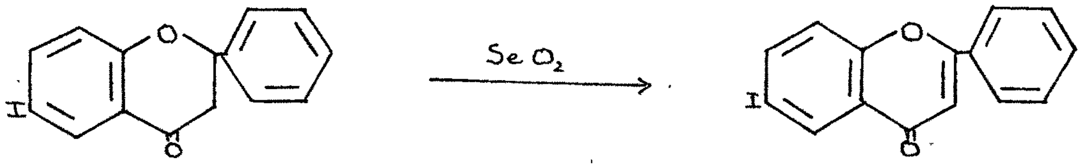
Part I

Section I (i)

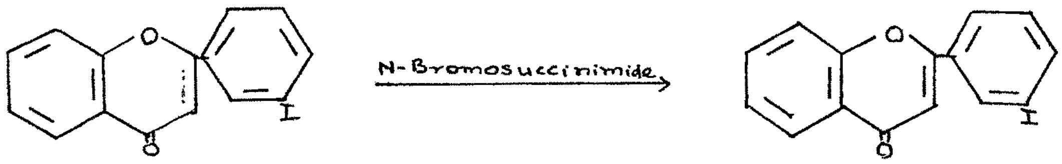
THEORETICAL

Iodination of some chromones and flavones

In the review of the work done on the halogenation of chromones and flavones, it has been seen that iodination of chromones and flavones has not been systematically studied. A few iodo flavones have been synthesised by other methods. Mulchandani and Shah (Ber., 1960, 93, 1913) synthesised 6-iodoflavone and 6-iodo-4'-methoxyflavone by dehydrogenation of the



corresponding flavanones with selenium dioxide and 6-iodo-3',4'-methylenedioxyflavone from ~~the~~ 2'-hydroxy-5'-iodo-3,4-methylenedioxychalcone ~~by~~ treat~~ed~~ment with selenium dioxide. They also obtained 6-iodo-3-hydroxyflavone from 2'-hydroxy-5'-iodochalcone by alkaline hydrogen peroxide treatment. Chen and Yang (J. Taiwan Pharm. Assoc., 1951, 3, 39; C.A.,1955, 49, 2432) prepared 3'-iodo- and 4'-iodoflavone by dehydrogenation of the corresponding



flavanone with N-bromo-succinimide. Chen and Chang (J. Chinese Chem. Soc., 1954, series II, I, 159 C.A. 1955, 49, 13932) synthesised 6-iodo-4'-methoxy-3-hydroxyflavone from 2'-hydroxy-5'-iodo-4-methoxychalcone by alkaline hydrogen peroxide treatment. The same authors (J. Chem. Soc., 1958, 146) obtained 7-iodoflavone from 2'-hydroxy-4'-iodochalcone by selenium dioxide and (ii) by the dehydrogenation of 7-iodoflavanone obtained from 2'-hydroxy-4'-iodochalcone with N-bromo-succinimide. 7-Iodo-4'-methoxyflavone was obtained from 2'-hydroxy-4'-iodo-4-methoxychalcone by treatment with selenium dioxide. ~~treatment~~. 7-Iodo-3-hydroxyflavone and 7-iodo-4'-methoxy-3-hydroxyflavone were obtained from the corresponding chalcones by alkaline hydrogen peroxide treatment.

Very recently, after the work on the iodination of chromones and flavones described in this thesis was published (J. Chem. Soc., 1959, 2676 ; 1960, 3899) Jurd (Chem. and Ind., 1961, 322) reported the synthesis of 7-hydroxy-8-iodo flavone, 3'-iodo-4'-methoxyflavone and 8-iodo-4',7-dimethoxy flavone by the cyclisation of the β-diketones obtained by the Baker- Venkataraman transformation of the corresponding iodo-*o*-benzoyloxyacetophenones.

No other work on the synthesis of iodochromone and flavone derivatives appears to have been reported. The iodination of 2-methylchromone, flavone, 5-hydroxy-2-methyl-chromone, 5-hydroxyflavone, 7-hydroxy-2-methylchromone and 7-hydroxyflavone ~~now~~ has now been studied and the structures of the iodo compounds obtained established.

The iodination of chromones has been studied with three different iodinating agents (i) iodine and iodic acid, (ii) iodine and ammonia and (iii) iodine monochloride.

The iodination is assumed to take place according to the following equations :

(i) In iodine and iodic acid :

$$5\ RH + 4I + HIO_3 \longrightarrow 5\ RI + 3\ H_2O$$

(ii) In iodine and ammonia :

$$3\ I_2 + NH_3 \longrightarrow NI_3 + 3\ HI$$

$$3\ RH + NI_3 \longrightarrow 3\ RI + NH_3$$

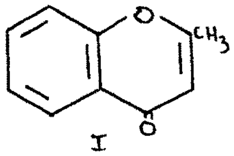
(iii) In iodine monochloride :

$$RH + ICl \longrightarrow RI + HCl$$

Iodination with iodine and iodic acid was found to be quite smooth and better yields were obtained by this method in most of the cases than by the other two methods and therefore the iodination of flavones has been studied mainly with iodine and iodic acid. Further, higher iodo derivative was obtained in the case of 7-hydroxy-2-methylchromone only by this method.

Attempted iodination of 2-methylchromone and flavones

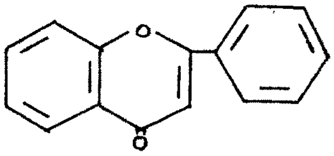
2-Methylchromone (I) and flavone (II) were subjected to the action of the above iodinating agents under varying conditions of time, temperature and quantities. Neither of these compounds gave an iodo derivative with iodine and iodic acid or iodine and ammonia. With iodine monochloride chloro



I

↓

No iodo derivative



II

↓

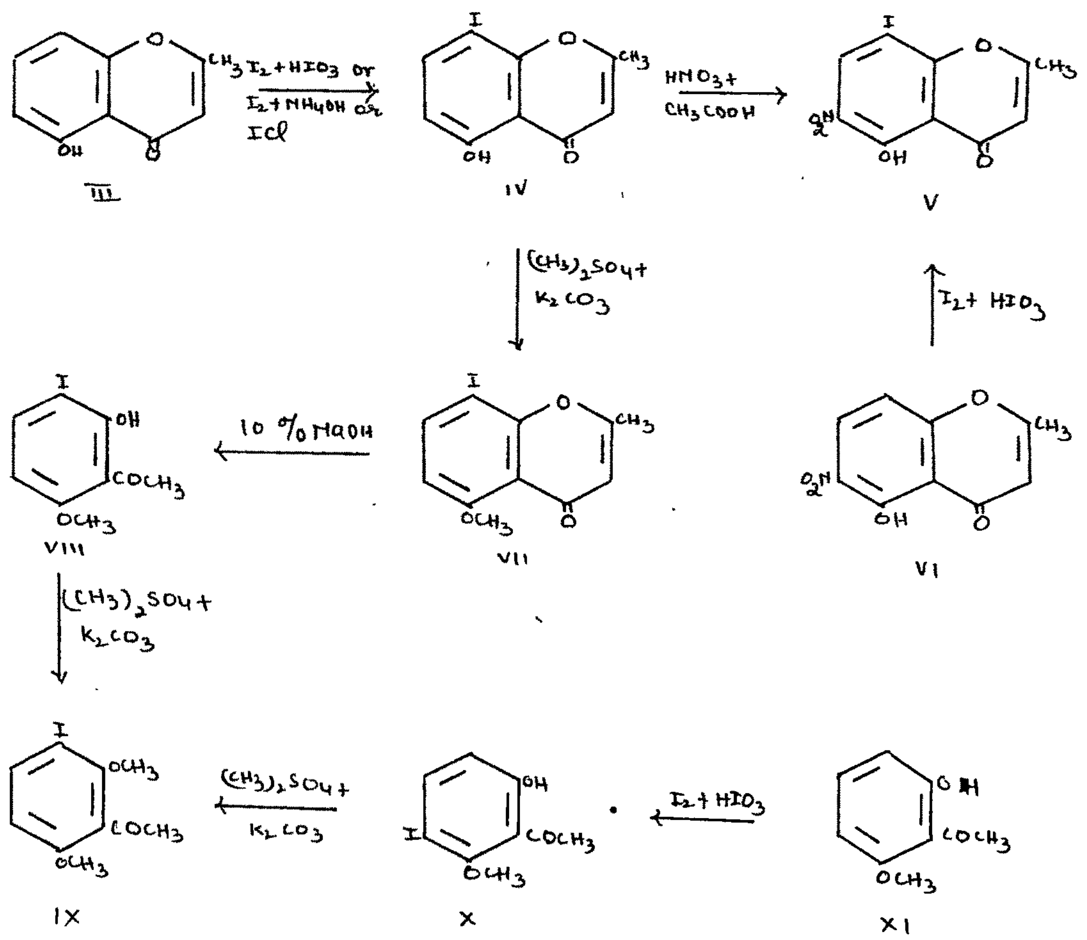
No iodo derivative

derivatives were obtained in both the cases but these have not been investigated further.

