THEORETICAL

Section (ii)

Kostanecki-Robinson Acylation of some Iodo-derivatives of 2,4-and 2,6-Dihydroxyacetophenone

The effect of the presence of various substituents such as chloro-, bromo-, alkyl- etc. in the o-hydroxyacetophenones has been studied, but no work has been carried out so far to study the effect of an iodine atom in the o-hydroxyacetophenone on the course of this reaction as will be seen from the discussion of the Kostanecki-Robinson reaction. The present work deals with the synthesis of some iodo-chromones and -flavones, by the Kostanecki-Robinson acetylation and benzoylation of the mono-iodo and di-iodo-o-hydroxyacetophenones.

The iodo ketones required for this purpose were first synthesised from 2,4- and 2,6-dihydroxyacetophenone and their structures established.

Iodination of 2,4-dihydroxyacetophenone

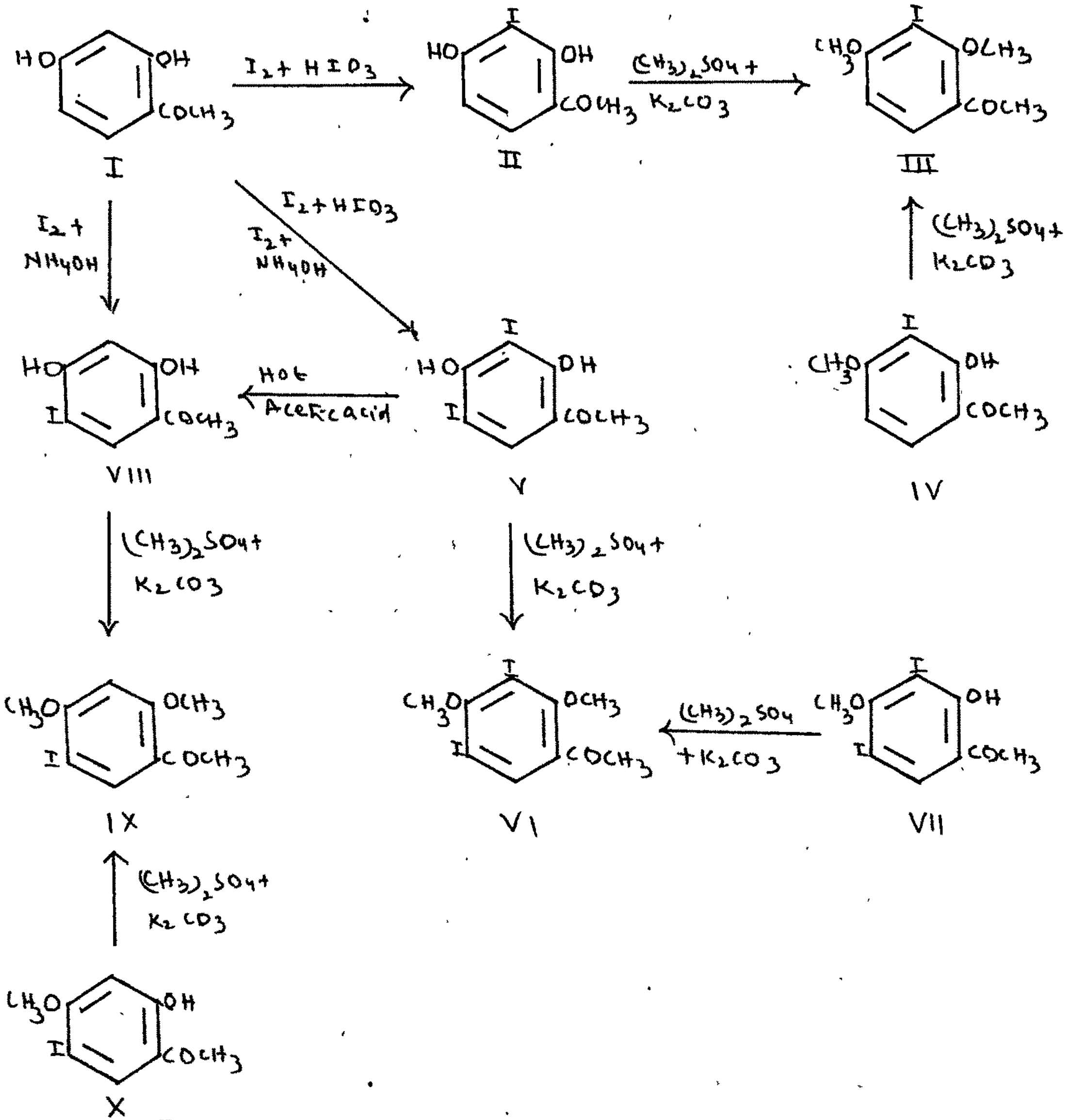
Segalle (Monatsh., 1896, 17, 314) iodinated 2,4-dihydroxyacetophenone with potassium iodate and potassium iodide in acetic acid solution and obtained a mono-iodo derivative, m.p. 158°, to which no definite structure was assigned. In the present work 2,4-dihydroxyacetophenone (I) on iodination with iodine and iodic acid afforded a mono-iodo derivative, m.p. 164°. Its dimethyl ether was found on direct comparison to be identical with the methyl ether of

2-hydroxy-3-iodo-4-methoxyacetophenone (IV) described in section (i). Segalle's iodo derivative was therefore 2,4-dihydroxy-3-iodo-acetophenone (II).

2,4-Dihydroxyacetophenone (I) on iodination with twice the theoretical amounts of iodine and iodic acid gave the 3,5-di-iodo derivative (V). Its dimethyl ether was identical with the methyl ether of 2-hydroxy-3,5-di-iodo-4-methoxyacetophenone (VII) described in section (i).

2,4-Dihydroxyacetophenone (I) on iodination with one mole of iodine in presence of ammonia gave a mixture from which mono-iodo and di-iodo derivatives were isolated by fractional crystallisation from ethyl alcohol in which the mono-iodo derivative was more soluble than the di-iodo derivative. The mono-iodo derivative was different from 2,4-dihydroxy-3-iodo-acetophenone (II) obtained by iodination with iodine and iodic acid. Further, its dimethyl ether agreed with the methyl ether of 2-hydroxy-4-methoxy-5-iodo-acetophenone (X) described in section (i). Therefore the mono-iodo derivative was 2,4-dihydroxy-5-iodo-acetophenone (VIII). The di-iodo derivative was the 3,5-di-iodo derivative (V) described above.

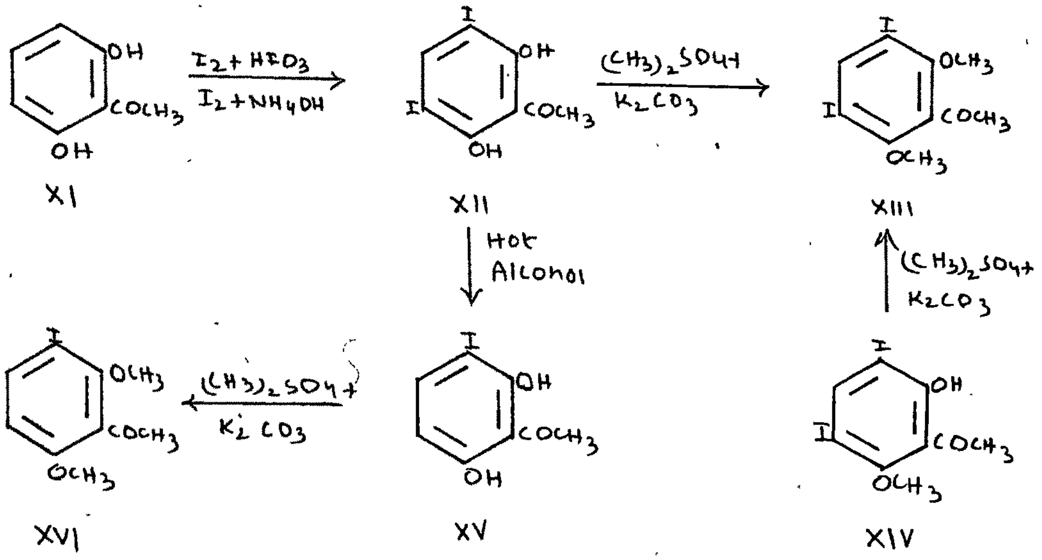
2,4-Dihydroxy-5-iodo-acetophenone (VIII) was obtained in better yield by refluxing2,4-dihydroxy-3,5-di-iodo-acetophenone (V) in acetic acid solution. It underwent decomposition losing the iodine atom from the 3-position.



