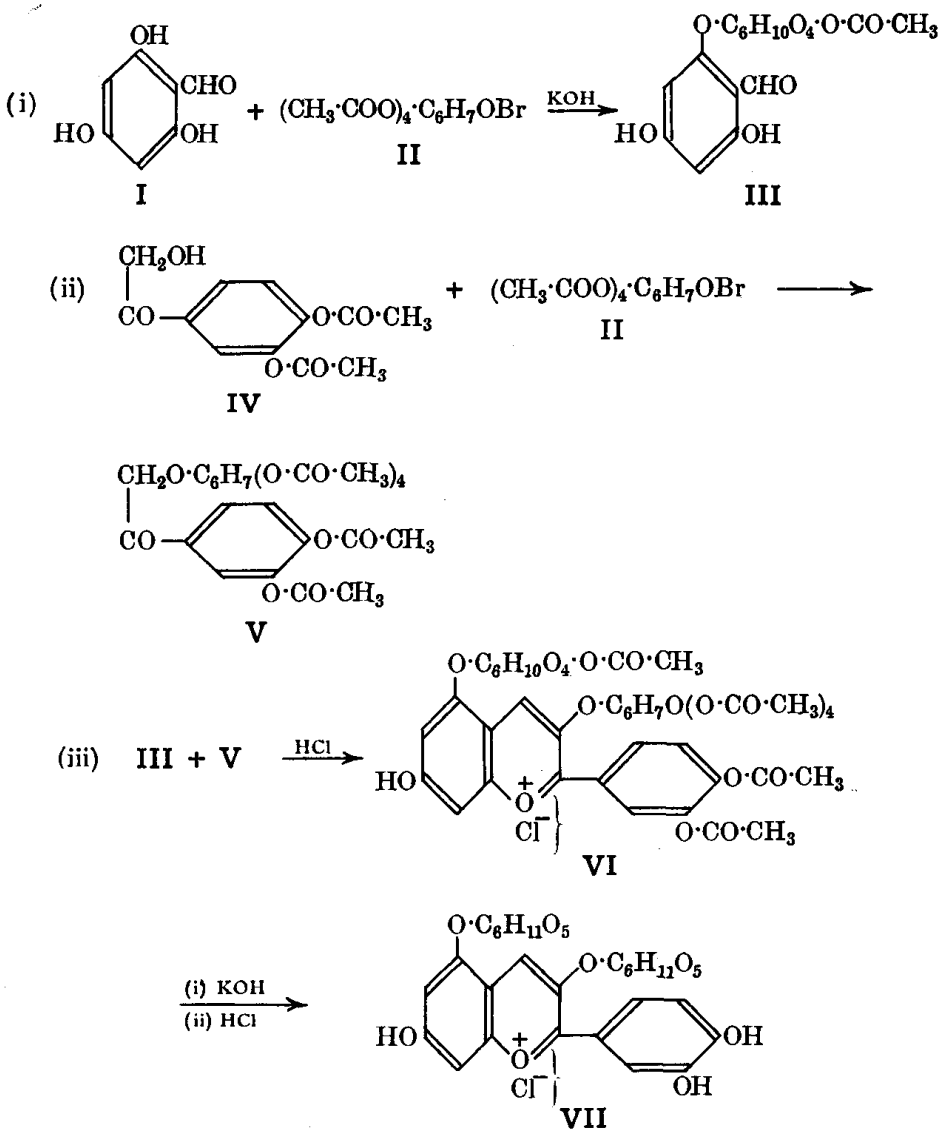


pseudo-base

base), and according to Markakis, it is this form which probably predominates at the isoelectric point. This structure has an interrupted conjugated bond system, and hence will be less coloured than the colour base itself.

Cyanin was the first anthocyanin to be isolated and its structure determined. It has been synthesised by Robinson *et al.* (1932). Phloroglucin-

aldehyde, I, is condensed with tetra-acetyl-α-bromoglucose, II (*cf.* §24. VII), in acetone solution to which has been added aqueous potassium hydroxide; the product is 2-*O*-monoacetyl-β-glucosidylphloroglucinaldehyde, III. ω-Hydroxy-3 : 4-diacetoxyacetophenone, IV, is also condensed with tetra-acetyl-α-bromoglucose (II) in benzene solution to give ω-*O*-tetra-acetyl-β-glucosidoxy-3 : 4-diacetoxyacetophenone, V. Compounds III and V are then dissolved in ethyl acetate and the solution saturated with hydrogen chloride; the product, VI, is treated first with cold aqueous potassium hydroxide and then with hydrochloric acid, whereby cyanin chloride, VII, is produced.

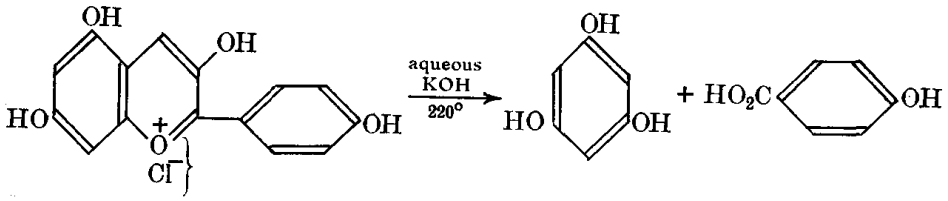


§6. **Pelargonidin chloride,** $C_{15}H_{11}O_5Cl$. This is formed, together with two molecules of glucose, when pelargonin chloride is hydrolysed with hydrochloric acid.

$$C_{27}H_{31}O_{15}Cl + 2H_2O \xrightarrow{HCl} C_{15}H_{11}O_5Cl + 2C_6H_{12}O_6$$

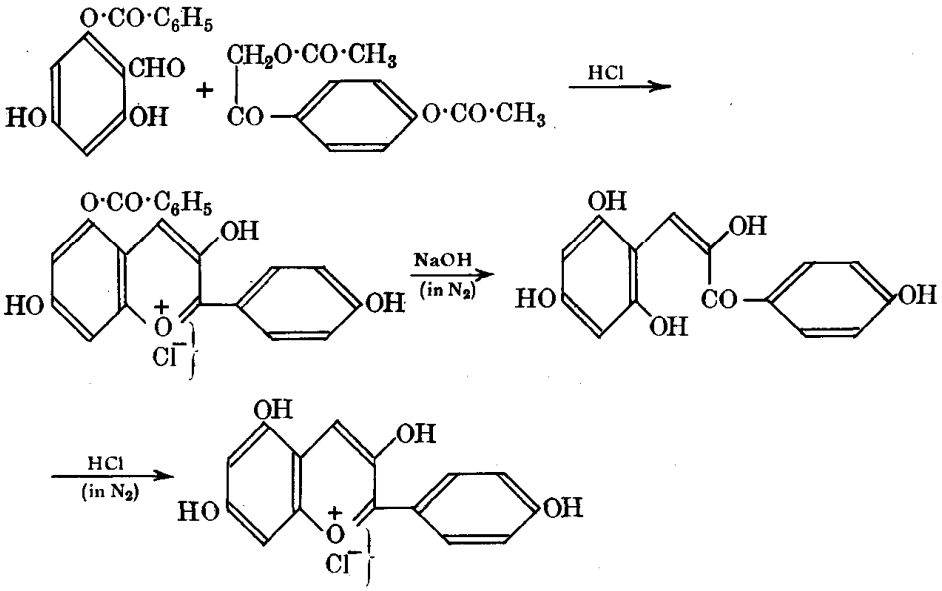
Since pelargonidin chloride forms a tetra-acetate, the molecule contains four hydroxyl groups. Furthermore, since there are no methoxyl groups