Iodination of 5-hydroxy-2-methylchromone and its methyl ether

5-Hydroxy-2-methylchromone (III) (Limaye and Kelkar J. Indian Chem. Soc., 1935, 12, 788) on iodination with the theoretical amounts of iodine and iodic acid according to equation (i) gave a mono-iodo derivative the methyl ether of which on hydrolysis with hot alkali gave a mono-iodophenolic ketone, indicating that the iodine atom had entered the benzenoid part of the molecule. This iodo ketone was found to be different from the mono-iodination product obtained from 2-hydroxy-6-methoxyacetophenone (XI) by iodination with iodine and iodic acid. The methyl ethers of both were however found to be identical. The position of the iodine atom in the chromone molecule was determined as follows :

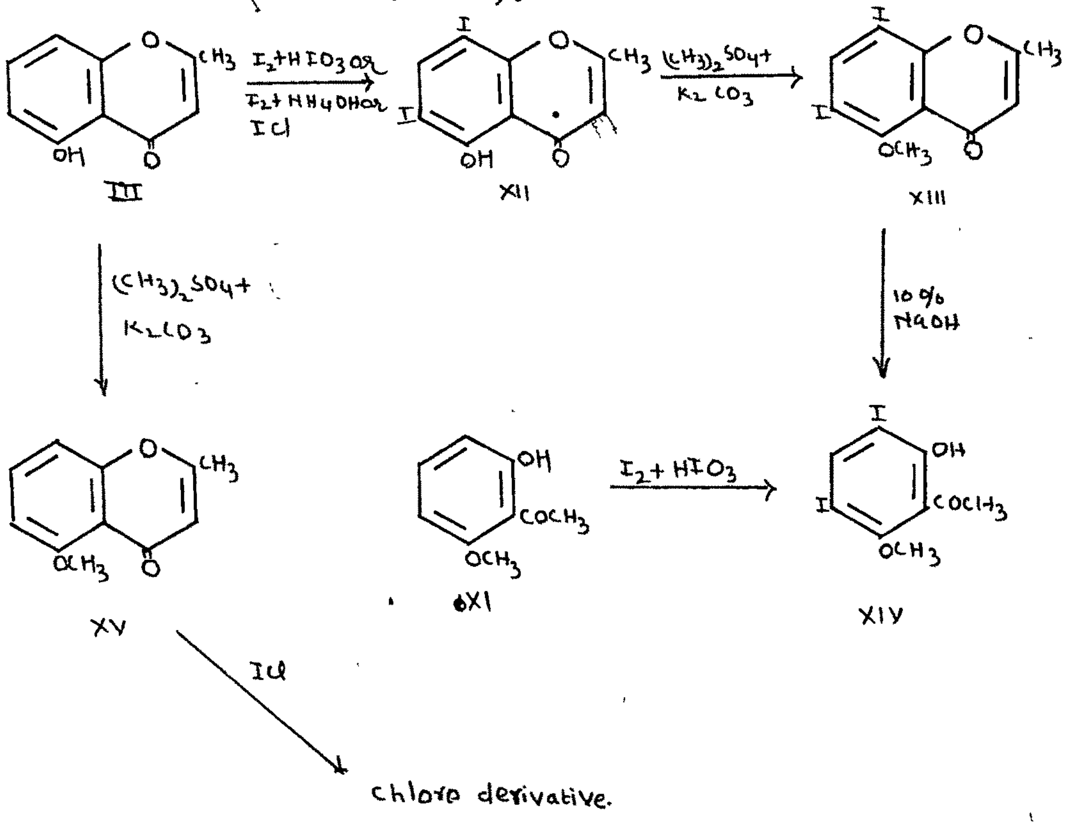
The mono-iodochromone on nitration with nitric acid gave a mono-iodonitrochromone identical with the iodo derivative obtained from 5-hydroxy-6-nitro-2-methylchromone (VI) (Naik and Thakor, Proc. Indian Acad. Sci., 1953, 37A, 774) by reaction with iodine and iodic acid. The iodochromone was therefore 5-hydroxy-8-iodo-2-methylchromone (IV) and the nitration product 5-hydroxy-8-iodo-6-nitro-2-methylchromone (V). The iodo ketone obtained in the hydrolysis was therefore 2-hydroxy-3-iodo-6-methoxyacetophenone (VIII) and the iodo derivative obtained from 2-hydroxy-6-methoxyacetophenone (XI) was the isomeric-2-hydroxy-5-iodo-6-methoxyacetophenone (X).



5-Hydroxy-2-methylchromone (III) on iodination with twice the theoretical amounts of iodine and iodic acid according to equation (i) gave a di-iodo derivative. Its methyl ether on treatment with hot alkali gave a di-iodo-phenolic ketone indicating that both the iodine atoms had entered the benzenoid part. The di-iodo ketone was identical with the di-iodo ketone obtained on iodination of 2-hydroxy-6-methoxyacetophenone (XI) with twice the theoretical amounts of iodine and iodic acid. The di-iodo ketone must therefore be 2-hydroxy-3,5-di-iodo-6-methoxy-acetophenone (XIV) and the di-iodochromone must have 5-hydroxy-6,8-di-iodo-2-methylchromone structure (XII).

5-Hydroxy-2-methylchromone (III) on iodination with one mole of iodine in presence of ammonia using dioxan as a solvent gave a mixture of the 8-iodo derivative (IV) and the 6,8-di-iodo derivative (XII) in poor yield but with two moles and excess of iodine it gave the 6,8-di-iodochromone (XII) in good yield.

5-Hydroxy-2-methylchromone (III) on iodination with one mole of iodine monochloride gave the 8-iodo derivative and with two moles and excess of iodine monochloride it gave the 6,8-di-iodo derivative (XII).

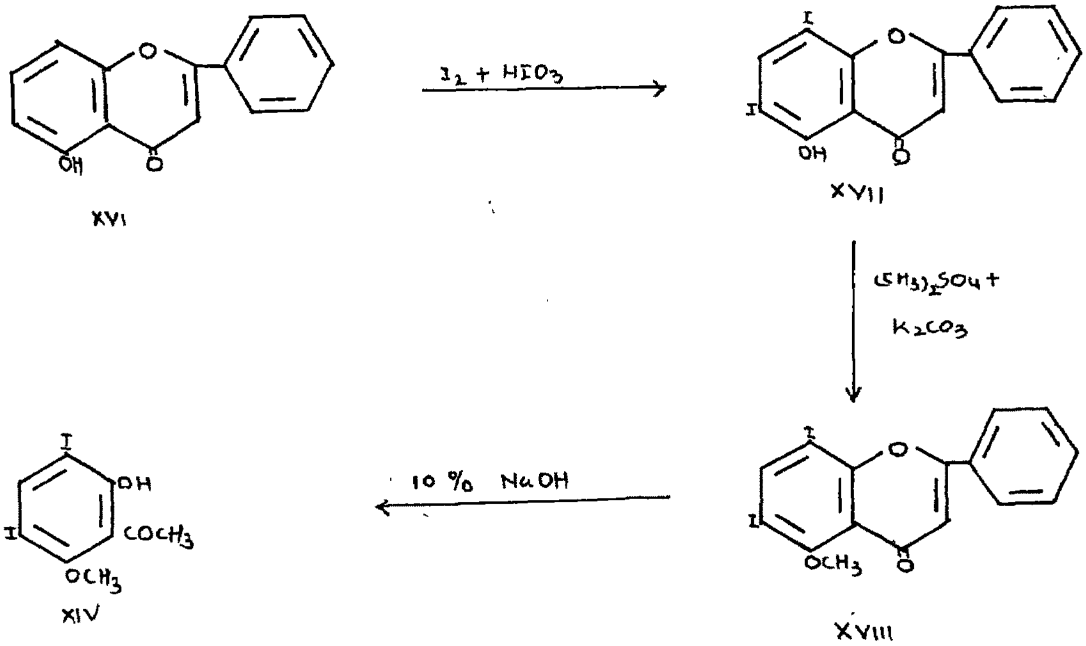


No tri-iodo derivative could be obtained by any of the three methods even with a large excess of the iodinating reagents.

5-Methoxy-2-methylchromone (XV) could not be iodinated either with iodine and iodic acid or with iodine and ammonia at all. With iodine monochloride it gave a chlorinated product which has not been investigated further.

Iodination of 5-hydroxyflavone

5-Hydroxyflavone (XVI) on iodination with iodine and iodic acid directly gave a di-iodo derivative. No mono-iodo derivative could be isolated. Its methyl ether on alkaline hydrolysis gave 2-hydroxy-3,5-di-iodo-6-methoxyacetophenone (XIV) . The iodo derivative has therefore been assigned 5-hydroxy-6,8-di-iodoflavone (XVII) structure. With twice the theoretical amounts of iodine and iodic acid the



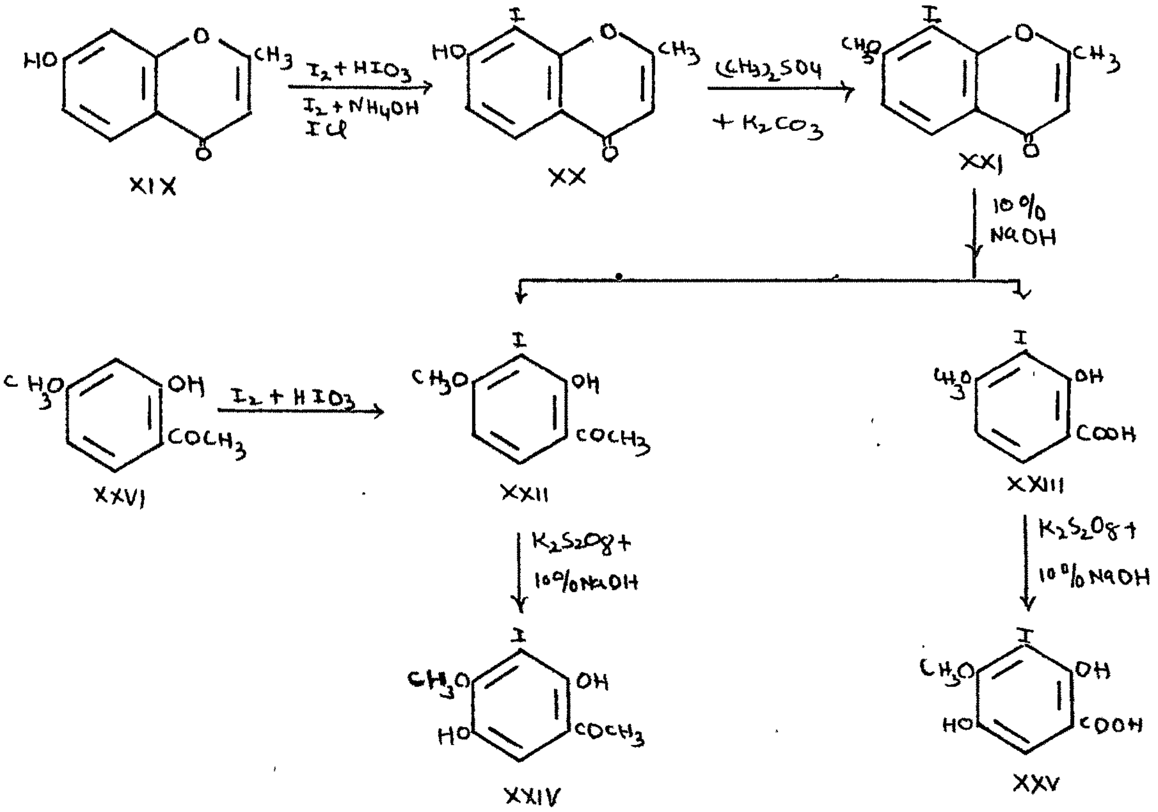
same di-iodoflavone was obtained in good yield. No tri-iodoflavone could be obtained even with a large excess of the iodinating reagents.