Iodination of 2,6-dihydroxyacetophenone

2,6-Dihydroxyacetophenone (XI) on iodination with the theoretical amounts of iodine and iodic acid gave a di-iodo-ketone in poor yield. But with twice the theoretical amounts of iodine and iodic acid it gave the di-iodo derivative in better yield. The dimethyl ether of the di-iodo ketone was identical with the methyl ether of 2-hydroxy-3,5-di-iodo-6-methoxyacetophenone (XIV) described in section (i). The di-iodo ketone was therefore 2,6-dihydroxy-3,5-di-iodo-acetophenone (XII)..

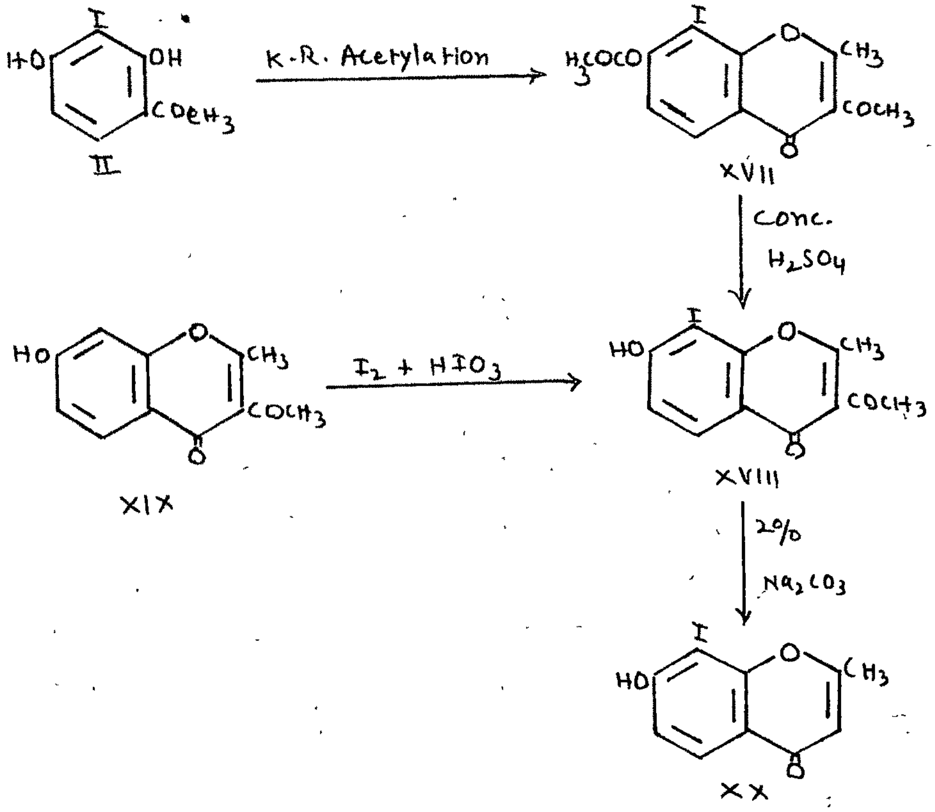
The above di-iodo ketone (XII) when refluxed with ethyl alcohol lost one iodine atom and gave a mono-iodo-acetophenone. As this can result in only one mono-iodo derivative, the mono-iodo-acetophenone has been assigned 2,6-dihydroxy-3-iodo-acetophenone (XV) structure. The dimethyl ether of this was identical with the 2,6-dimethoxy-3-iodo-acetophenone (XVI) described in section (i).



Kostanecki-Robinson acetylation of 2,4-dihydroxy-3-iodo-acetophenone

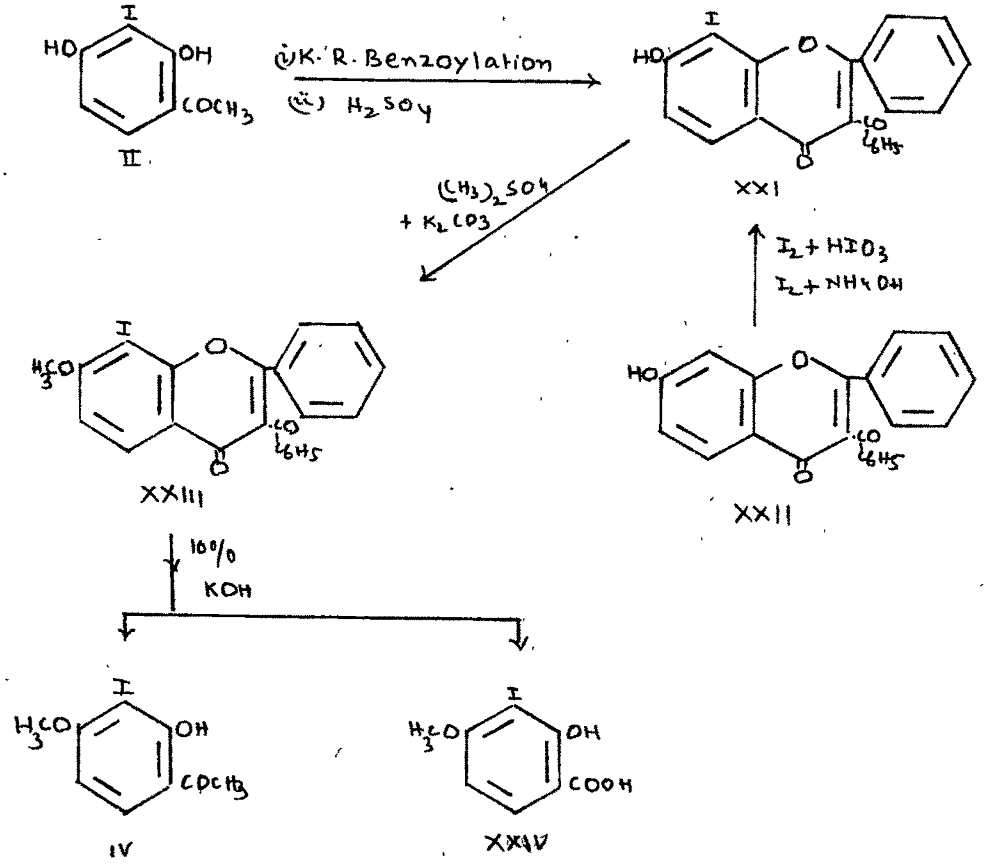
2,4-Dihydroxy-3-iodo-acetophenone (II) on Kostanecki-Robinson acetylation with sodium acetate and acetic anhydride gave a product which has been assigned 7-acetoxy-8-iodo-3-acetyl-2-methylchromone (XVII) structure. On treatment with concentrated sulphuric acid it gave 7-hydroxy-3-acetyl-8-iodo-2-methylchromone (XVIII) identical with the product obtained on iodination of

7-hydroxy-3-acetyl-2-methylchromone (XIX) with the theoretical amounts of iodine and iodic acid. This on heating with alkali gave a de-acetylated product identical with 7-hydroxy-8-iodo-2-methylchromone (XX) prepared by the iodination of 7-hydroxy-2-methylchromone as described in section (i).