present, the potassium hydroxide fusion or boiling with concentrated potassium hydroxide solution may be used to degrade the compound; the products are phloroglucinol and *p*-hydroxybenzoic acid, and so the structure is probably as shown:

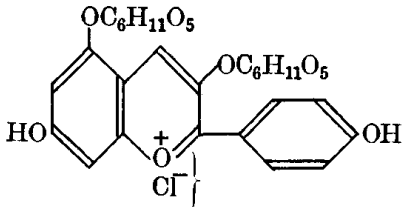


pelargonidin chloride

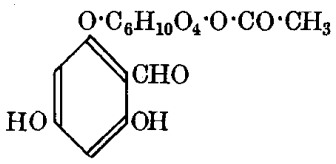
This structure has been confirmed by synthesis, *e.g.*, Robinson *et al.* (1928).



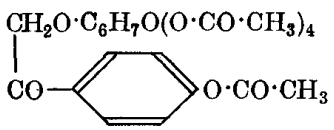
Pelargonin chloride, I, has been synthesised by Robinson *et al.* (1932) from 2-*O*-monoacetyl-*β*-glucosidylphloroglucinaldehyde, II, and *ω*-*O*-tetraacetyl-*β*-glucosidoxy-4-acetoxyacetophenone, III (*cf.* cyanin chloride, §5).



I

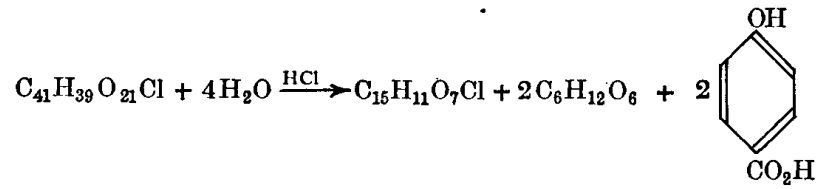


II

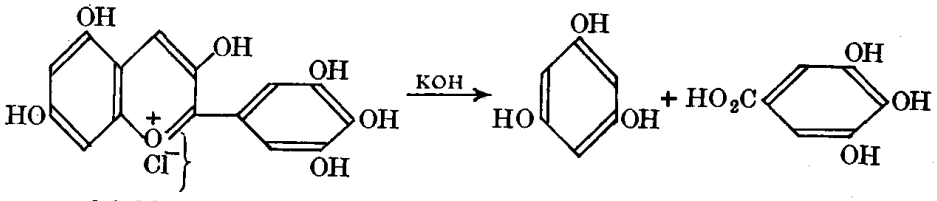


III

§7. **Delphinidin chloride,** $C_{15}H_{11}O_7Cl$, is obtained, together with two molecules of glucose and two molecules of *p*-hydroxybenzoic acid, when delphinin chloride is hydrolysed with hydrochloric acid.



Delphinidin chloride contains six hydroxyl groups, and no methoxyl groups; on fusion with potassium hydroxide, the products are phloroglucinol and gallic acid.



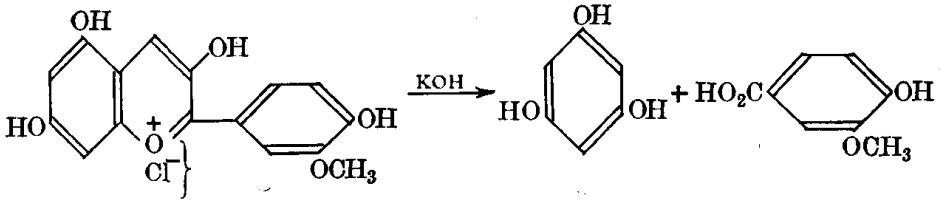
delphinidin chloride

This structure has been confirmed by synthesis, starting from 2-benzoylphloroglucinaldehyde and $\omega : 3 : 4 : 5$-tetra-acetoxyacetophenone (Robinson *et al.*, 1930).

§8. **Peonidin chloride,** $C_{16}H_{13}O_6Cl$, is produced, together with two molecules of glucose, when peonin chloride is hydrolysed with hydrochloric acid.

$$C_{28}H_{33}O_{16}Cl + 2H_2O \xrightarrow{HCl} C_{16}H_{13}O_6Cl + 2C_6H_{12}O_6$$

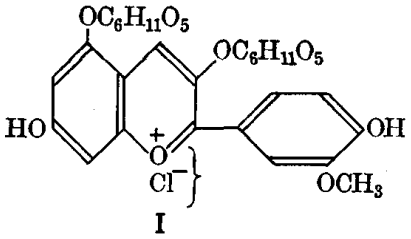
When heated with hydrogen iodide in the presence of phenol, peonidin chloride is demethylated to give cyanidin chloride. Thus peonidin is the monomethyl ether of cyanidin. Heating peonidin chloride with potassium hydroxide solution produces 4-hydroxy-3-methoxybenzoic acid and phloroglucinol. Thus:



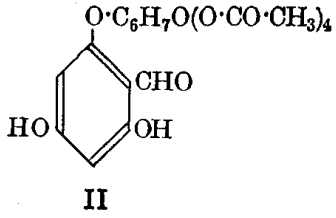
peonidin chloride

This structure has been confirmed by synthesis from 2-benzoylphloroglucinaldehyde and ω : 4-diacetoxy-3-methoxyacetophenone (Robinson *et al.*, 1926).

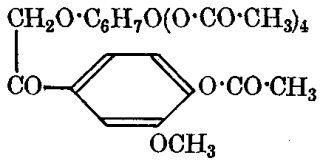
Peonin chloride, I, has been synthesised by Robinson *et al.* (1931), using 2-*O*-tetra-acetyl-β-glucosidylphloroglucinaldehyde, II, and ω-tetra-acetyl-β-glucosidoxy-4-acetoxy-3-methoxyacetophenone, III.