Iodination of 7-hydroxy-2-methylchromone and its methyl ether

7-Hydroxy-2-methylchromone (XIX) on iodination with the theoretical amounts of iodine and iodic acid gave a mono-iodo derivative. Attempts to prove the structure of the mono-iodo compound by nitration as in the previous case did not succeed as on treatment with nitric acid the iodochromone decomposed. The structure was therefore proved as follows:

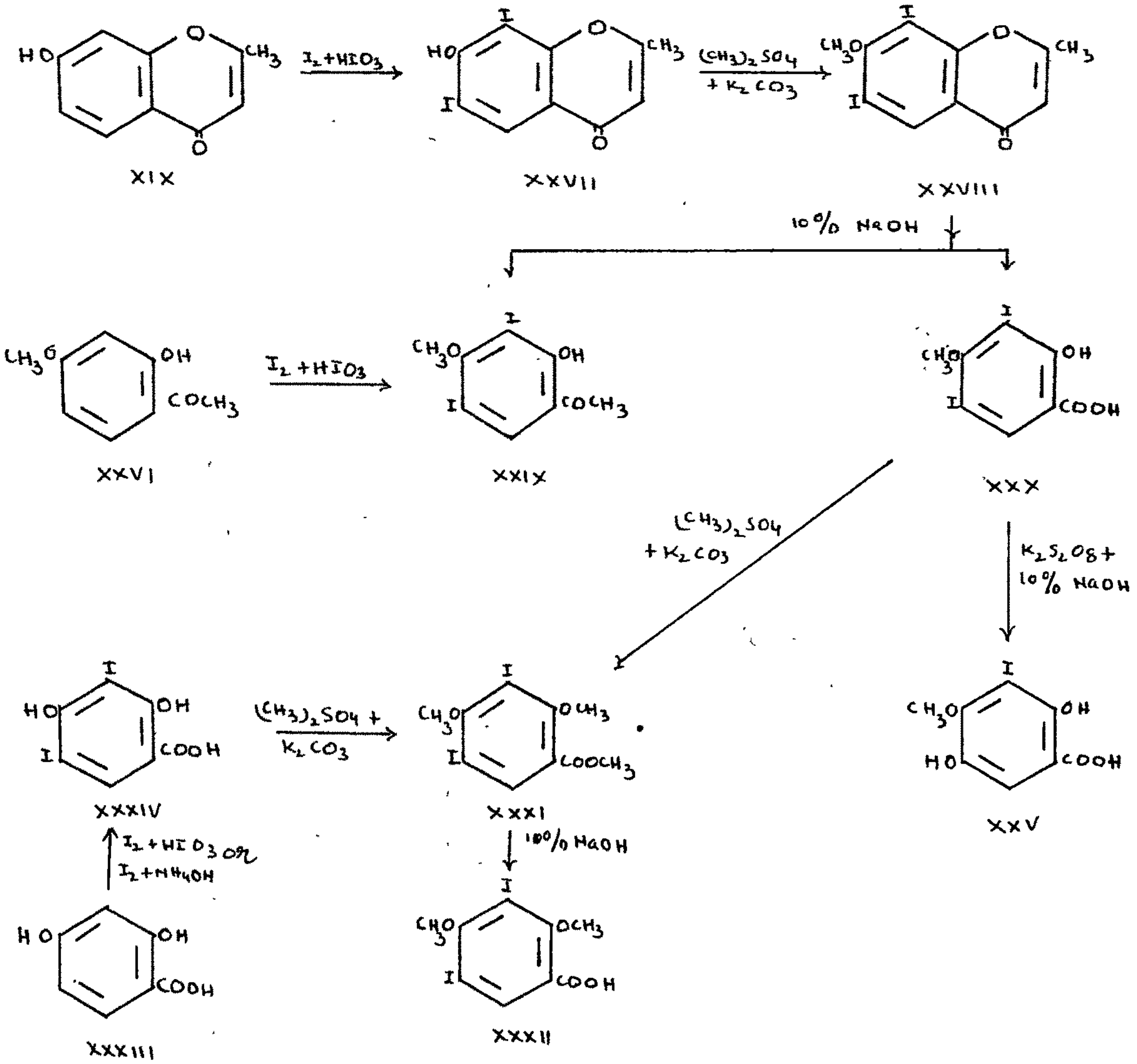
The methyl ether of the iodochromone on treatment with hot alkali gave a mixture of an iodophenolic ketone (A) and an iodophenolic acid (B) which showed that the iodine was in the benzenoid part of the chromone molecule. The same iodo ketone was obtained on iodination of 2-hydroxy-4-methoxyacetophenone (XXVI) with iodine and iodic acid. The iodophenolic ketone (A) when subjected to Elbs Persulphate Oxidation gave an oxidation product in good yield, in which the iodine was retained, showing that the para-position to the hydroxyl must be free for the Elbs Persulphate Oxidation of para-substituted products is difficult (cf. Baker and Brown , J. Chem. Soc., 1948, 2303). The oxidation product must therefore be 2,5-dihydroxy-3-iodo-4-methoxyacetophenone (XXIV) and the iodo ketone (A) must be 2-hydroxy-3-iodo-4-methoxyacetophenone (XXII). The iodo acid (B) also underwent Elbs Persulphate Oxidation smoothly and gave the oxidation product in good yield. The oxidation product is assigned 2,5-dihydroxy-3-iodo-4-methoxybenzoic acid (XXV) structure and the iodo acid (B) 2-hydroxy-3-iodo-4-methoxybenzoic acid (XXIII) structure. The mono-iodochromone was therefore 7-hydroxy-8-iodo-2-methylchromone (XX) .

Attempts to iodinate 2,5-dihydroxy-4-methoxyacetophenone to prepare 2,5-dihydroxy-3-iodo-4-methoxyacetophenone with varying amounts of iodine and iodic acid did not succeed, the original compound was recovered unchanged.



7-Hydroxy-2-methylchromone (XIX) on iodination with twice the theoretical amounts of iodine and iodic acid gave only the 8-iodo derivative (XX), in good yield. But with three times the amounts of iodine and iodic acid it gave a di-iodo derivative. Its methyl ether on hydrolysis with hot alkali gave a di-iodophenolic ketone (C) and a di-iodophenolic acid (D) indicating that both the iodine atoms were in the benzenoid part. The di-iodo ketone (C) was found to be identical with the di-iodo derivative obtained from 2-hydroxy-4-methoxyacetophenone (XXVI) by iodination with iodine and iodic acid. It must therefore be 2-hydroxy-3,5-di-iodo-4-methoxyacetophenone (XXIX). The di-iodo acid (D) on Elbs Persulphate Oxidation lost an iodine atom and gave 2,5-dihydroxy-3-iodo-4-methoxybenzoic acid (XXV) described above. The acid (D) has been assigned 2-hydroxy-3,5-di-iodo-4-methoxybenzoic acid (XXX) structure. The methyl ether of the methyl ester of the di-iodo acid was found to be identical with the completely methylated and esterified product from the di-iodo acid prepared by the iodination of 2,4-dihydroxybenzoic acid (XXXIII) with iodine and iodic acid, previously prepared by Nicolet and Sampey (J. Amer. Chem. Soc., 1927, 49, 1767), the iodination product must therefore be 2,4-dihydroxy-3,5-di-iodobenzoic acid (XXXIV) and the methylated and esterified product must be methyl 2,4-dimethoxy-3,5-di-iodobenzoate (XXXI). The di-iodo ester (XXXI) on alkaline hydrolysis yielded the 3,5-di-iodo acid (XXXII). On the basis of all this data the di-iodochromone obtained above has been assigned 7-hydroxy-6,8-di-iodo-2-methylchromone (XXVII) structure.

Iodination of 7-hydroxy-2-methylchromone with even large excess of iodine and iodic acid did not give the tri-iodo derivative.