Kostanecki-Robinson benzoylation of 2,4-dihydroxy-3-iodo-acetophenone

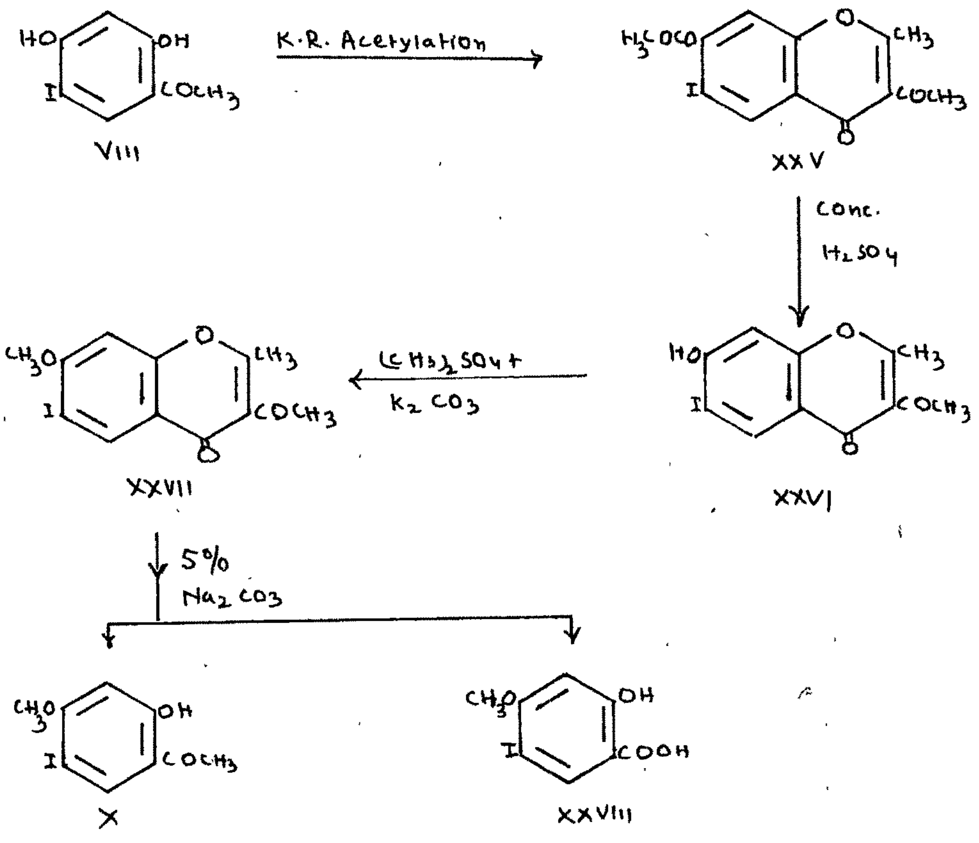
2,4-Dihydroxy-3-iodo-acetophenone (II) on Kostanecki-Robinson benzoylation with sodium benzoate and benzoic anhydride gave a product which could not be purified hence it was treated directly with concentrated sulphuric acid. It yielded a hydroxy-iodoflavone identical with the mono-iodo product obtained from 7-hydroxy-3-benzoylflavone(XXII) by iodination with the theoretical amounts of iodine and iodic acid and has therefore been assigned 7-hydroxy-8-iodo-3-benzoylflavone (XXI) structure. Attempts to debenzoylate this product with alkali gave unsatisfactory results. Its methyl ether on alkaline hydrolysis did not give any debenzoylated flavone but gave instead an iodo phenolic ketone and an iodo phenolic acid which were found on direct comparison to be 2-hydroxy-3-iodo-4-methoxyacetophenone (IV) and 2-hydroxy-3-iodo-4-methoxybenzoic acid (XXIV) respectively, described in section (i).



Kostanecki-Robinson acetylation of 2,4-dihydroxy-5-iodo-acetophenone

2,4-Dihydroxy-5-iodo-acetophenone (VIII) on

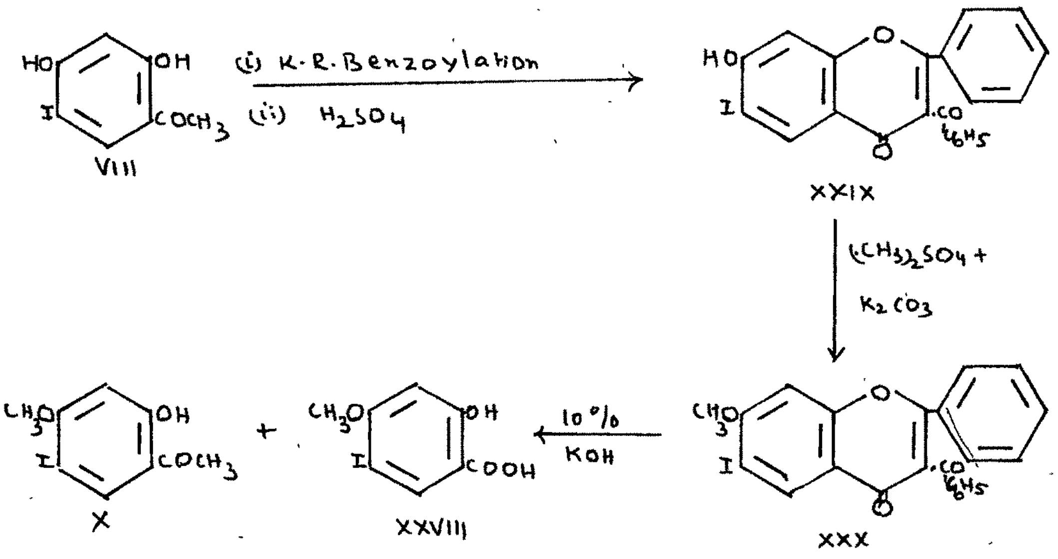
Kostanecki-Robinson acetylation with sodium acetate and acetic anhydride gave a product which has been assigned 7-acetoxy-6-iodo-3-acetyl-2-methylchromone (XXV) structure. On de-esterification with sulphuric acid it gave 7-hydroxy-6-iodo-3-acetyl-2-methylchromone (XXVI). Attempts to de-acetylate this compound did not succeed. The methyl ether of this 3-acetylchromone on heating with alkali decomposed to give a mixture of 2-hydroxy-4-methoxy-5-iodo-acetophenone (X) and 2-hydroxy-4-methoxy-5-iodobenzoic acid (XXVIII) described in section (i).