I



II

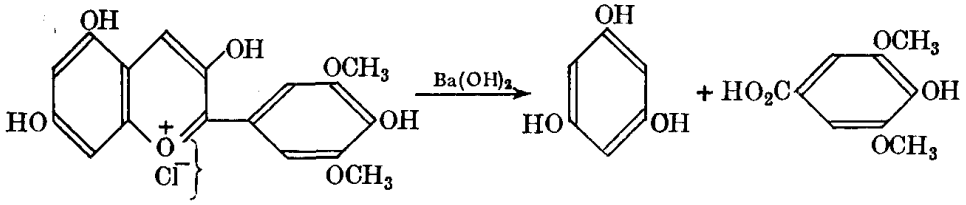


III

§9. **Malvidin chloride,** $C_{17}H_{15}O_7Cl$, is produced, together with two molecules of glucose, when malvin chloride is hydrolysed with hydrochloric acid.

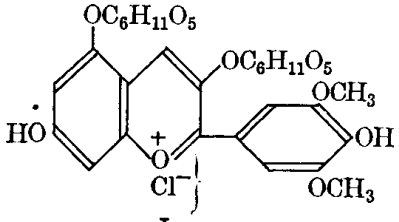
$$C_{29}H_{35}O_{17}Cl + 2H_2O \xrightarrow{HCl} C_{17}H_{15}O_7Cl + 2C_6H_{12}O_6$$

Malvidin chloride contains four hydroxyl groups and two methoxyl groups. When degraded by boiling barium hydroxide solution in an atmosphere of hydrogen, the products are phloroglucinol and *syringic acid* (4-hydroxy-3 : 5-dimethoxybenzoic acid). Thus:

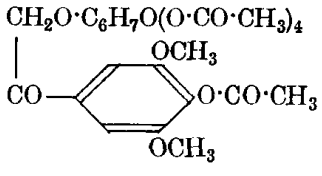


malvidin chloride

Robinson *et al.* (1928) confirmed this structure by synthesis, starting from 2-benzoylphloroglucinaldehyde and ω-acetoxy-4-benzyloxy-3 : 5-dimethoxyacetophenone (*cf.* §10). Robinson *et al.* (1932) have also synthesised **malvin chloride,** I, by condensing 2-*O*-tetra-acetyl-β-glucosidylphloroglucinaldehyde with ω-*O*-tetra-acetyl-β-glucosidoxy-4-acetoxy-3 : 5-dimethoxyacetophenone, II.



I



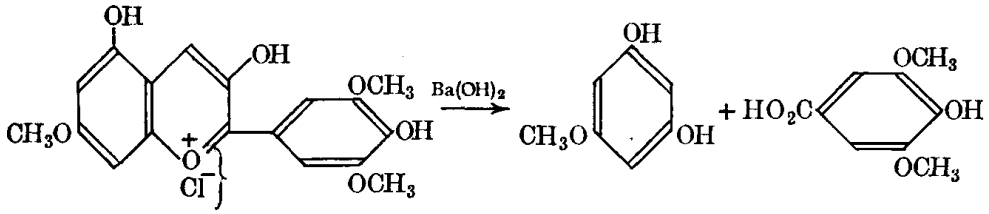
II

§10. **Hirsutidin chloride,** $C_{18}H_{17}O_7Cl$, is produced by the hydrolysis of hirsutin chloride with hydrochloric acid; two molecules of glucose are also produced.

$$C_{30}H_{37}O_{17}Cl + 2H_2O \xrightarrow{HCl} C_{18}H_{17}O_7Cl + 2C_6H_{12}O_6$$

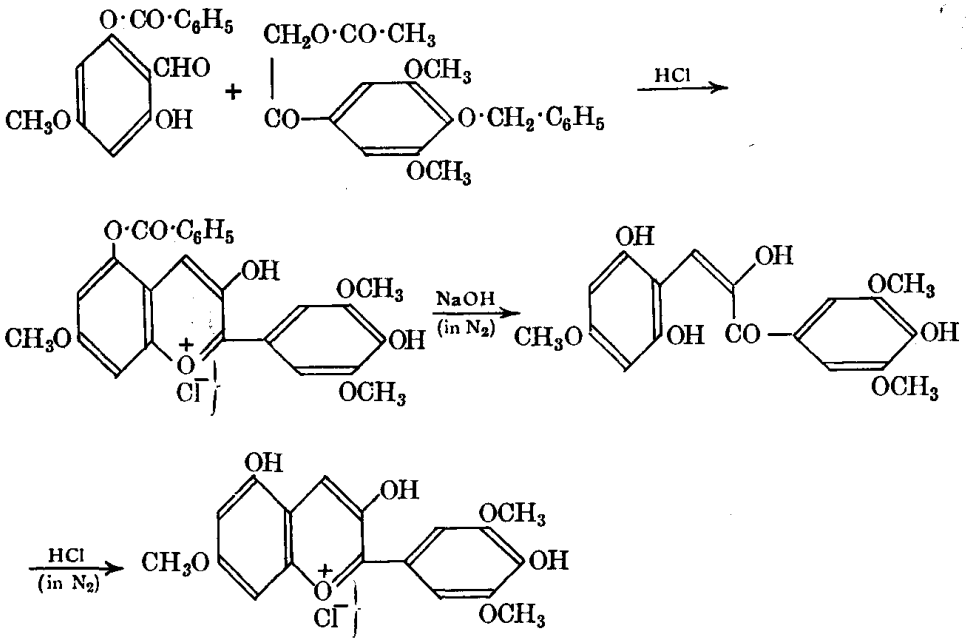
Hirsutidin chloride contains three hydroxyl groups and three methoxyl groups. Its structure is shown from the fact that on hydrolysis with barium

hydroxide solution in an atmosphere of hydrogen, the products are monomethylphloroglucinol and syringic acid. The formation of these products

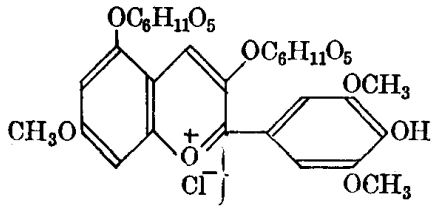


hirsutidin chloride

does not prove conclusively that the methoxyl group at position 7 is actually there; had this position been interchanged with the hydroxyl group at position 5, monomethylphloroglucinol would still have been obtained (*cf.* §3). The formula given for hirsutidin chloride, however, has been confirmed by synthesis, starting from 2-benzoyl-4-*O*-methylphloroglucinaldehyde and ω-acetoxy-4-benzyloxy-3 : 5-dimethoxyacetophenone (Robinson *et al.*, 1930).



Hirsutin chloride has also been synthesised by Robinson *et al.* (1932) from 2-*O*-tetra-acetyl-β-glucosidyl-4-*O*-methylphloroglucinaldehyde and ω-*O*-tetra-acetyl-β-glucosidoxy-4-acetoxy-3 : 5-dimethoxyacetophenone.