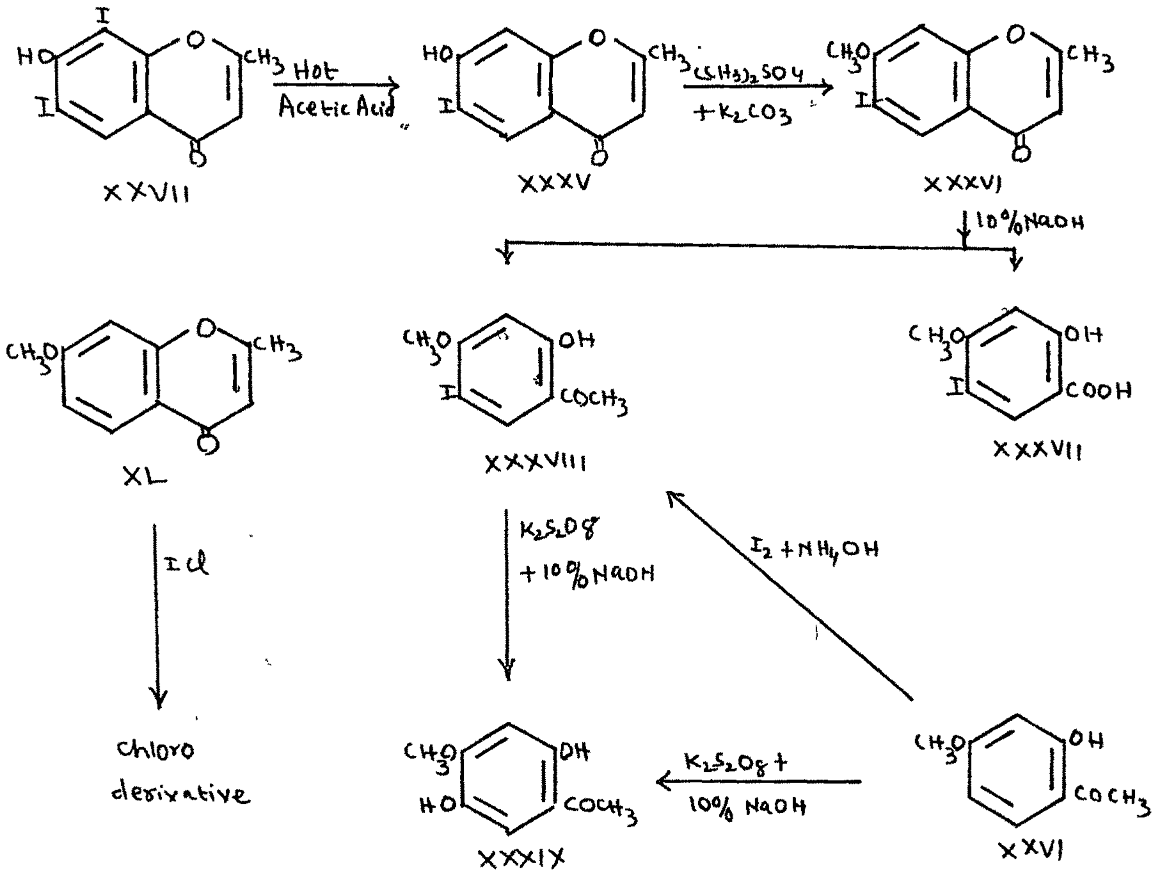
7-Hydroxy-6,8-di-iodo-2-methylchromone on prolonged refluxing with glacial acetic acid lost one iodine atom and gave a mono-iodo derivative different from 7-hydroxy-8-iodo-2-methylchromone (XX). Its methyl ether on hydrolysis with sodium hydroxide gave a mixture of a mono-iodophenolic ketone (E) and a mono-iodophenolic acid (F). The iodo ketone (E) was different from 2-hydroxy-3-iodo-4-methoxyacetophenone (XXII) but was identical with the iodination product obtained from 2-hydroxy-4-methoxyacetophenone (XXVI). on iodination with iodine in presence of ammonia. On Elbs Persulphate Oxidation the iodophenolic ketone (E) lost the iodine atom and gave the iodine free product - 2,5-dihydroxy-4-methoxyacetophenone (XXXIX) previously synthesised by Bargellini and Aurelli (Atti Accad. Lincei., 1911, 20 (i), 118) from 2-hydroxy-4-methoxyacetophenone (XXVI) by Elbs Persulphate Oxidation. On the basis of all this data the mono-iodo ketone (E) is assigned 2-hydroxy-4-methoxy-5-iodoacetophenone (XXXVIII) structure. The mono-iodo acid (F) was different from 2-hydroxy-3-iodo-4-methoxybenzoic acid (XXIII) and is therefore assigned the alternate structure - 2-hydroxy-4-methoxy-5-iodobenzoic acid (XXXVII). The mono-iodochromone obtained from the decomposition of the di-iodochromone is therefore 7-hydroxy-6-iodo-2-methylchromone (XXXV).

7-Methoxy-2-methylchromone (XL) could not be iodinated at all even with excess of iodine and iodic acid.

7-Hydroxy-2-methylchromone on iodination with one molecular equivalent of iodine in potassium iodide solution in presence of ammonia gave the 8-iodo derivative (XX). Iodination using large excess of iodine in presence of ammonia did not give amy higher iodination product.

7-Methoxy-2-methylchromone (XL) could not be iodinated at all by this method.

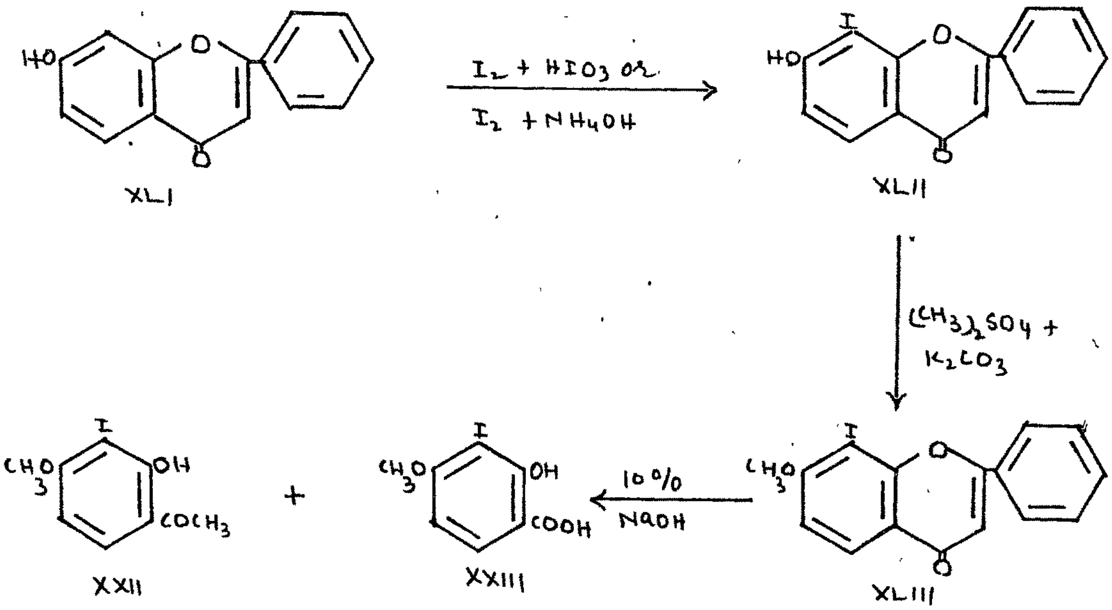
7-Hydroxy-2-methylchromone did not react with one mole of iodine monochloride. With two moles of iodine monochloride it gave only the 8-iodo derivative (XX). With excess of iodine monochloride it did not give any di-iodo derivative. 7-Methoxy-2-methylchromone (XL) on iodination with iodine monochloride gave a chlorinated product which has not been investigated further.



Iodination of 7-hydroxyflavone

7-Hydroxyflavone (XLI) on iodination with the theoretical amounts of iodine and iodic acid gave ~~the~~ a mono-iodo derivative. Its methyl ether, on heating with alkali gave 2-hydroxy-3-iodo-4-methoxyacetophenone (XXII) and 2-hydroxy-3-iodo-4-methoxybenzoic acid (XXIII) described before. Therefore the mono-iodoflavone was 7-hydroxy-8-

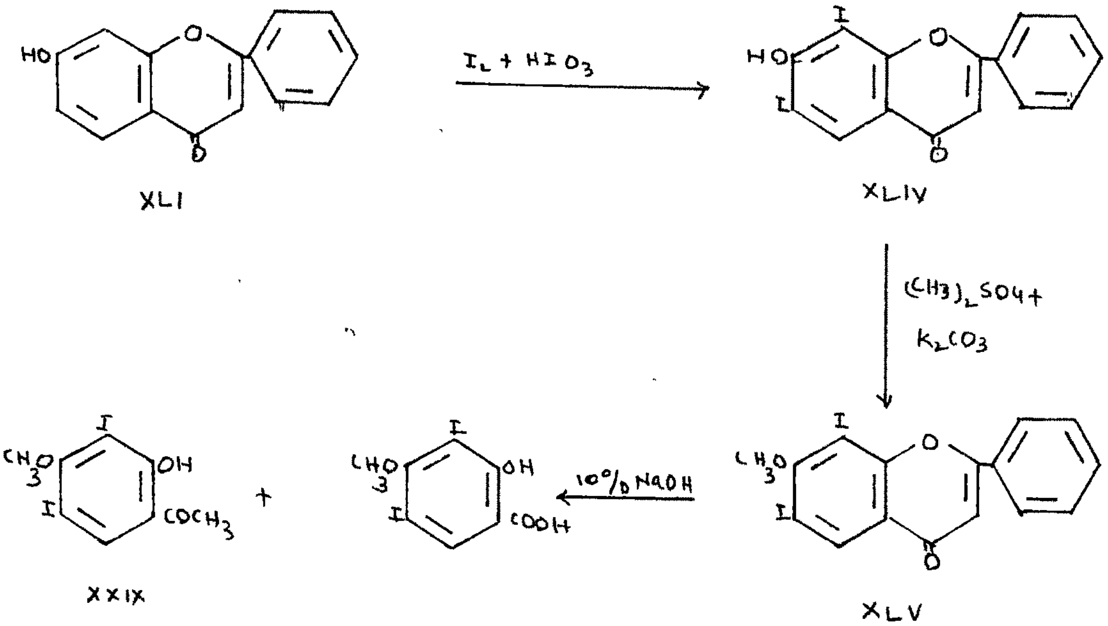
iodoflavone (XLII).



On iodination with twice the theoretical amounts of iodine and iodic acid 7-hydroxyflavone (XLI) gave only the 8-iodo derivative but in better yield. On iodination with three times the amounts of iodine and iodic acid it gave a di-iodo derivative, the methyl ether of which on alkaline hydrolysis gave 2-hydroxy-3,5-di-iodo-4-methoxyacetophenone (XXIX) and 2-hydroxy-3,5-di-iodo-4-methoxybenzoic acid (XXX) described before. The di-iodo derivative was therefore 7-hydroxy-6,8-di-iodoflavone (XLIV).

No tri-iodoflavone could be obtained even with a large excess of the iodinating reagents.

7-Hydroxyflavone on iodination with iodine and ammonia gave the 8-iodo derivative (XLII) in good yield. No higher iodo derivative could be obtained even with excess of iodine and ammonia.



XLI

XLIV

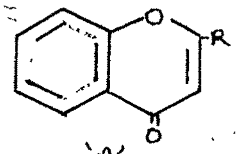
XLV

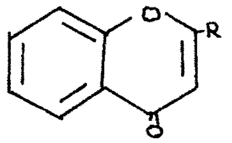
XXIX

The results obtained in this work may be compared with those obtained in other substitution reactions. As seen before 2-methylchromone, flavone, 5-methoxy-2-methylchromone and 7-methoxy-2-methylchromone do not undergo iodination. However, 2-methylchromone, flavone and 7-methoxy-2-methylchromone undergo bromination in the 3-position (Winter and Hamilton, J. Amer. Chem. Soc., 1952, 3999 ; Limaye et al., Rasayanam, 1956, 2, 121 ; Seshadri and co-workers, J. Sci. Ind. Research, India, 1954, 13B, 160) . No higher bromination products have been reported. Further, it has been seen that iodination of 5-hydroxy-2-methylchromone, 7-hydroxy-2-methylchromone and 7-hydroxyflavone give the 8-iodo and the 6,8-di-iodo derivatives and the iodination of 5-hydroxyflavone directly gives the 6,8-di-iodo derivative. No tri-iodo compound could be obtained even with a large excess of the iodinating agents. The work of Naik and Sethna (J. Indian Chem. Soc., 1952, 29, 493) shows that the bromination of 5-hydroxy-2-methylchromone and 7-hydroxy-2-methylchromone also takes a similar course and the 6-bromo and the 6,8-dibromo derivatives are obtained. With liquid bromine a tribromo derivative is obtained to which they tentatively assigned the 3,6,8-tribromo structure. Naik (unpublished work) has found in this laboratory that 5-hydroxyflavone and its methyl ether on bromination gives 5-hydroxy-6,8-dibromo flavone and 7-hydroxyflavone yields the 8-bromo and the 6,8-dibromo derivatives. With liquid bromine both 5-hydroxy- and 7-hydroxyflavone give the tribromo derivatives to which the 3,6,8-tribromo structures have been tentatively assigned.