Kostanecki-Robinson benzoylation of 2,4-dihydroxy-5-iodo-acetophenone

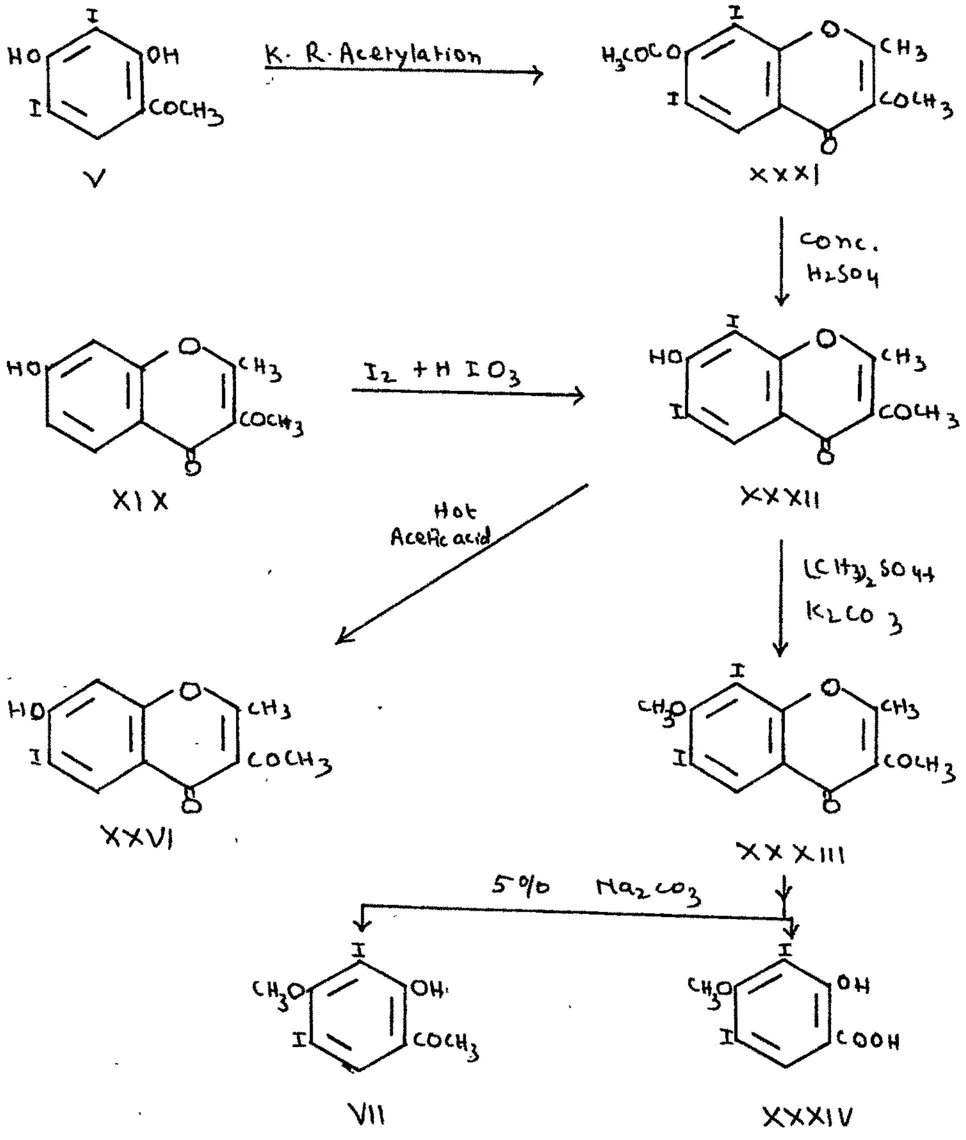
2,4-Dihydroxy-5-iodo-acetophenone (VIII) on

Kostanecki-Robinson benzoylation with sodium benzoate and benzoic anhydride gave an impure reddish brown product which could not be purified. The crude product was therefore treated with sulphuric acid when a hydroxy-iodoflavone was obtained. This has been assigned 7-hydroxy-6-iodo-3-benzoylflavone (XXIX) structure. It could not be debenzoylated with alkali. Its methyl ether gave 2-hydroxy-4-methoxy-5-iodo-acetophenone (X) and 2-hydroxy-4-methoxy-5-iodobenzoic acid (XXVIII) instead of the debenzoylated product on treatment with alcoholic potassium hydroxide.



Kostanecki-Robinson acetylation of 2,4-dihydroxy-3,5-di-iodo-acetophenone

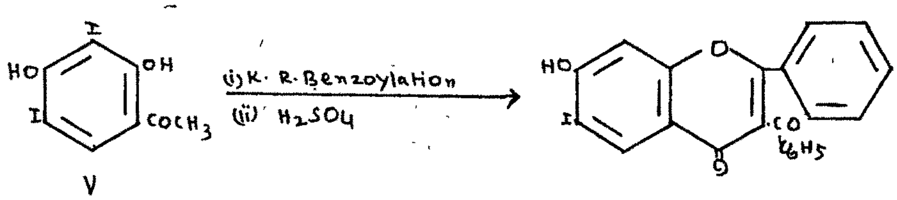
2,4-Dihydroxy-3,5-di-iodo-acetophenone (V) on Kostanecki-Robinson acetylation with acetic anhydride and sodium acetate gave 7-acetoxy-6,8-di-iodo-3-acetyl-2-methylchromone (XXXI). This on de-esterification with sulphuric acid gave a hydroxychromone identical with the di-iodo-chromone obtained from 7-hydroxy-3-acetyl-2-methylchromone (XIX) by iodination with iodine and iodic acid. The product obtained on de-esterification with sulphuric acid has therefore been assigned 7-hydroxy-6,8-di-iodo-3-acetyl-2-methylchromone (XXXII) structure. On alkaline hydrolysis no pure product could be obtained. Its methyl ether on alkaline hydrolysis gave a mixture of 2-hydroxy-3,5-di-iodo-4-methoxyacetophenone (VII) and 2-hydroxy-3,5-di-iodo-4-methoxybenzoic acid (XXXIV) described in section (i).



7-Hydroxy-6,8-di-iodo-3-acetyl-2-methylchromone (XXXII) on prolonged refluxing with glacial acetic acid lost one iodine atom and gave 7-hydroxy-6-iodo-3-acetyl-2-methylchromone (XXVI) described before.

Kostanecki-Robinson benzoylation of 2,4-dihydroxy-3,5-di-iodo-acetophenone

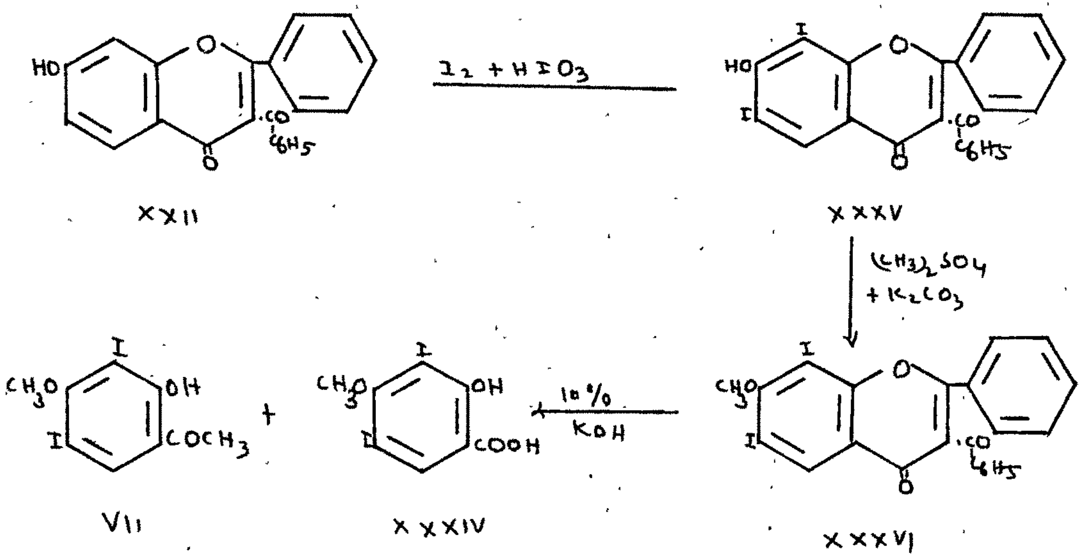
2,4-Dihydroxy-3,5-di-iodo-acetophenone (V) on Kostanecki-Robinson benzoylation with sodium benzoate and benzoic anhydride gave a deep reddish brown product which could not be purified and so was treated with sulphuric acid. It gave a mono-iodo-hydroxyflavone identical with 7-hydroxy-6-iodo-3-benzoylflavone (XXIX) described before. The iodine atom from the 3-position of the ketone was eliminated in the course of the reaction.