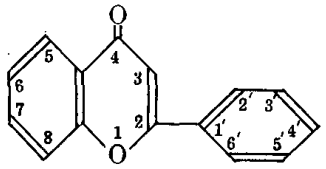


hirsutin chloride

FLAVONES

§11. Introduction. The flavones, which are also known as the **anthoxanthins,** are yellow pigments which occur in the plant kingdom. Flavones

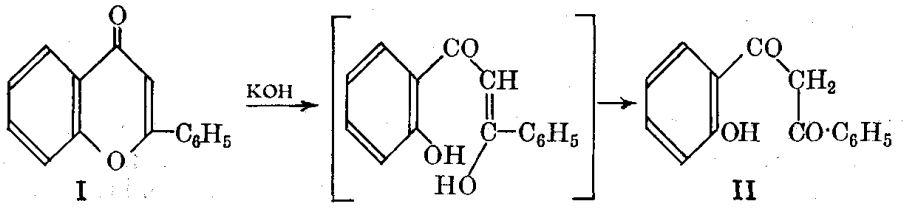
occur naturally in the free state, or as glycosides (the aglycon is the *anthoxanthidin* and the sugar is glucose or rhamnose), or associated with tannins. Chemically, the flavones are very closely related to the anthocyanins; the flavones are hydroxylated derivatives of *flavone* (2-phenyl-4-chromone) which may be partially alkylated. In almost all cases positions 5 and 7 are



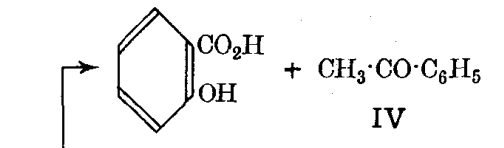
flavone

hydroxylated, and frequently one or more of positions 3′, 4′ and 5′. The general method of ascertaining the structure of the flavones is similar to that used for the anthocyanins: the number of free phenolic groups and the number of methoxyl groups are first determined, and then the products obtained by alkaline fusion or hydrolysis are examined. Finally, the structure is confirmed by synthesis. Recently, Simpson *et al.* (1954) have shown that methoxyflavones may be demethylated selectively by hydrobromic acid, the relative rates being $3' > 4' > 7$. These authors have also shown that the relative rates of methylation of flavone-hydroxyl groups with methyl sulphate and sodium hydrogen carbonate in acetone solution are $7 > 4' > 3' > 3$. With methyl sulphate and aqueous alcoholic sodium carbonate, the exact reverse of this order is obtained. These results thus offer a method of ascertaining the positions of methoxyl groups in various methoxyflavones.

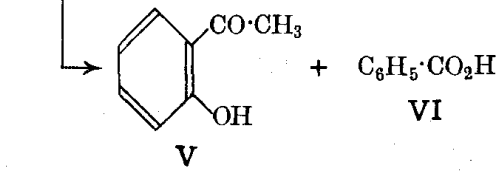
§12. Flavone, $C_{15}H_{10}O_2$, occurs naturally as " dust " on flowers, leaves, etc. When boiled with concentrated potassium hydroxide solution, flavone, I, gives a mixture of four products, salicylic acid (III), acetophenone (IV), *o*-hydroxyacetophenone (V) and benzoic acid (VI). The products, which are produced in the pairs III and IV, and V and VI, arise from the fact that the opening of the pyrone ring produces *o*-hydroxydibenzoylmethane, II, which then undergoes scission in two different ways (II is a β-diketone).



I II



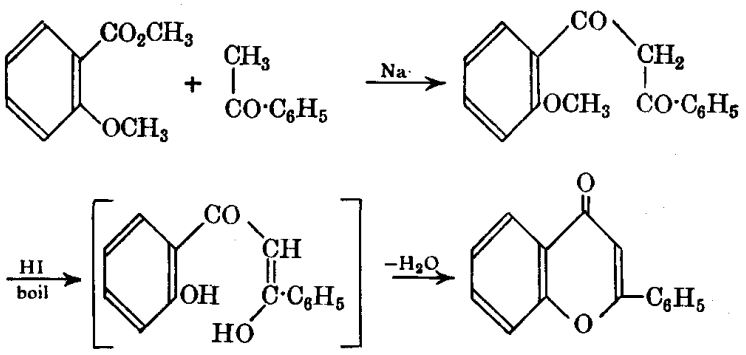
III IV



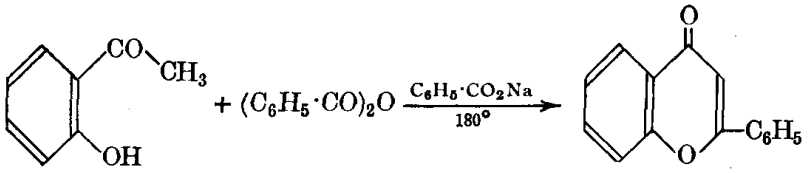
V VI

In general, all the flavones give a mixture of four products when degraded with potassium hydroxide. The intermediate *o*-hydroxy-*β*-diketone can be isolated if *cold* alkali or an ethanolic solution of sodium ethoxide is used. On the other hand, if a normal solution of barium hydroxide is used as the degrading agent, then the products are usually salicylic acid and acetophenone (Simonis, 1917).

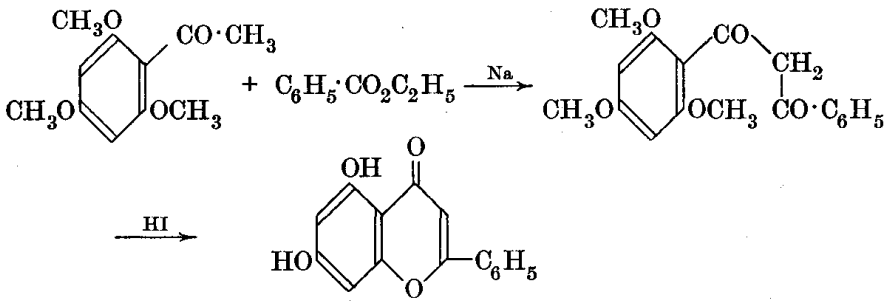
The structure given for flavone has been confirmed by synthesis. Many syntheses are known, *e.g.*, *the Kostanecki synthesis* (1900). This is a general method for synthesising flavones, and consists in condensing the ester of an alkylated salicylic acid with an acetophenone in the presence of sodium (this is an example of the Claisen condensation; this synthesis is a reversal of the formation of III and IV). Thus, for flavone itself, the reaction is carried out with methyl *o*-methoxybenzoate and acetophenone.