In 7-hydroxychromone and flavone derivatives formylation (Rangaswami and Seshadri, Proc. Indian Acad. Sci., 1939, 9A, 7), nitration (Mehta, Jadhav and Shah, Proc. Indian Acad. Sci., 1949, 29, 314) and sulphonation (Shah and co-workers, J. Org. Chem., 1956, 21, 1104) takes place mainly in the 8-position. Further, Fries migration of 7-acyloxy-chromone and-flavone derivatives (Wittig, Bangert and Reichert, Ann. 1925, 446, 105 ; Ber., 1926, 59B, 116 ; Kelkar and Limaye, Rasayanam 1936, 1, 60) or the rearrangement of their 7-allyloxy derivatives (Seshadri and Rangaswami, Proc. Indian Acad. Sci., 1939, 9A, 1) occur preferentially in the 8-position. This has been explained on the basis of the existence of a double bond between 7 and 8 positions. If we assume on the basis of the Mills-Nixon theory (J. Chem.

Soc., 1930, 2510) that the structure 'A' with a double bond


'A'


'B'

~~R = CH_3 or C_6H_5~~

Common to both the rings possesses lower energy due to less distortion of valence bonds and hence is more likely there would be a double bond between the carbon atoms 7 and 8 and therefore in 7-hydroxy-chromone and -flavone substitution would take place in 8 position. However, it has been found that 7-hydroxy-chromone and -flavone derivatives with an alkyl or allyl substituent in 8-position easily couple with diazotised p-nitraniline in the 6-position and their allyl ethers rearrange to furnish the 6-allyl derivatives (Rangaswami and Seshadri, loc.cit.). This leads to the conclusion that though in chromone normally the bond structure is as in 'A' the bonds are capable of redistribution as in structure 'B'.

According to modern concepts it can be said that in chromones there is a resonance between the two structures 'A' and 'B' with predominant contribution by the structure 'A'.

In the case of 5-hydroxy-2-methylchromone nitration first occurs in the 8-position and then in the 6-position to give the 6,8-dinitro derivative (Mehta, Jadhav and Shah, loc.cit.). 5-Hydroxyflavone on nitration (Mehta, Jadhav and Shah, loc.cit.), sulphonation (Shah and co-workers loc.cit.) and coupling (Iyer and Venkataraman, Proc. Indian Acad.Sci., 1953, 37A, 629) gives first the 8-substituted compound. Further nitration and sulphonation leads to the 6,8-di~~nitro~~substituted derivative. However, in the Fries rearrangement of 5-acetoxyflavone Baker (J. Chem.Soc., 1934, 1953) found that the 6-acetyl derivative was obtained.

EXPERIMENTAL

Iodination of 5-hydroxy-2-methylchromone :

5-Hydroxy-8-iodo-2-methylchromone

(a) With iodine and iodic acid 5-Hydroxy-2-methylchromone (1.76 g. ; 0.01 mole) was dissolved in warm alcohol (40 ml.) and iodine crystals (1.01 g. ; 0.004 mole) were added with stirring. Iodic acid (0.35 g.) dissolved in minimum quantity of water was then added to the reaction mixture at room temperature and the stirring continued for 2 hours. The separated product was filtered and crystallised from ethyl alcohol in yellow needles, m.p. 171°. Yield 1.4 g. Its alcoholic solution gave a deep red colouration with alcoholic ferric chloride.

Analysis :

10.432 mg. of the substance gave 8.180 mg. of silver iodide.

Found : I = 42.39 %.
$C_{10}H_7O_3I$ requires : I = 42.05 %.

(b) With iodine and ammonia 5-Hydroxy-2-methylchromone (1.76 g. ; 0.01 mole)was dissolved in dioxan (70 ml.) and ammonia (22 % ;60 ml.). A solution of iodine (2.54 g. ; 0.01 mole) and potassium iodide (5.1 g.) was then added drop-wise to the stirred ammoniacal solution of the chromone at room temperature during half an hour. The separated product was filtered, washed with ammonia and finally acidified with ice cold dilute sulphuric acid. The product obtained crystallised from ethyl alcohol. This was the di-iodo derivative m.p. 238° (See p.52). From the mother liquor the mono-iodo derivative was obtained on dilution. Yield 1.2 g.

Some 5-hydroxy-2-methylchromone was recovered on acidification of the original ammoniacal mother liquor.

(c) With iodine monochloride : A mixture of 5-hydroxy-2-methylchromone (1.76 g. ; 0.01 mole) in acetic acid (40 ml.) and hydrochloric acid (d.1.11 ; 15 ml.) was added to iodine monochloride (1.62 g. ; 0.01 mole) and the reaction mixture left over-night at 60° in an oven. Next day it was vigorously stirred and added to ice-cold sodium hydrogen sulphite solution. The product obtained crystallised from alcohol in yellow needles, m.p. 171°. Yield 1 g.

The methyl ether : The above iodochromone (1 g.) in acetone (100 ml.) was refluxed with dimethyl sulphate (1 g.) and anhydrous potassium carbonate (2 g.)for 12 hours. The product obtained on removal of acetone was washed with dilute sodium hydroxide solution and the residue crystallised from aqueous methanol (charcoal) in colourless needles, m.p. 92-95°.

Analysis :

4.423 mg. of the substance gave 6.762 mg. of carbon dioxide and 1.112 mg. of water.

11.642 mg. of the same substance gave 8.576 mg. of silver iodide.

Found : C = 41.72 % ; H = 2.81 % ; I = 39.82 %.

$C_{11}H_9O_3I$ requires : C = 41.77 % ; H = 2.85 % ; I = 40.19 %.

Nitration of 5-hydroxy-8-iodo-2-methylchromone : 5-Hydroxy-8-iodo-6-nitro-2-methylchromone

5-Hydroxy-8-iodo-2-methylchromone (1 g.) was disslolved in glacial acetic acid (40 ml.) and externally cooled. Nitric acid (d.1.42 ; 10 ml.)was then added drop-wise with stirring maintaining the temperature below 10° during the addition. The reaction mixture was kept for 24 hours at room temperature and then added to crushed ice. The precipitated solid crystallised from acetic acid in thick yellow needles, m.p. 215-216° (decomp.). Yield 0.6 g. Its alcoholic solution gave a violet blue colouration with alcoholic ferric chloride.

Analysis :

7.442 mg. of the substance gave 0.288 ml. of nitrogen at 29° and 762 mm.

14.660 mg. of the same substance gave 9.826 mg. of silver iodide.

Found : N = 4.39 % ; I = 36.33 %.

$C_{10}H_6O_5NI$ requires : N = 4.03 % ; I = 36.60 %.

The same iodo-nitrochromone was obtained by iodination of 5-hydroxy-6-nitro-2-methylchromone (1.1 g. ;0.005 mole) in warm ethyl alcohol with iodine (1.01 g. ;0.004 mole)and iodic acid (0.5 g.) dissolved in water. Yield 1.1 g.

Alkaline hydrolysis of 5-methoxy-8-iodo-2-methylchromone : 2-Hydroxy-3-iodo-6-methoxyacetophenone

5-Methoxy-8-iodo-2-methylchromone (0.5 g.) was refluxed with aqueous alcoholic sodium hydroxide solution (10 % ; 20 ml.) for 4 hours. The product obtained on acidification crystallised from petroleum ether (b.p. 60-80°) in yellow needles, m.p. 57°. Its alcoholic solution gave a deep red colouration with alcoholic ferric chloride.

Analysis :

4.828 mg. of the substance gave 6.528 mg. of carbon dioxide and 1.338 mg. of water.

16.52 mg. of the same substance gave 13.256 mg. of silver iodide.

Found : C = 36.90 % ; H = 3.10 % ; I = 43.38 %.

$C_9H_9O_3I$ requires : C = 36.98 % ; H = 3.08 % ; I = 43.50 %.

No definite product could be isolated from a similar hydrolysis of 5-hydroxy-8-iodo-2-methylchromone.

2,6-Dimethoxy-3-iodo-acetophenone The above mono-iodo-acetophenone (0.5 g.) was refluxed in acetone with dimethyl sulphate (0.5 ml.) and anhydrous potassium carbonate (1 g.) for 10 hours. The product obtained crystallised from aqueous ethyl alcohol in white plates, m.p. 71-72°.

Analysis :

4.074 mg. of the substance gave 5.768 mg. of carbon dioxide and 1.346 mg. of water.

13.352 mg. of the same substance gave 10.204 mg. of silver iodide.

Found : C = 38.64 % ; H = 3.70 % ; I = 41.31 %.

$C_{10}H_{11}O_3I$ requires : C = 39.21 % ; H = 3.60 % ; I = 41.50 %.

5-Hydroxy-6,8-di-iodo-2-methylchromone

5-Hydroxy-2-methylchromone (1.76 g. ; 0.01 mole) was dissolved in warm alcohol (50 ml.) and iodine crystals (2.03 g. ; 0.008 mole) were added. To the vigorously stirred reaction mixture iodic acid (0.8 g.) dissolved in water was added and stirring continued for 2 hours. The separated product crystallised from acetic acid in yellow needles, m.p. 238°. Yield 2.2 g. Its alcoholic solution gave a violet blue colouration with alcoholic ferric chloride. The di-iodo derivative was stable in boiling glacial acetic acid.

Analysis :

10.98 mg. of the substance gave 12.124 mg. of silver iodide.

Found : I = 59.68 %.