V

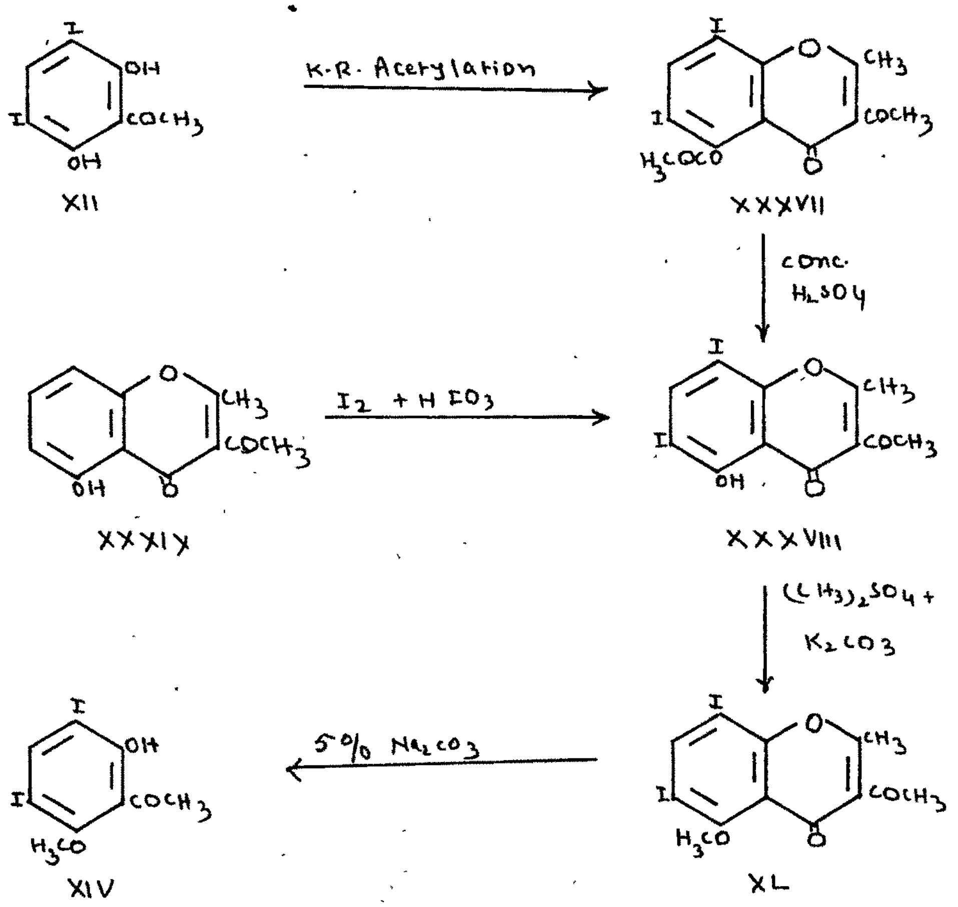
XXIX

The desired 7-hydroxy-6,8-di-iodo-3-benzoylflavone (XXXV) has however been obtained by iodinating 7-hydroxy-3-benzoylflavone (XXII) with iodine and iodic acid. The methyl ether of this on alkaline hydrolysis gave 2-hydroxy-3,5-di-iodo-4-methoxyacetophenone (VII) and 2-hydroxy-3,5-di-iodo-4-methoxybenzoic acid (XXXIV) described in section (i).



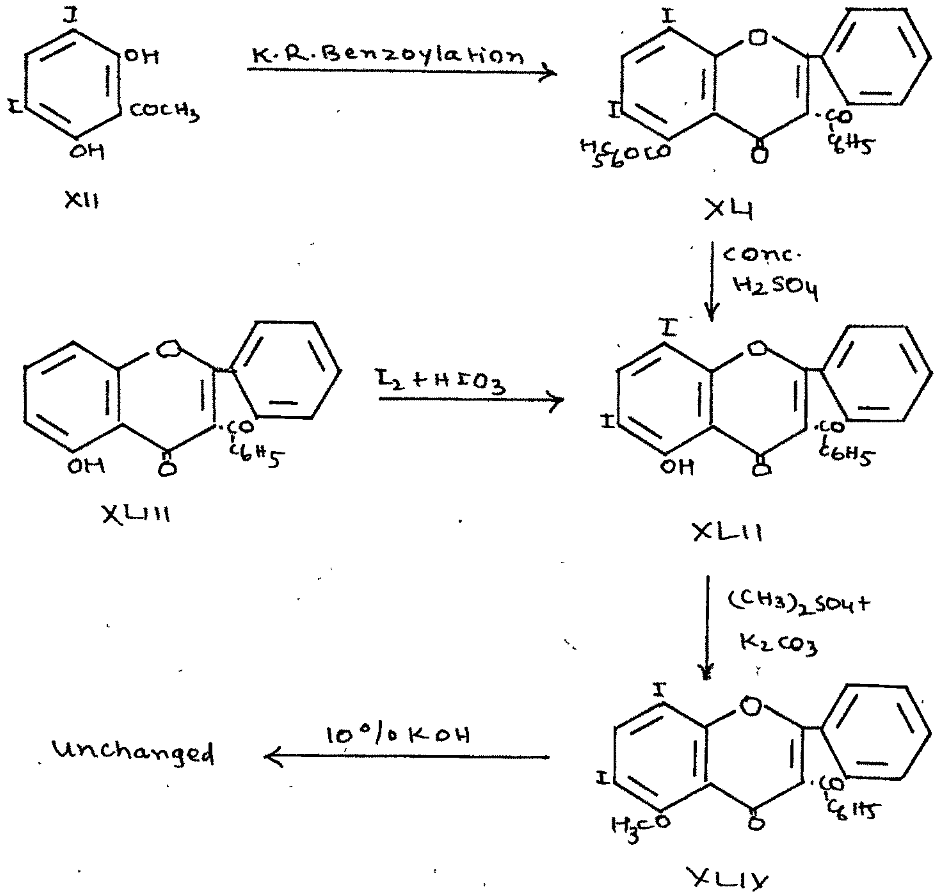
Kostanecki-Robinson acetylation of 2,6-dihydroxy-3,5-di-iodo-acetophenone

2,6-Dihydroxy-3,5-di-iodo-acetophenone (XII) when subjected to Kostanecki-Robinson acetylation with sodium acetate and acetic anhydride gave a product which has been assigned 5-acetoxy-6,8-di-iodo-3-acetyl-2-methylchromone (XXXVII) structure. On de-esterification with sulphuric acid it gave a hydroxy-di-iodo derivative identical with the one obtained on iodination of 5-hydroxy-3-acetyl-2-methylchromone (XXXIX) with iodine and iodic acid. The product obtained on de-esterification with sulphuric acid has therefore been assigned 5-hydroxy-6,8-di-iodo-3-acetyl-2-methylchromone (XXXVIII) structure. Its methyl ether on alkaline hydrolysis gave 2-hydroxy-3,5-di-iodo-6-methoxyacetophenone (XIV) described in section (i) and no de-acetylated product could be isolated.



Kostanecki-Robinson benzoylation of 2,6-dihydroxy-3,5-di-iodo-acetophenone

2,6-Dihydroxy-3,5-di-iodo-acetophenone (XII) on Kostanecki-Robinson benzoylation with sodium benzoate and benzoic anhydride gave a product which has been assigned 5-benzoyloxy-6,8-di-iodo-3-benzoylflavone (XLI) structure. On de-esterification with sulphuric acid it gave 5-hydroxy-6,8-di-iodo-3-benzoylflavone (XLII) identical with the product obtained in the iodination of 5-hydroxy-3-benzoylflavone (XLIII). Its methyl ether on treatment with hot alkali remained unchanged.