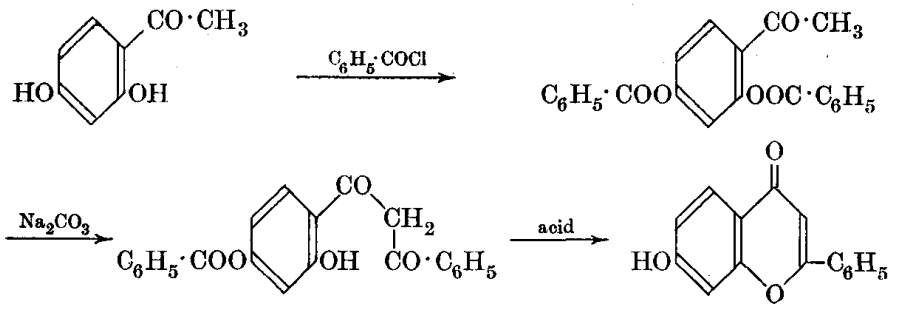
The most useful general synthetic method for preparing flavones is that of Robinson (1924). This is a reversal of the formation of V and VI; an *o*-hydroxyacetophenone is heated at about 180° with the anhydride and sodium salt of a substituted benzoic acid, *e.g.*, flavone:



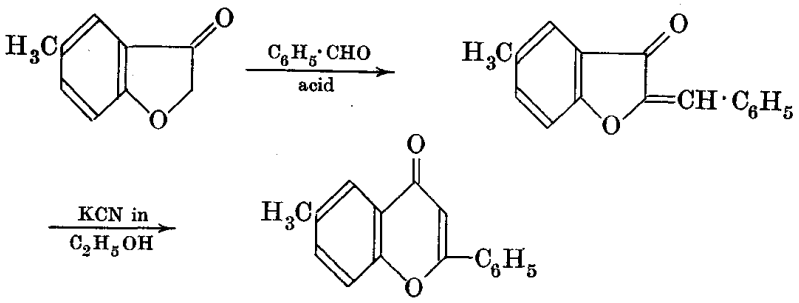
Another general method which is also a reversal of the formation of V and VI is illustrated by the preparation of *chrysin* (5 : 7-dihydroxyflavone) from 2 : 4 : 6-trimethoxyacetophenone and ethyl benzoate.



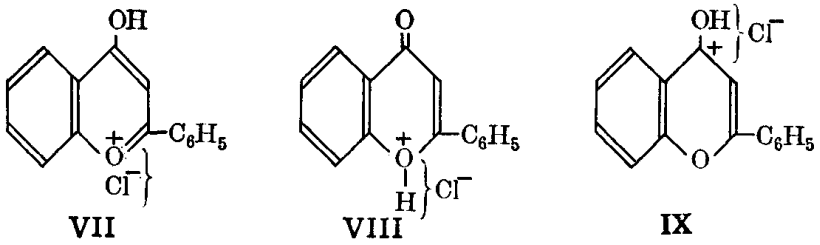
This preparation involves a Claisen condensation, and the following is also another general method which involves an " internal " Claisen condensation.



A recent method for synthesising flavones is by the ring expansion of 2-benzylidenecoumaran-3-ones (Wheeler *et al.*, 1955), *e.g.*,

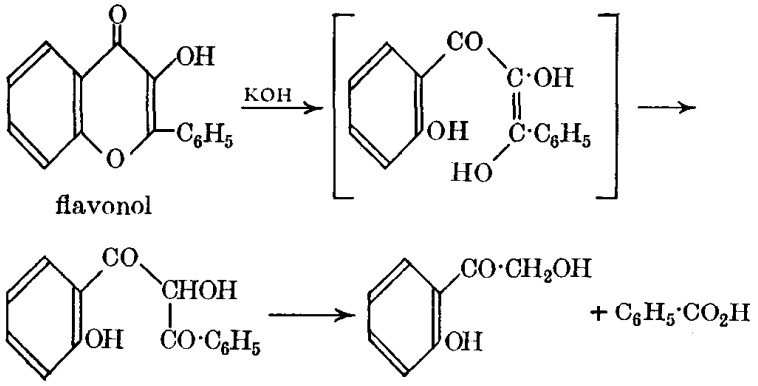


Most flavones are yellow solids which are soluble in water, ethanol and dilute acids and alkalis. The oxonium salts are usually more highly coloured than the free bases; the flavones do not occur naturally as salts (*cf.* anthocyanins). The structure of flavone salts is not certain; VII, VIII and IX are possibilities, and according to calculations of charge distribution (in γ-pyrone salts), IX appears to be most likely (Brown, 1951).

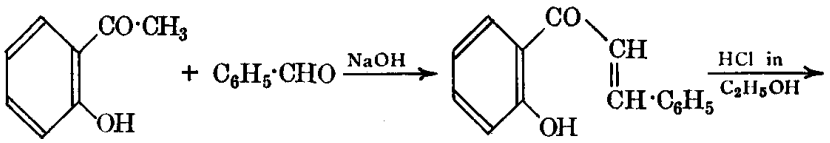


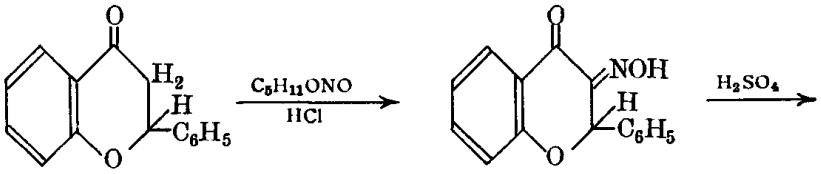
§13. Flavonol (3-hydroxyflavone), $C_{15}H_{10}O_3$. Flavonol is widely distributed in the plant kingdom, usually in the form of glycosides.

When boiled with an ethanolic solution of potassium hydroxide, flavonol gives *o*-hydroxybenzoylmethanol and benzoic acid. This suggests that flavonol is 3-hydroxyflavone (3-hydroxy-2-phenyl-γ-chromone).

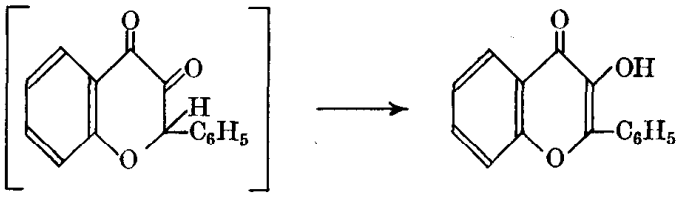


This structure has been confirmed by various syntheses, *e.g.*, Kostanecki *et al.* (1904). This is a general method, and uses the Claisen reaction between *o*-hydroxyacetophenones and substituted benzaldehydes, *e.g.*, flavonol.