$C_{10}H_6O_3I_2$ requires : I = 59.34 %.

The same di-iodochromone was obtained when 5-hydroxy-2-methylchromone (1.76 g. ; 0.01 mole) was iodinated with iodine monochloride (3.24 g. ; 0.02 mole) (Yield 1.5 g.) and also when the chromone (0.88 g. ; 0.005 mole) in dioxan (40 ml.) and ammonia solution was treated with iodine (2.54 g. ; 0.01 mole) solution (Yield 0.9 g.) as seen on p.49.

The methyl ether, prepared by refluxing the di-iodochromone (2 g.) in acetone with dimethyl sulphate (2 g.) in presence of anhydrous potassium carbonate (4 g.) for 15 hours, crystallised from rectified spirit in yellowish needles, m.p. 207-208°.

Analysis :

4.774 mg. of the substance gave 5.244 mg. of carbon dioxide and 0.838 mg. of water.

13.676 mg. of the same substance gave 14.528 mg. of silver iodide.

Found : C = 29.98 % ; H = 1.96 % ; I = 57.42 %.

$C_{11}H_8O_3I_2$ requires : C = 29.86 % ; H = 1.81 % ; I = 57.47 %.

Alkaline hydrolysis of 5-methoxy-6,8-di-iodo-2-methylchromone : 2-Hydroxy-3,5-di-iodo-6-methoxyacetophenone

5-Methoxy-6,8-di-iodo-2-methylchromone (2 g.) was refluxed with sodium hydroxide solution (10 % ; 40 ml.) as before. The product obtained on acidification crystallised from aqueous ethyl alcohol in tiny yellow needles, m.p.111°. Its alcoholic solution gave a deep red colouration with alcoholic ferric chloride. The same product was obtained on iodination of 2-hydroxy-6-methoxyacetophenone as described on p. 70.

Analysis :

13.404 mg. of the substance gave 14.978 mg. of silver iodide.

Found : I = 60.40 %.

$C_9H_8O_3I_2$ requires : I = 60.76 %.

Iodination of 5-hydroxyflavone : 5-Hydroxy-6,8-di-iodoflavone

5-Hydroxyflavone (1.19 g. ; 0.005 mole) was dissolved in warm ethyl alcohol and iodine crystals (0.5 g. ; 0.002 mole) were added. To the stirred solution iodic acid (0.3 g.) in water was added and the reaction mixture stirred for 2 hours. The separated product crystallised from ethyl alcohol in yellow needles, m.p. 252°. Yield 0.9 g. Its alcoholic solution gave a violet blue colouration with alcoholic ferric chloride.

No mono-iodo derivative could be isolated.

Analysis :

11.390 mg. of the substance gave 10.822 mg. of silver iodide.

Found : I = 51.36 %.

$C_{15}H_8O_3I_2$ requires : I = 51.71 %.

The same di-iodoflavone was obtained in better yield by iodination of 5-hydroxyflavone (1.19 g. ; 0.005 mole) with iodine (1.01 g. ; 0.004 mole) and iodic acid (0.5 g.) under vigorous stirring. Yield 1.7 g.

The product was stable in boiling acetic acid.

The methyl ether, obtained as before by refluxing the di-iodo-flavone (0.5 g.) in acetone with dimethyl sulphate (0.5 ml.) in presence of anhydrous potassium carbonate (1 g.) for 18 hours crystallised from dilute ethyl alcohol in buff coloured needles, m.p. 246°.

Analysis :

9.16 mg. of the substance gave 12.70 mg. of carbon dioxide and 1.32 mg. of water.

10.984 mg. of the same substance gave 10.260 mg. of silver iodide.

Found : C = 37.83 % ; H = 1.61 % ; I = 50.49 %.

$C_{16}H_{10}O_3I_2$ requires : C = 38.10 % ; H = 1.99 % ; I = 50.28 %.

Alkaline hydrolysis of 5-methoxy-6,8-di-iodoflavone :

2-Hydroxy-3,5-di-iodo-6-methoxyacetophenone

5-Methoxy-6,8-di-iodoflavone (0.5 g.) was refluxed with aqueous alcoholic sodium hydroxide solution (10 % ; 20 ml.) for 4 hours. The product obtained on acidification crystallised from dilute alcohol in yellow needles, m.p. 111°. Mixed m.p. with 2-hydroxy-3,5-di-iodo-6-methoxyacetophenone described earlier was not depressed.

Iodination of 7-hydroxy-2-methylchromone :

7-Hydroxy-8-iodo-2-methylchromone

(a) With iodine and iodic acid

7-Hydroxy-2-methylchromone (1.76 g. ; 0.01 mole) was dissolved in warm alcohol (50 ml.) and iodinated with iodine (1.01 g. ; 0.004 mole) and iodic acid (0.6 g.) The separated product crystallised from acetic acid in colourless needles, m.p. 213° (decomp.). Yield 1.4 g.

Analysis :

The product was dried in vacuo at 110° for 3 hours and then analysed.

17.424 mg. of the substance gave 13.698 mg. of silver iodide.

Found : I = 42.50 %.

$C_{10}H_7O_3I$ requires : I = 42.05 %.

The same product was obtained in better yield (1.8 g.) when more iodine (2.03 g. ; 0.008 mole) and ~~iodine and~~ iodic acid (0.8 g.) in water were used.

(b) With iodine and ammonia

The hydroxychromone (1.76 g. ; 0.01 mole) was dissolved in aqueous ammonia and treated with iodine (2.54 g. ; 0.01 mole) solution with stirring. On acidification with cold dilute sulphuric acid it gave the above 8-iodochromone. Yield 2.3 g.

(c) With iodine monochloride

The hydroxychromone (1.76 g. ; 0.01 mole) on iodination with iodine monochloride (3.24 g. ; 0.02 mole) in acetic acid by keeping it in an oven at 60° over-night gave the same 8-iodo derivative. Yield 0.7 g.

The methyl ether, prepared by refluxing the acetone solution of the above hydroxy-iodochromone (3 g.) with dimethyl sulphate (3 ml.) in presence of anhydrous potassium carbonate (6 g.) for 4 hours, crystallised from alcohol in colourless needles, m.p. 191-192°.

Analysis :

4.294 mg. of the substance gave 6.598 mg. of carbon dioxide and 1.066 mg. of water.

14.040 mg. of the same substance gave 10.592 mg. of silver iodide.

Found : C = 41.93 % ; H = 2.77 % ; I = 40.78 %.

$C_{11}H_9O_3I$ requires : C = 41.77 % ; H = 2.85 % ; I = 40.19 %.

Alkaline hydrolysis of 7-methoxy-8-iodo-2-methylchromone : 2-Hydroxy-3-iodo-4-methoxyacetophenone and 2-hydroxy-3-iodo-4-methoxybenzoic acid

7-Methoxy-8-iodo-2-methylchromone (2 g.) was refluxed with aqueous alcoholic sodium hydroxide solution (10 % ; 40 ml.) for 4 hours. The product obtained on acidification was first treated with sodium hydrogen carbonate solution and the residue treated with sodiun hydroxide solution. The sodium hydrogen carbonate extract on acidification gave an iodo acid which crystallised from dilute ethyl alcohol in colourless needles, m.p. 218° (efferv.) Its alcoholic solution gave a deep red colouration with alcoholic ferric chloride.

Analysis :

5.076 mg. of the substance gave 6.136 mg. of carbon dioxide and 1.138 mg. of water.

13.586 mg. of the same substance gave 10.934 mg. of silver iodide.

Found : C = 32.99 % ; H = 2.50 % ; I = 43.50 %.
$C_8H_7O_4I$ requires : C = 32.66 % ; H = 2.39 % ; I = 43.20 %.

The sodium hydroxide extract on acidification gave the iodo-ketone which crystallised from rectified spirit in colourless thick needles, m.p. 152°. Its alcoholic solution gave a deep red colouration with alcoholic ferric chloride. The same iodo ketone was obtained on iodination of 2-hydroxy-4-methoxyacetophenone as described on p.71.

Analysis :

11.560 mg. of the substance gave 9.376 mg. of silver iodide.

Found : I = 43.84 %.

$C_9H_9O_3I$ requires : I = 43.50 %.

Elbs Persulphate Oxidation of 2-hydroxy-3-iodo-4-methoxyacetophenone : 2,5-Dihydroxy-3-iodo-4-methoxyacetophenone

2-Hydroxy-3-iodo-4-methoxyacetophenone (1 g.) was dissolved in sodium hydroxide solution (10 % ; 40 ml.) and the solution cooled. Saturated solution of potassium persulphate (0.9 g. in 20 ml. water) was then added gradually from a separating funnel during 2 hours. The solution was mechanically stirred and the temperature was not allowed to rise above 10°. The reaction mixture was stirred for one hour more and then left over-night. The next day it was acidified with concentrated hydrochloric acid till it was just acidic, when the original substance precipitated out. This was removed by filtration and the filtrate was twice extracted with ether. The aqueous layer was then heated on a steam bath for about an hour with concentrated hydrochloric acid (25 ml.). The product which separated on cooling crystallised from aqueous acetic acid in thick yellow needles, m.p. 174° (decomp.). Yield 0.22 g. Its alcoholic solution gave a deep red colouration with alcoholic ferric chloride.

Analysis :

4.086 mg. of the substance gave 5.248 mg. of carbon dioxide and 1.042 mg. of water.

13.584 mg. of the same substance gave 10.340 mg. of silver iodide.

Found : C = 35.05 % ; H = 2.85 % ; I = 41.15 %.
$C_9H_9O_4I$ requires : C = 35.06 % ; H = 2.92 % ; I = 41.23 %.

This compound could not be obtained by the iodination of 2,5-dihydroxy-4-methoxyacetophenone (0.091 g. ; 0.005 mole) (Bergellini and Aurelli, Atti. Accad. Lincei., 1911, 20 (i), 118) with iodine (0.5 g. ; 0.002 mole) and iodic acid (0.2 g.) in water. No iodination took place.

Elbs Persulphate Oxidation of 2-hydroxy-3-iodo-4-methoxybenzoic acid : 2,5-Dihydroxy-3-iodo-4-methoxybenzoic acid

2-Hydroxy-3-iodo-4-methoxybenzoic acid (1.5 g.) was dissolved in sodium hydroxide solution (10 % ; 60 ml.) and oxidised with potassium persulphate solution (1.3 g. in 30 ml. water) as above. The product obtained crystallised from water in yellowish needles, m.p. 212° (efferv.) . Yield 0.3 g. Its alcoholic solution gave a deep red colouration with alcoholic ferric chloride.