General observations :

The best temperature for both the acetylation and benzoylation was found to be 155-160°. Higher temperatures led to decomposition of the iodo ketone and gave unworkable products. Larger quantities of the sodium salts of the acids also had a deleterious effect on the reaction and led to decomposition of the iodo ketones and highly coloured products were obtained which could not be purified. Yields in the Kostanecki-Robinson acetylation and benzoylation varied ~~vary~~ from 13 to 20%.

EXPERIMENTAL

Section (ii)

Iodination of 2,4-dihydroxyacetophenone : 2,4-Dihydroxy-3-iodoacetophenone

2,4-Dihydroxyacetophenone (1.52 g. ; 0.01 mole) was iodinated in ethyl alcohol with iodine (1.01 g. ; 0.004 mole) and iodic acid (0.5 g.) in water by stirring for half an hour at room temperature. The shining product obtained on dilution of the reaction mixture, crystallised from benzene in colourless plates, m.p. 164° (decomp.). Yield 2.3 g. Its alcoholic solution gave a deep red colouration with alcoholic ferric chloride.

Analysis :

13.088 mg. of the substance gave 11.026 mg. of silver iodide.

Found : I = 45.54 %.

$C_8H_7O_3I$ requires : I = 45.68 %.

The dimethyl ether, prepared by refluxing the above iodo ketone (0.5 g.) in acetone with dimethyl sulphate (0.6 ml.) in presence of anhydrous potassium carbonate (1.2 g.) for 10 hours, crystallised from petroleum ether (b.p. 60-80°) in colourless needles, m.p. 101-102°. It agreed when compared directly with the methyl ether of 2-hydroxy-3-iodo-4-methoxyacetophenone.

Analysis :

4.070 mg. of the substance gave 5.898 mg. of carbon dioxide and 1.332 mg. of water.

8.124 mg. of the same substance gave 6.282 mg. of silver iodide.

Found : C = 39.53 % ; H = 3.66 % ; I = 41.80 %.
$C_{10}H_{11}O_3I$ requires : C = 39.21 % ; H = 3.60 % ; I = 41.50 %.

2,4-Dihydroxy-5-iodo-acetophenone

2,4-Dihydroxyacetophenone (1.52 g. ; 0.01 mole) was dissolved in aqueous ammonia solution and iodine (2.54 g. ; 0.01 mole) was added with vigorous stirring of the reaction mixture within 15 minutes. The solution was immediately acidified with ice cold dilute sulphuric acid other wise the product starts decomposing. The solid obtained was extracted with hot ethyl alcohol (15 ml.) and filtered. The filtrate on dilution gave colourless needles, m.p. 184° (decomp.). Yield 0.4 g. Its alcoholic solution gave a deep red colouration with alcoholic ferric chloride.

Analysis :

10.150 mg. of the substance gave 8.602 mg. of silver iodide.

Found : I = 45.81 %.
$C_8H_7O_3I$ requires : I = 45.68 %.

The residue from above crystallised from acetic acid in tiny needles, and was found to be identical with 2,4-dihydroxy-3,5-di-iodo-acetophenone described below.

The dimethyl ether, prepared by refluxing the

5-iodo ketone (0.5 g.) in acetone with dimethyl sulphate (0.6 ml.) in presence of anhydrous potassium carbonate (1.2 g.) for 10 hours, crystallised in colourless stout needles from petroleum ether (b.p. 60-80°). M.P. and mixed m.p. with the methyl ether of 2-hydroxy-4-methoxy-5-iodo-acetophenone was 145°.

Analysis :

4.480 mg. of the substance gave 6.412 mg. of carbon dioxide and 1.512 mg. of water.

11.160 mg. of the same substance gave 8.572 mg. of silver iodide.

Found : C = 39.06 % ; H = 3.78 % ; I = 41.52 %.
$C_{10}H_{11}O_3I$ requires : C = 39.21 % ; H = 3.60 % ; I = 41.50 %.

2,4-Dihydroxy-3,5-di-iodo-acetophenone

2,4-Dihydroxyacetophenone (1.52 g. ; 0.01 mole) was iodinated with iodine (2.03 g. ; 0.008 mole) and iodic acid (0.8 g.) in water with stirring. After one hour the separated product was crystallised from acetic acid in tiny needles, m.p. 180° (decomp.). Yield 3.5 g. Its alcoholic solution gave a deep red colouration with alcoholic ferric chloride.

Analysis :

19.578 mg. of the substance gave 22.802 mg. of silver iodide.

Found : I = 62.96 %.
$C_8H_6O_3I_2$ requires : I = 62.87 %.

The di-iodo ketone was obtained on iodination of

2,4-dihydroxyacetophenone (1.52 g. ; 0.01 mole) with iodine (5.08 g. ; 0.02 mole) in presence of aqueous ammonia. The iodine solution was added within 15 minutes and the reaction mixture immediately acidified otherwise the product starts decomposing and the solution becomes reddish in colour. Yield 3.2 g.

The same di-iodo ketone was also obtained by iodination of 2,4-dihydroxyacetophenone (1.52 g. ; 0.01 mole) with iodine monochloride (3.24 g. ; 0.02 mole) in ethyl alcohol. Yield 2.4 g.

On refluxing the di-iodo ketone in glacial acetic acid for 2 hours, the solution became deep violet. The product obtained on pouring it in ice-cold sodium hydrogen sulphite solution was found to be 2,4-dihydroxy-5-iodoacetophenone.

The dimethyl ether, prepared by refluxing the di-iodo ketone (0.5 g.) in acetone with dimethyl sulphate (0.6 ml.) in presence of anhydrous potassium carbonate (1.2 g.) for 10 hours, crystallised from petroleum ether (b.p. 40-60°) in colourless plates. M.P. and mixed m.p. with the methyl ether of 2-hydroxy-3,5-di-iodo-4-methoxyacetophenone was 59-60° (~~opalascence~~).

Analysis :

4.204 mg. of the substance gave 4.260 mg. of carbon dioxide and 0.884 mg. of water.

10.07 mg. of the same substance gave 11.026 mg. of silver iodide.

Found : C = 27.65 % ; H = 2.35 % ; I = 59.19 %.

$C_{10}H_{10}O_3I_2$ requires : C = 27.77 % ; H = 2.32 % ; I = 58.80 %.

Iodination of 2,6-dihydroxyacetophenone : 2,6-Dihydroxy-3,5-di-iodoacetophenone

2,6-Dihydroxyacetophenone (1.52 g. ; 0.01 mole) was dissolved in alcohol at room temperature. To the stirred reaction mixture iodine crystals (1.01 g. ; 0.004 mole) and iodic acid (0.4 g.) in water were added. A product immediately separated. It crystallised from aqueous acetone in yellow needles, m.p. 133°. Yield 1.6 g. It decomposed in boiling ethyl alcohol. Its alcoholic solution gave a deep red colouration with alcoholic ferric chloride.

Analysis :

11.086 mg. of the substance gave 12.790 mg. of silver iodide.

Found : I = 62.37 %.

$C_8H_6O_3I_2$ requires : I = 62.87 %.

Attempts to synthesise a mono-iodo derivative from 2,6-dihydroxyacetophenone by carrying out the above iodination at 0° did not succeed. Only the above di-iodo derivative was obtained.

The same di-iodo ketone was obtained in better yield on iodination with iodine (2.03 g. ; 0.008 mole) and iodic acid (0.8 g.) (Yield 3.2 g.) or with iodine (5.08 g. ; 0.02 mole) and ammonia (Yield 3.0 g.).

The dimethyl ether, prepared from the di-iodo ketone (2 g.) by refluxing its acetone solution with dimethyl sulphate (2 ml.) in presence of anhydrous potassium carbonate (4 g.) for 8 hours, crystallised from petroleum ether (b.p. 40-60°) in colourless needles, m.p. 83-84°. The same product was obtained on methylation of 2-hydroxy-3,5-di-iodo-6-methoxyacetophenone.