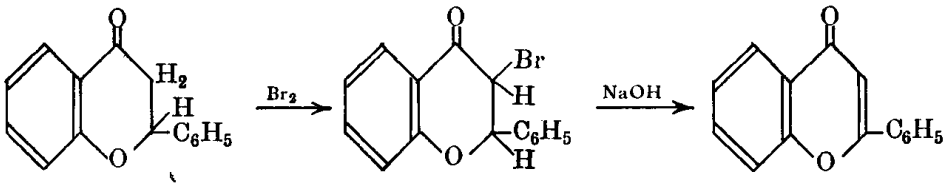


flavanone



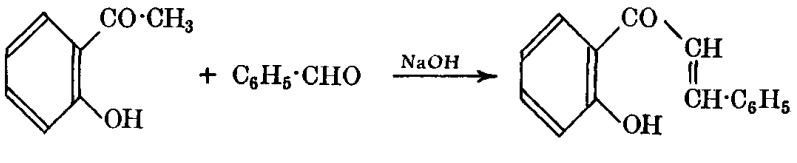
keto form enol form; flavonol

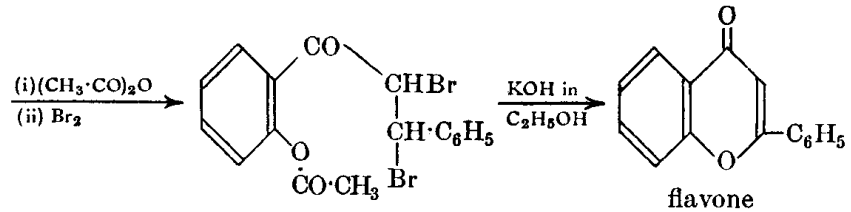
The synthesis, starting from flavanone, has been adapted to the preparation of flavones.



flavanone flavone

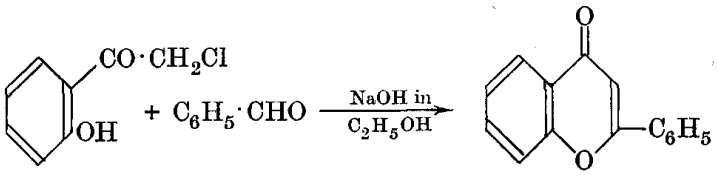
An alternative general method for preparing flavones based on the flavonol synthesis is as follows (Kostanecki *et al.*, 1898):





flavone

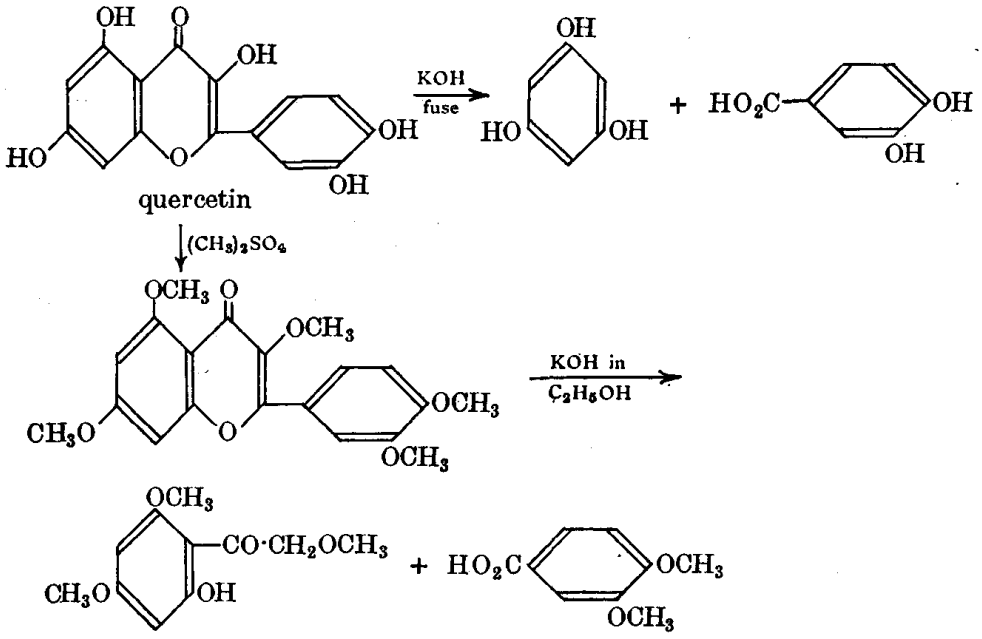
This synthesis has been simplified by Wheeler *et al.* (1955); these authors prepared flavones by condensing ω-chloro-*o*-hydroxyacetophenones with aromatic aldehydes in the presence of ethanolic sodium hydroxide, *e.g.*,



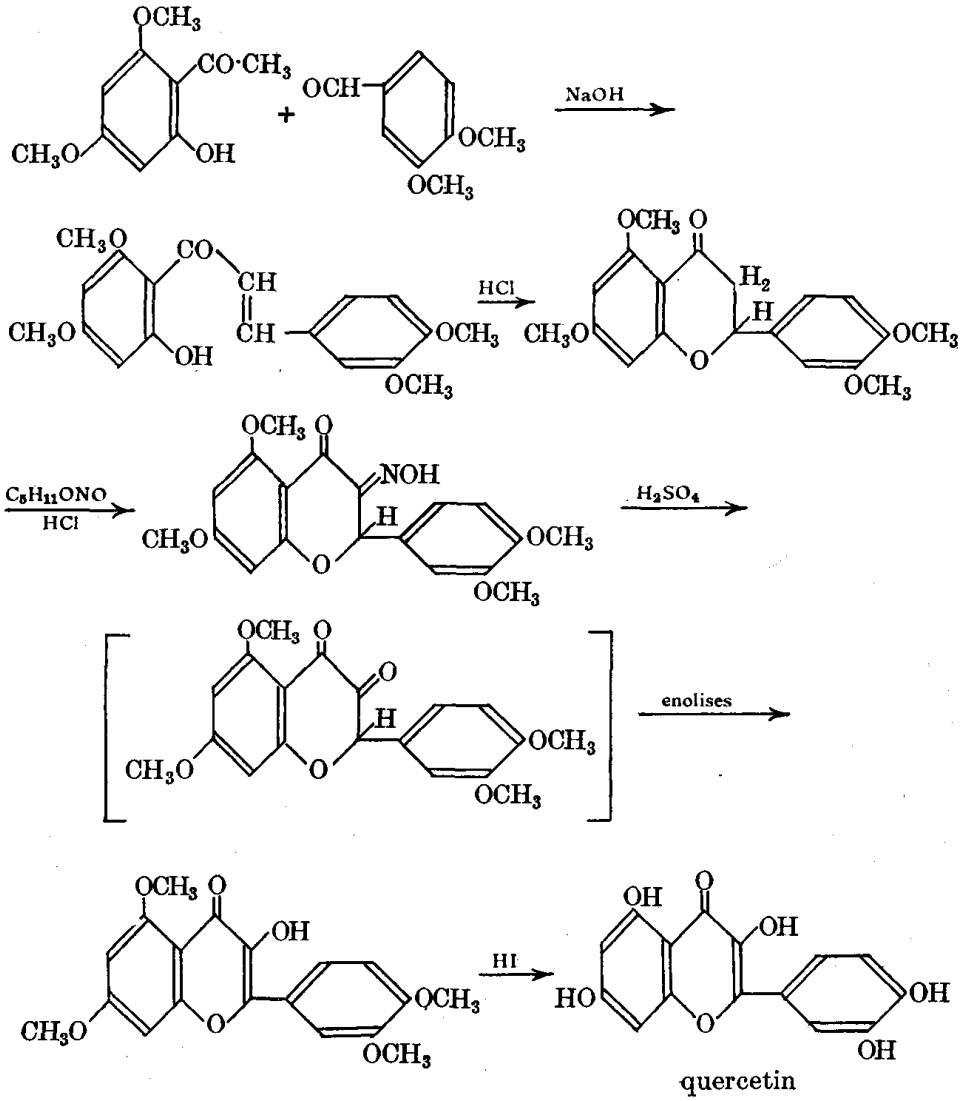
§14. Quercetin, $C_{15}H_{10}O_7$, occurs as the glycoside *quercitrin* in the bark of *Quercus tinctoria*; quercitrin appears to be the most widely distributed natural pigment. On hydrolysis with acids, quercitrin forms quercetin and one molecule of rhamnose.