Analysis :

3.524 mg. of the substance gave 4.046 mg. of carbon dioxide and 0.772 mg. of water.

9.814 mg. of the same substance gave 7.578 mg. of silver iodide.

Found : C = 31.33 % ; H = 2.45 % ; I = 41.74 %.

$C_8H_7O_5I$ requires : C = 30.96 % ; H = 2.26 % ; I = 40.97 %.

7-Hydroxy-6,8-di-iodo-2-methylchromone

7-Hydroxy-2-methylchromone (0.88 g. ; 0.005 mole) dissolved in warm alcohol was iodinated with iodine (1.52 g. ; 0.006 mole) and iodic acid (0.8 g.) in water. The ~~separated~~ shining product which separated after vigorous stirring for 2 hours crystallised from ethyl alcohol in yellow needles, m.p. 212° (decomp.). Yield 1.24 g.

Analysis :

12.258 mg. of the substance gave 13.568 mg. of silver iodide.

Found : I = 59.83 %.

$C_{10}H_6O_3I_2$ requires : I = 59.34 %.

It was found to decompose on heating with acetic acid.

The same di-iodochromone was also obtained on iodination of 7-hydroxy-8-iodo-2-methylchromone (1.51 g. ; 0.005 mole) with iodine (1.52 g. ; 0.006 mole) and iodic acid (0.8 g.) in water.

This di-iodochromone could not be obtained on iodination of 7-hydroxy-2-methylchromone with even large excess of either iodine in presence of ammonia or iodine monochloride in acetic acid.

The methyl ether, prepared by refluxing the di-iodochromone (2 g.) in acetone on a steam bath with dimethyl sulphate (2 ml.) in presence of anhydrous potassium carbonate (4 g.) for 3 hours, crystallised from ethyl alcohol in colourless needles, m.p. 162°.

Analysis :

4.098 mg. of the substance gave 4.540 mg. of carbon dioxide and 0.632 mg. of water.

10.858 mg. of the same substance gave 11.582 mg. of silver iodide.

Found : C = 30.23 % ; H = 1.73 % ; I = 57.66 %.

$C_{11}H_8O_3I_2$ requires : C = 29.86 % ; H = 1.81 % ; I = 57.47 %.

Alkaline hydrolysis of 7-methoxy-6,8-di-iodo-2-methylchromone : 2-Hydroxy-3,5-di-iodo-4-methoxyacetophenone and 2-hydroxy-3,5-di-iodo-4-methoxybenzoic acid

7-Methoxy-6,8-di-iodo-2-methylchromone (2 g.) was heated with sodium hydroxide solution (10 % ; 40 ml.) for 4 hours when the solution became clear. The product obtained on acidification was extracted first with sodium hydrogen carbonate solution and then with dilute sodium hydroxide solution.

The sodium hydrogen carbonate extract on acidification gave the iodo acid which crystallised from rectified spirit in colourless needles, m.p. 217° (efferv.). Its alcoholic solution gave a deep red colouration with alcoholic ferric chloride.

Analysis :

3.626 mg. of the substance gave 3.002 mg. of carbon dioxide and 0.882 mg. of water.

5.052 mg. of the same substance gave 5.710 mg. of silver iodide.

Found : C = 22.59 % ; H = 1.18 % ; I = 61.10 %.
$C_8H_6O_4I_2$ requires : C = 22.87 % ; H = 1.43 % ; I = 60.47 %.

The methyl ether of the methyl ester of the above di-iodo acid agreed directly with the methylated and esterified product of the di-iodo acid obtained by iodination of β-resorcylic acid as described on p.71.

The sodium hydroxide extract from above on acidification gave the iodo ketone which crystallised from alcohol in colourless needles, m.p. 98-99°. Its alcoholic solution gave a red colouration with alcoholic ferric chloride. The same di-iodo ketone was obtained on iodination of a-hydroxy-4-methoxyacetophenone as described on p.71.

Analysis :

4.352 mg. of the substance gave 4.156 mg. of carbon dioxide and 0.790 mg. of water.

9.172 mg. of the same substance gave 10.390 mg. of silver iodide.

Found : C = 26.06 % ; H = 2.03 % ; I = 61.23 %.
$C_9H_8O_3I_2$ requires : C = 25.83 % ; H = 1.91 % ; I = 60.76 %.

Elbs Persulphate Oxidation of 2-hydroxy-3,5-di-iodo-4-methoxybenzoic acid : 2,5-Dihydroxy-3-iodo-4-methoxybenzoic acid

2-Hydroxy-3,5-di-iodo-4-methoxybenzoic acid (2 g.) was dissolved in sodium hydroxide solution (10 % ; 80 ml.)

and oxidised with potassium persulphate solution (1.8 g. ; in 40 ml. water) as usual. The product obtained crystallised from water in yellowish needles, m.p. 212° (efferv.). ~~M.P.~~ ~~and~~ ~~m~~Mixed m.p. with 2,5-dihydroxy-3-iodo-4-methoxybenzoic acid described before was not depressed. Yield 0.33 g.

Decomposition of 7-hydroxy-6,8-di-iodo-2-methylchromone by prolonged boiling with acetic acid : 7-Hydroxy-6-iodo-2-methylchromone

7-Hydroxy-6,8-di-iodochromone (2 g.) was refluxed in glacial acetic acid (120 ml.) for 4 hours, on a wire gauze. The solution became deep violet. It was cooled, filtered and added to ice-cold sodium hydrogen sulphite solution. The product obtained crystallised from alcohol in colourless needles, m.p. 258-260° (decomp.). Yield 0.4 g.

Analysis :

7.076 mg. of the substance gave 5.560 mg. of silver iodide.

Found : I = 42.48 %.

$C_{10}H_7O_3I$ requires : I = 42.05 %.

The methyl ether, prepared by refluxing the 6-iodo-derivative (2 g.) in acetone with dimethyl sulphate (2 ml.) in presence of anhydrous potassium carbonate (4 g.) for 3 hours, crystallised from ethyl alcohol in colourless needles, m.p. 238°.

Analysis :

4.298 mg. of the substance gave 6.524 mg. of carbon dioxide and 1.110 mg. of water.

7.038 mg. of the same substance gave 5.294 mg. of silver iodide.

Found : C = 41.42 % ; H = 2.89 % ; I = 40.66 %.
$C_{11}H_9O_3I$ requires : C = 41.77 % ; H = 2.85 % ; I = 40.19 %.

Alkaline hydrolysis of 7-methoxy-6-iodo-2-methylchromone : 2-Hydroxy-4-methoxy-5-iodo-acetophenone and 2-hydroxy-4-methoxy-5-iodobenzoic acid

7-Methoxy-6-iodo-2-methylchromone (1 g.) was refluxed with sodium hydroxide solution (10 % ; 40 ml.) for 4 hours when it completely went in solution. The iodo ketone and the iodo acid obtained were separated as before.

The iodo acid crystallised from dilute acetic acid in yellow needles, m.p. 245° (efferv.). Its alcoholic solution gave a red colouration with alcoholic ferric chloride.

Analysis :

4.452 mg. of the substance gave 5.376 mg. of carbon dioxide and 0.932 mg. of water.

8.832 mg. of the same substance gave 7.002 mg. of silver iodide.

Found : C = 32.95 % ; H = 2.34 % ; I = 42.86 %.
$C_8H_7O_4I$ requires : C = 32.66 % ; H = 2.34 % ; I = 43.20 %.

The ketone crystallised from ethyl alcohol in colourless long needles, m.p. 161°. Its alcoholic solution gave a red colouration with alcoholic ferric chloride. The same iodo ketone was obtained on iodination of 2-hydroxy-4-methoxyacetophenone as described on p.71.

Analysis :

11.068 mg. of the substance gave 8.784 mg. of silver iodide.

Found : I = 42.90 %.

$C_9H_9O_3I$ requires : I = 43.50 %.

Elbs Persulphate Oxidation of 2-hydroxy-4-methoxy-5-iodo-acetophenone : 2,5-Dihydroxy-4-methoxyacetophenone

2-Hydroxy-4-methoxy-5-iodo-acetophenone (1 g.) in sodium hydroxide solution (10 % ; 40 ml.) on oxidation with potassium persulphate (0.9 g. in 20 ml. water) as usual, gave an iodine free product. It crystallised from aqueous ethyl alcohol in yellowish needles. M.P. and mixed m.p. with 2,5-dihydroxy-4-methoxyacetophenone (Bargellini and Aurelli loc.cit.) was 169-170° (decomp.). Yield 0.16 g.

Iodination of 7-hydroxyflavone :

7-Hydroxy-8-iodoflavone

7-Hydroxyflavone (1.19 g. ; 0.005 mole) was dissolved in warm alcohol (30 ml.) and treated with iodine (0.5 g. ; 0.002 mole) and iodic acid (0.3 g.) in water with stirring for 2 hours. The separated product crystallised in colourless needles from alcohol, m.p. 230°. Yield 0.8 g.

Analysis :

9.998 mg. of the substance gave 6.196 mg. of silver iodide.

Found : I = 33.50 %.

$C_{15}H_9O_3I.H_2O$ requires : I = 33.24 %.

It decomposed on drying in vacuo.

The same iodo derivative was obtained on iodination of 7-hydroxyflavone (1.19 g. ; 0.005 mole) with iodine (1.27 g. ; 0.005 mole) in presence of ammonia (30 ml.). Yield 1.2 g.

Iodination with twice the above ammounts of iodine (1.0 g. ; 0.004 mole) and iodic acid (0.6 g.) gave only the above 8-iodo derivative in better yield. Yield 1.1 g.

The methyl ether , prepared by refluxing 7-hydroxy-8-iodoflavone (2 g.) in acetone on a steam bath with dimethyl sulphate (2 ml.) and anhydrous potassium carbonate (4 g.) for 7 hours, crystallised from ethyl alcohol in colourless needles, m.p. 210-211°.

Analysis :

8.92 mg. of the substance gave 16.52 mg. of carbon dioxide and 2.32 mg. of water.

9.076 mg. of the same substance gave 5.678 mg. of silver iodide.