Analysis :

4.310 mg. of the substance gave 4.426 mg. of carbon dioxide and 0.786 mg. of water.

10.104 mg. of the same substance gave 10.942 mg. of silver iodide.

Found : $C = 28.03\ \%$; $H = 2.04\ \%$; $I = 58.54\ \%$.

$\overset{C_{10}H_{10}}{\cancel{C_9H_8}}O_3I_2$ requires : $C = 27.77\ \%$; $H = 2.31\ \%$; $I = 58.80\ \%$.

Decomposition of 2,6-dihydroxy-3,5-di-iodo-acetophenone with boiling alcohol : 2,6-Dihydroxy-3-iodo-acetophenone

2,6-Dihydroxy-3,5-di-iodo-acetophenone (2 g.) was boiled in ethyl alcohol (30 ml.) for one hour and the reaction mixture was added after cooling to sodium hydrogen sulphite solution. The product obtained crystallised in yellow needles, m.p. 162°. Yield 0.2 g. Its alcoholic solution gave a deep red colouration with alcoholic ferric chloride.

Analysis :

8.374 mg. of the substance gave 7.00 mg. of silver iodide.

Found : $I = 45.19\ \%$.

$C_8H_7O_3I$ requires : $I = 45.68\ \%$.

The dimethyl ether, prepared by refluxing 2,6-dihydroxy-3-iodo-acetophenone (0.5 g.) in acetone with dimethyl sulphate (1.0 ml.) in presence of anhydrous potassium carbonate (2 g.) for 10 hours was found identical with 2,6-dimethoxy-3-iodo-acetophenone described in section (i).

Kostanecki-Robinson acetylation of 2,4-dihydroxy-3-iodo-acetophenone : 7-Acetoxy-8-iodo-3-acetyl-2-methylchromone

2,4-Dihydroxy-3-iodo-acetophenone (4 g.) was mixed with freshly fused and powdered sodium acetate (18 g.) and distilled acetic anhydride (60 ml.). The reaction mixture, protected from moisture, was heated in an oil bath at 125-130° for half an hour and then the temperature was slowly raised to 155-160° during one hour and maintained there for 5 hours. Excess of acetic anhydride was distilled under vacuum and the reaction mixture added to ice cold water. The product obtained was crystallised first from acetic acid (charcoal) and then from ethyl alcohol in colourless needles, m.p. 190-191°. Yield 1.2 g. Higher temperatures or longer heating time gave poor yields or non-crystallisable deep brown coloured mass.

Analysis :

9.56 mg. of the substance gave 15.36 mg. of carbon dioxide and 2.30 mg. of water.

17.18 mg. of the same substance gave 10.40 mg. of silver iodide.

Found : C = 43.85 % ; H = 2.69 % ; I = 32.72 %.

$C_{14}H_{11}O_5I$ requires : C = 43.52 % ; H = 2.85 % ; I = 32.91 %.

7-Hydroxy-8-iodo-3-acetyl-2-methylchromone

The above chromone (2 g.) was dissolved in minimum quantity of concentrated sulphuric acid (15 ml.), occasionally stirred and kept at room temperature for 4 hours. The product obtained on pouring the reaction mixture over crushed ice was purified through sodium hydroxide solution. The product obtained crystallised from ethyl alcohol in colourless needles, m.p. 240°.

Analysis :

13.88 mg. of the substance gave 13.88 mg. of carbon dioxide and 1.90 mg. of water.

10.396 mg. of the same substance gave 7.092 mg. of silver iodide.

Found : C = 42.37 % ; H = 2.38 % ; I = 36.88 %.

$C_{12}H_9O_4I$ requires : C = ~~42.64~~ 41.85 % ; H = 2.62 % ; I = 36.92 %.

The same iodo product was obtained on iodination of 7-hydroxy-3-acetyl-2-methylchromone (2.18 g. ; 0.01 mole) in warm alcohol with iodine crystals (1.01 g. ; 0.004 mole) and iodic acid (0.5 g.) in water with stirring for 2 hours. The separated product crystallised from ethyl alcohol in colourless needles, Yield 2 g.

The methyl ether , prepared by refluxing 7-hydroxy-8-iodo-3-acetyl-2-methylchromone (1 g.) in dry benzene with dimethyl sulphate (1 g.) in presence of anhydrous potassium carbonate (2 g.) for 3 hours on a steam bath.

The product obtained on removal of benzene crystallised from ethyl alcohol in colourless needles, m.p. 164°. Methylation in acetone solution led to decomposition of the iodo derivative.

Analysis :

8.59 mg. of the substance gave 13.57 mg. of carbon dioxide and 2.00 mg. of water.

13.78 mg. of the same substance gave 8.96 mg. of silver iodide.

Found : C = 43.12 % ; H = 2.61 % ; I = 35.14 %.

$C_{13}H_{11}O_4I$ requires : C = 43.57 % ; H = 3.07 % ; I = 35.47 %.

Desacetylation of 7-hydroxy-8-iodo-3-acetyl-2-methylchromone : 7-Hydroxy-8-iodo-2-methylchromone

The above 3-acetylchromone (1 g.) was heated with aqueous alcoholic sodium carbonate solution (2 % ; 20 ml.) on a steam bath for fifteen minutes. The product obtained on acidification with cold dilute hydrochloric acid crystallised from alcohol in colourless needles. M.P. and mixed m.p. with 7-hydroxy-8-iodo-2-methylchromone (described in section (i)) was 213° (decomp.)

Kostanecki-Robinson benzoylation of 2,4-dihydroxy-3-iodo-acetophenone : 7-Hydroxy-8-iodo-3-benzoylflavone

2,4-Dihydroxy-3-iodo-acetophenone (2 g.) was thoroughly mixed with freshly fused and powdered sodium benzoate (1 g.) and benzoic anhydride (20 g.). The reaction mixture was heated in an oil bath first at 125-130° for half an hour and then at 155-160° for 5 hours. Higher reaction temperatures or longer heating time led to the decomposition of the iodo derivative..More of sodium benzoate also accelerated the decomposition. The reaction mixture was then treated repeatedly with hot water to remove sodium benzoate and benzoic anhydride and finally washed with sodium hydrogen carbonate solution. The residue obtained could not be crystallised.and so was treated with concentrated sulphuric acid (20 ml.) and kept at room temperature over-night. Next day it was poured over crushed ice and the separated product purified by extraction with sodium hydroxide solution. The product obtained on acidification crystallised from ethyl alcohol in colourless needles, m.p. 246°. Yield 0.2 g.

Analysis :

9.48 mg. of the substance gave 19.46 mg. of carbon dioxide and 2.56 mg. of water.

9.764 mg. of the same substance gave 4.880 mg. of silver iodide.

Found : C = 56.02 % ; H = 3.02 % ; I = 27.02 %.

$C_{22}H_{13}O_4I$ requires : C = 56.41 % ; H = 2.78 % ; I = 27.16 %.

The same product was obtained on iodination of 7-hydroxy-3-benzoylflavone (1.71 g. ; 0.005 mole) in warm alcohol with iodine (0.5 g. ; 0.002 mole) and iodic acid (0.2 g.) in water. The separated product crystallised in needles, from alcohol. Yield 1.1 g. It was also obtained on iodination with iodine and ammonia as follows.

7-Hydroxy-3-benzoylflavone (1.71 g. ; 0.005 mole) was partly dissolved by stirring in ammonia(22 % ; 30 ml.) and water (120 ml.). The solution was filtered and the residue was repeatedly treated with ammonia till all of it dissolved. To the clear solution was added the iodine solution (1.27 g. ; 0.005 mole) with stirring for half an hour and the reaction mixture acidified. The product obtained crystallised in needles from alcohol. Yield 1.4 g.