$$C_{21}H_{20}O_{11} + H_2O \xrightarrow{HCl} C_{15}H_{10}O_7 + CH_3{\cdot}(CHOH)_4{\cdot}CHO$$

Quercetin contains five hydroxyl groups; no methoxyl groups are present; on fusion with potassium hydroxide, phloroglucinol and protocatechuic acid are obtained (*cf.* cyanidin, §5). Also, when quercetin is methylated and the product, pentamethylquercetin, boiled with an ethanolic solution of potassium hydroxide, 6-hydroxy-ω : 2 : 4-trimethoxyacetophenone and veratric acid are obtained. These results suggest that quercetin is 3 : 3′ : 4′ : 5 : 7-pentahydroxyflavone.

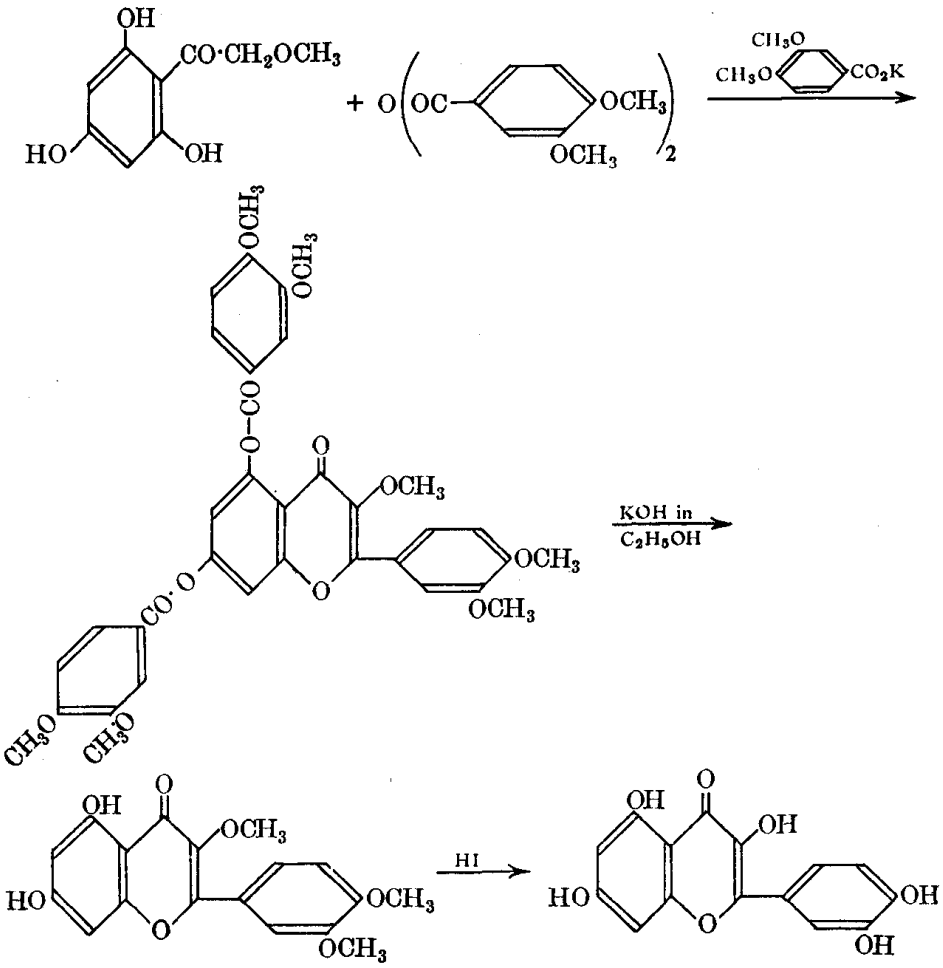


This structure has been confirmed by synthesis, *e.g.*, Kostanecki *et al.* (1904).



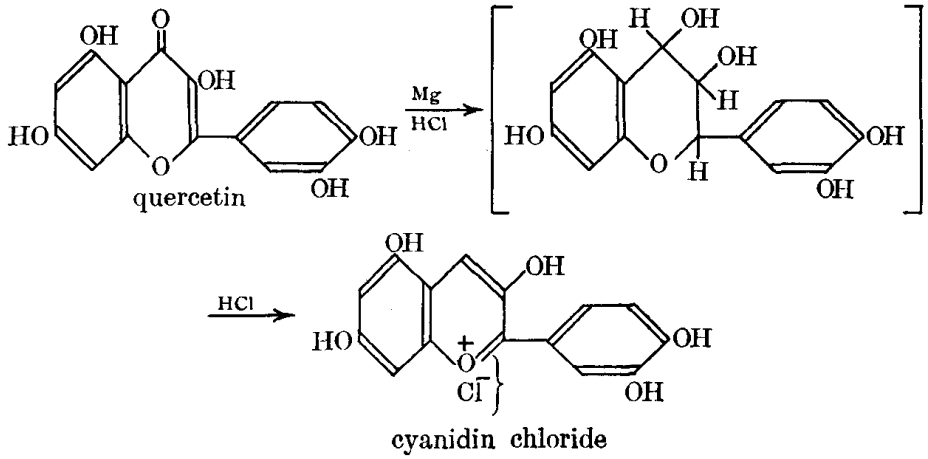
quercetin

Another synthesis is that of Robinson *et al.* (1926); it is a general method for flavonols (*cf.* flavone, §12): ω-methoxyphloroacetophenone is condensed with veratric anhydride in the presence of the potassium salt of veratric acid.



The position of the rhamnose residue in quercitrin has been shown to be **3** (Herzig *et al.*, 1912).