Found : C = 50.54 % ; H = 2.92 % ; I = 33.82 %.

$C_{16}H_{11}O_3I$ requires : C = 50.79 % ; H = 2.91 % ; I = 33.59 %.

Alkaline hydrolysis of 7-methoxy-8-iodoflavone : 2-Hydroxy-3-iodo-4-methoxyacetophenone and 2-hydroxy-3-iodo-4-methoxybenzoic acid

7-Methoxy-8-iodoflavone (0.7 g.) was refluxed with aqueous alcoholic sodium hydroxide solution (10 % ; 30 ml.) for 4 hours. On working up as usual 2-hydroxy-3-iodo-4-methoxyacetophenone and 2-hydroxy-3-iodo-4-methoxybenzoic acid were obtained as seen by direct comparison.

7-Hydroxy-6,8-di-iodoflavone

7-Hydroxyflavone (1.19 g. ; 0.005 mole) was dissolved in warm alcohol and iodinated with iodine (1.52 g. ; 0.006 mole) and iodic acid (0.7 g.) in water with vigorous stirring for 2 hours. The product obtained crystallised in colourless needles, from acetic acid, m.p. 282-283° (decomp.). Yield 1.5 g.

Analysis :

11.002 mg. of the substance gave 10.606 mg. of silver iodide.

Found : I = 52.11 %.

$C_{15}H_8O_3I_2$ requires : I = 51.71 %.

The product was stable in boiling acetic acid.

With excess of the iodinating reagents the same product was obtained in better yield.

The methyl ether, prepared by refluxing the above di-iodoflavone (2 g.) in acetone with dimethyl sulphate (2 ml.) in presence of anhydrous potassium carbonate (4 g.)

for 8 hours, crystallised from dilute alcohol in colourless needles, m.p. 198-199°.

Analysis :

7.88 mg. of the substance gave 10.98 mg. of carbon dioxide and 1.32 mg. of water.

7.682 mg. of the same substance gave 7.112 mg. of silver iodide.

Found : C = 38.03 % ; H = 1.87 % ; I = 50.05 %.
$C_{16}H_{10}O_3I_2$ requires : C = 38.10 % ; H = 1.99 % ; I = 50.28 %.

Alkaline hydrolysis of 7-methoxy-6,8-di-iodoflavone : 2-Hydroxy-3,5-di-iodo-4-methoxyacetophenone and 2-hydroxy-3,5-di-iodo-4-methoxybenzoic acid

7-Methoxy-6,8-di-iodoflavone (1 g.) was refluxed with sodium hydroxide solution (10 % ; 30 ml.) for 4 hours. The product obtained on acidification on working up as usual gave 2-hydroxy-3,5-di-iodo-4-methoxybenzoic acid and 2-hydroxy-3,5-di-iodo-4-methoxyacetophenone as seen by direct comparison.

Iodination of 2-hydroxy-6-methoxyacetophenone : 2-Hydroxy-5-iodo-6-methoxyacetophenone

2-Hydroxy-6-methoxyacetophenone (0.83 g. ; 0.005 mole) was dissolved in warm alcohol and iodine crystals (0.5 g. ; 0.002 mole) were added. To the stirred reaction mixture iodic acid (0.2 g.) in water was added. The reaction mixture was stirred for 2 hours and the separated product crystallised from ethyl alcohol in thick yellow needles, m.p. 116°. Yield 1 g. Its alcoholic solution gave a red colouration with alcoholic ferric chloride.

Analysis :

11.80 mg. of the substance gave 5.548 mg. of silver iodide.

Found : I = 43.74 % .

$C_9H_9O_3I$ requires : I = 43.50 %.

The same iodo derivative was obtained on iodination of 2-hydroxy-6-methoxyacetophenone (1.62 g. ; 0.01 mole) either with iodine (2.54 g. ; 0.01 mole) and ammonia (Yield 2.1 g.) or with iodine monochloride (1.62 g. ; 0.01 mole) in acetic acid. Yield 0.8 g.

2-Hydroxy-5-iodo-6-methoxyacetophenone (0.2 g.) on methylation with dimethyl sulphate (0.2 ml.) in acetone solution in presence of anhydrous potassium carbonate (0.4 g.) by refluxing for 8 hours on a steam bath gave 2,6-dimethoxy-5-iodo-acetophenone (same as 2,6-dimethoxy-3-iodo-acetophenone) described earlier.

2-Hydroxy-3,5-di-iodo-6-methoxyacetophenone

2-Hydroxy-6-methoxyacetophenone (0.83 g. ; 0.005 mole) was treated in warm alcohol with iodine crystals (1.01 g. ; 0.004 mole) with stirring followed by iodic acid (0.5 g.) in water. The separated shining product crystallised from ethyl alcohol in tiny yellow needles, m.p. 111°. Yield 1.6 g.

The di-iodo ketone did not decompose even on prolonged refluxing (5 hr.) with glacial acetic acid.

The same di-iodo derivative was obtained on iodination of 2-hydroxy-6-methoxyacetophenone (0.83 g. ; 0.005 mole) with iodine (2.54 g. ; 0.01 mole) in presence of ammonia (yield 1.4 g.) or with iodine monochloride (1.62 g. ; 0.01 mole) in acetic acid (yield 1.2 g.).

Iodination of 2-hydroxy-4-methoxyacetophenone : 2-Hydroxy-3-iodo-4-methoxyacetophenone and 2-hydroxy-3,5-di-iodo-4-methoxyacetophenone

2-Hydroxy-4-methoxyacetophenone (1.66 g. ; 0.01 mole) in warm alcohol was treated with iodine crystals (1.01 g. ; 0.004 mole) and iodic acid (0.5 g.) in water with vigorous stirring for 2 hours. The separated shining solid crystallised from ethyl alcohol in thick white needles, m.p. 152°. Yield 0.4 g.

The mother liquor on dilution gave a little 2-hydroxy-3,5-di-iodo-4-methoxyacetophenone, m.p. 98-99°. Yield 0.2 g.

2-Hydroxy-4-methoxy-5-iodo-acetophenone

2-Hydroxy-4-methoxyacetophenone (1.66 g. ; 0.01 mole) was iodinated with iodine (2.5 g. ; 0.01 mole) in presence of ammonia. The product obtained on acidification crystallised from ethyl alcohol in colourless long needles, m.p. 161°. Yield 0.4 g.

Iodination of 2,4-dihydroxybenzoic acid : 2,4-Dihydroxy-3,5-di-iodobenzoic acid

2,4-Dihydroxybenzoic acid (1.54 g. ; 0.01 mole) was iodinated with iodine (2.03 g. 0.008 mole) and iodic acid (0.8 g.) in water. The separated product crystallised from benzene in brown needles, m.p. 218° (efferv.). Yield 2.8 g. Some decomposition was observed on heating with acetic acid.

<u>Analysis</u> :

27.230 mg. of the substance gave 31.708 mg. of silver iodide.

Found : I = 62.94 %.

$C_7H_4O_4I_2$ requires : I = 62.56 %.

The same di-iodo acid was obtained on iodination of β-resorcylic acid (1.54 g. ; 0.01 mole) with iodine (5.08 g. ; 0.02 mole) in presence of aqueous ammonia. Yield 3 g.

Nicolet and Sampey (J. Am. Chem. Soc., 1927, 49, 1796) prepared the above di-iodo acid by iodination of β-resorcylic acid with iodine in ether using litharge as an oxidising agent. They reported m.p. 193-196° (decomp.)

<u>Methyl-2,4-dimethoxy-3,5-di-iodo-benzoate</u>

The above di-iodo acid (1.5 g.) was methylated and esterified simultaneously by refluxing its acetone solution with dimethyl sulphate (2 ml.) in the presence of anhydrous potassium carbonate (4 g.) for 10 hours. The product obtained was pasty and solidified after keeping for 48 hours. It was repeatedly washed with cold petroleum ether (b.p. 60-80°) and crystallised from a mixture of benzene and petroleum ether (b.p. 60-80°) in colourless needles, m.p. 60°.

Analysis :

3.956 mg. of the substance gave 3.818 mg. of carbon dioxide and 0.766 mg. of water.

11.028 mg. of the same substance gave 11.706 mg. of silver iodide.

Found : C = 26.34 % ; H = 2.17 % ; I = 57.41 %.

$C_{10}H_{10}O_4I_2$ requires : C = 26.79 % ; H = 2.23 % ; I = 56.67 %.

2,4-Dimethoxy-3,5-di-iodobenzoic acid

Methyl-2,4-dimethoxy-3,5-di-iodobenzoate (1 g.) was treated with sodium hydroxide solution (10 % ; 25 ml.) and kept in a hot water bath at 60° till all of it went in solution. The acid obtained on acidification crystallised from silute acetic acid in colourless needles, m.p. 183-184°.

Analysis :

4.518 mg. of the substance gave 4.132 mg. of carbon dioxide and 0.772 mg. of water.

18.040 mg. of the same substance gave 19.504 mg. of silver iodide.

Found : C = 24.96 % ; H = 1.91 % ; I = 58.57 %.

$C_9H_8O_4I_2$ requires : C = 24.88 % ; H = 1.84 % ; I = 58.53 %.

Attemoted iodination of 2-methylchromone, flavone, 5-methoxy-and 7-methoxy-2-methylchromone

(a) With iodine and iodic acid

The chromone or flavone derivative (0.01 mole) was dissolved in warm alcohol and treated with iodine (1.01 g. ; 0.004 mole) and iodic acid (0.35 g.) in minimum quantity of water. The reaction mixture after stirring for 2 hr. was poured in sodium hydrogen sulphite solution. The product isolated in every case was the starting material.

(b) With iodine and ammonia

The chromone or flavone derivative (0.01 mole) was dissolved in ammonia (40 ml.) and dioxan (25 ml.) and treated with iodine (2.54 g. ; 0.01 mole) solution with stirring for 1 hr. and the solution then acidified with cold dilute sulphuric acid. The product obtained in every case was the starting material.

(c) With iodine monochloride

The chromone or flavone derivative (0.01 mole) was treated with iodine monochloride (3.24 g. ; 0.02 mole) in acetic acid and kept in an oven at 60° over-night. On dilution with sodium hydrogen sulphite solution it gave a chloro derivative in all the cases.

Iodination in each case with excess of the above reagents and keeping the reaction mixture for different periods failed to yield any iodo derivative.