Before leaving this problem of quercetin, let us consider its relationship to cyanidin (§5). As we have seen, the relationship between the two compounds is suggested by the fact that both give the same products when fused with potassium hydroxide. Willstätter *et al.* (1914) reduced quercetin with magnesium in hydrochloric acid containing mercury, and thereby obtained a small amount of cyanidin chloride.



Bauer *et al.* (1954) have converted the penta-acetate of quercetin into cyanidin chloride by means of lithium aluminium hydride.

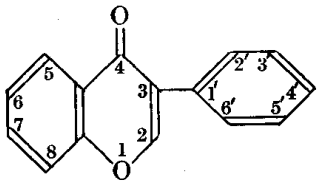
King *et al.* (1957) have shown that the reductive acetylation of a flavonol, followed by the action of hot hydrochloric acid, gives the corresponding anthocyanidin; thus:

$$\text{quercetin} \xrightarrow[\text{(ii) HCl}]{\text{(i) Zn-AcONa; } Ac_2O} \text{cyanidin chloride}$$

This appears to be a useful general method.

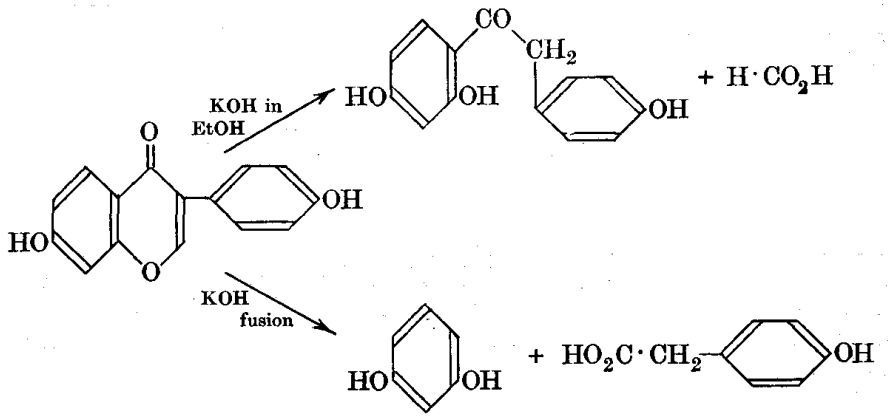
ISO*FLAVONES*

§14a. *iso*Flavones are hydroxylated derivatives of *iso*flavone (3-phenyl-4-chromone) which may be partially alkylated. The *iso*flavones occur



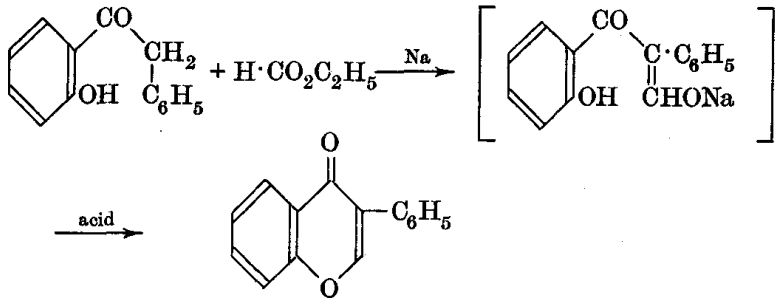
*iso*flavone

naturally, but are not so widespread as the flavones; they occur either in the free state or as glycosides. The general method of ascertaining the structure of *iso*flavones is similar to that used for the flavones (see §§3, 11). Thus fusion with potassium hydroxide breaks down the molecule into two fragments, and hydrolysis with ethanolic potassium hydroxide permits the isolation of intermediates. This may be illustrated with *daidzein* (Walz, 1931):

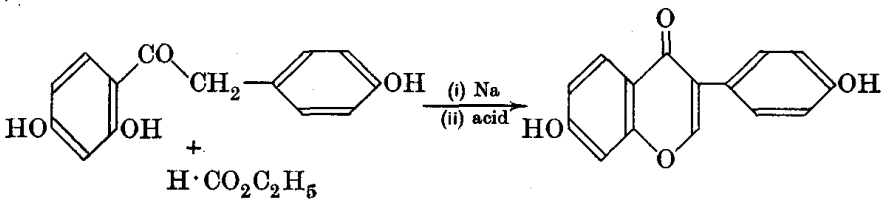


Oxidation with alkaline hydrogen peroxide may also be used in degrading *iso*flavones; recognisable fragments are not usually obtained by this method, but sometimes information may be obtained about the substituents in the 3-phenyl nucleus, *e.g.*, *genistein* (4′ : 5 : 7-trihydroxy*iso*flavone) gives *p*-hydroxybenzoic acid.

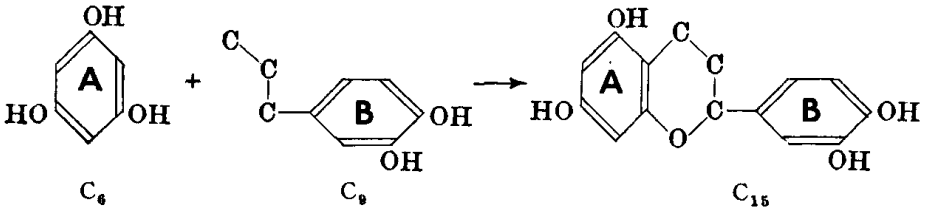
The final proof of the structure of an *iso*flavone lies in its synthesis. A general method of synthesising *iso*flavones is that of Späth *et al.* (1930); *e.g.*, *iso*flavone itself may be synthesised from benzyl *o*-hydroxyphenyl ketone and ethyl formate:



By using substituted ketones, various *iso*flavones may be synthesised, *e.g.*, daidzein from 2 : 4-dihydroxyphenyl *p*-hydroxybenzyl ketone (Wessely *et al.*, 1933):



§14b. Biosynthesis of the flavonoids. Robinson (1936) considered the C_{15} skeleton of flavonoids to be composed of two parts, C_6 and C_9:



Biosynthetic work has shown that rings A and B are derived from different sources. Birch *et al.* (1955) have carried out the biosynthesis of benzenoid compounds from acetate, *e.g.*, using cultures of *Penicillium griseofulvin*, it was shown that:

Underhill *et al.* (1957), using ^{14}C-labelled compounds, showed that in the biosynthesis of quercetin and cyanidin, rings A and B have different origins; ring A appears to be produced from acetate, but ring B is produced by the shikimic acid pathway (§18. XIII). Biosynthetic studies of cyanidin (Weygand *et al.*, 1957; Grisebach, 1958) also support the origin of phloroglucinol (ring A) from acetate units.

DEPSIDES

§15. Depsides. Phenolic acids, by the interaction of the carboxyl group of one molecule with the hydroxyl group of another, give rise to **depsides:**