Attempts to debenzoylate the hydroxyflavone (1 g.) with alcoholic potassium hydroxide solution (10 % ; 20 ml.) by refluxing on a steam bath for two hours led to decomposition and no definite product could be isolated from the acidified reaction mixture.

The methyl ether was prepared by refluxing the above iodo flavone (2 g.) in dry benzene with dimethyl sulphate (2 ml.) in presence of anhydrous potassium carbonate (4 g.) on a steam bath for 4 hours. The residue after removal of benzene was crystallised from ethyl alcohol in colourless needles, m.p. 235-236°.

Analysis :

8.920 mg. of the substance gave 18.88 mg. of carbon dioxide and 2.50 mg. of water.

20.76 mg. of the same substance gave 10.24 mg. of silver iodide.

Found : C = 57.76 % ; H = 3.14 % ; I = 26.66 %.

$C_{23}H_{15}O_4I$ requires : C = 57.27 % ; H = 3.11 % ; I = 26.35 %.

Hydrolysis of 7-methoxy-8-iodo-3-benzoylflavone : 2-Hydroxy-3-iodo-4-methoxyacetophenone and 2-hydroxy-3-iodo-4-methoxybenzoic acid

7-Methoxy-8-iodo-3-benzoylflavone (1 g.) was refluxed with alcoholic potassium hydroxide solution (10 % ; 25 ml.) on a steam bath for 2 hours. The excess of alcohol was distilled under vacuum and the reaction mixture acidified. The product obtained was extracted successively with sodium hydrogen carbonate and sodium hydroxide solution. The former gave on acidification 2-hydroxy-3-iodo-4-methoxybenzoic acid and the latter 2-hydroxy-3-iodo-4-methoxyacetophenone described in section (i).

Attempts to get the debenzoylated product by reduction ~~variation~~ in strength of alkali and heating time did not succeed, only the iodo ketone and the iodo acid were obtained.

Kostanecki-Robinson acetylation of 2,4-dihydroxy-5-iodo-acetophenone : 7-Acetoxy-6-iodo-3-acetyl-2-methylchromone

2,4-Dihydroxy-5-iodo-acetophenone (3 g.) was mixed with fused sodium acetate (15 g.) and acetic anhydride (50 ml.). The reaction mixture was heated in an oil bath at 125-130° for half an hour and then at 155-160° for 5 hours. The product obtained on working up as before crystallised from ethyl alcohol (charcoal) in colourless needles, m.p. 149°. Yield 0.7 g. Higher reaction temperature or longer heating time resulted in poor yields or unworkable mass.

Analysis :

9.32 mg. of the substance gave 14.70 mg. of carbon dioxide and 2.54 mg. of water.

11.850 mg. of the same substance gave 7.148 mg. of silver iodide.

Found : C = 43.04 % ; H = 3.05 % ; I = 32.61 %.
$C_{14}H_{11}O_5I$ requires : C = 43.52 % ; H = 2.85 % ; I = 32.91 %.

7-Hydroxy-6-iodo-3-acetyl-2-methylchromone

The above iodo chromone (1 g.) was dissolved in minimum quantity of concentrated sulphuric acid (10 ml.) and kept at room temperature for 4 hours. The product obtained on pouring the reaction mixture over crushed ice crystallised from ethyl alcohol in brown needles, m.p. 253-254°.

Analysis :

9.48 mg. of the substance gave 14.62 mg. of carbon dioxide and 2.36 mg. of water.

10.77 mg. of the same substance gave 7.25 mg. of silver iodide.

Found : C = 42.09 % ; H = 2.79 % ; I = 36.39 %.
$C_{12}H_9O_4I$ requires : C = ~~42.64~~ 41.85 % ; H = 2.62 % ; I = 36.92 %.

Attempts to de-acetylate the above hydroxy-3-acetylchromone (1 g.) with aqueous alcoholic sodium carbonate solution (5 % ; 25 ml.) by heating on a steam bath for 2 hours led to decomposition and no definite product was obtained on acidification of the reaction mixture.

The methyl ether, prepared by refluxing the above chromone (2.5 g.) in dry benzene with dimethyl sulphate (2.5 ml.) in presence of anhydrous potassium carbonate (5 g.) for 4 hours, crystallised in colourless needles, from ethyl alcohol, m.p. 177-178°.

Analysis :

9.56 mg. of the substance gave 15.14 mg. of carbon dioxide and 2.42 mg. of water.

21.06 mg. of the same substance gave 13.96 mg. of silver iodide.

Found : C = 43.22 % ; H = 2.83 % ; I = 35.83 %.

$C_{13}H_{11}O_4I$ requires : C = 43.57 % ; H = 3.07 % ; I = 35.47 %.

Hydrolysis of 7-methoxy-6-iodo-3-acetyl-2-methylchromone : 2-Hydroxy-4-methoxy-5-iodo-acetophenone and 2-hydroxy-4-methoxy-5-iodobenzoic acid

7-Methoxy-6-iodo-3-acetyl-2-methylchromone (1 g.) was heated with aqueous alcoholic sodium carbonate solution (5 % ; 20 ml.) for 2 hours on a steam bath. The product obtained on acidification was successively extracted with sodium hydrogen carbonate and sodium hydroxide solution. The former gave on acidification 2-hydroxy-4-methoxy-5-iodobenzoic acid and the latter gave 2-hydroxy-4-methoxy-5-iodo-acetophenone both described in section (i). No de-acetylated chromone was obtained.

Kostanecki-Robinson benzoylation of 2,4-dihydroxy-5-iodo-acetophenone : 7-Hydroxy-6-iodo-3-benzoylflavone

2,4-Dihydroxy-5-iodo-acetophenone (3 g.) was mixed with fused sodium benzoate (1.3 g.) and benzoic anhydride (18 g.). The reaction mixture was heated at 125-130° for half an hour and then at 155-160° in an oil bath for 5 hours as before. The reaction mixture became reddish brown in colour. It was treated repeatedly with hot water to remove sodium benzoate and benzoic anhydride and finally washed with sodium hydrogen carbonate solution. The residue (1.5 g.) could not be purified and so was kept with concentrated sulphuric acid at room temperature for 24 hours. Next day it was added to crushed ice and the separated product extracted with sodium hydroxide solution. The solid obtained on acidification was insoluble in most of the organic solvents and was therefore crystallised from nitrobenzene in buff coloured needles, m.p. 303° (decomp.). Yield 0.6 g. Higher reaction temperatures or longer heating time gave deeply coloured unworkable mass.

Analysis :

8.56 mg. of the substance gave 17.56 mg. of carbon dioxide and 1.76 mg. of water.

11.90 mg. of the same substance gave 5.844 mg. of silver iodide.

Found : C = 55.98 % ; H = 2.30 % ; I = 26.55 %.

$C_{22}H_{13}O_4I$ requires : C = 56.41 % ; H = 2.78 % ; I = 27.16 %.

Attempts to debenzoylate this compound (1 g.) by refluxing with alcoholic potash (10 % ; 20 ml.) for 2 hours led to decomposition of the product and no pure product could be isolated from the reaction mixture after acidification.

The methyl ether, prepared by refluxing 7-hydroxy-6-iodo-3-benzoylflavone (2 g.) in dry benzene with dimethyl sulphate (2 ml.) in presence of anhydrous potassium carbonate for 4 hours crystallised in colourless needles from acetic acid, m.p. 273-274°.

Analysis :

9.44 mg. of the substance gave 19.94 mg. of carbon dioxide and 2.88 mg. of water.

10.074 mg. of the same substance gave 4.826 mg. of silver iodide.

Found : C = 57.64 % ; H = 3.41 % ; I = 25.90 %.
$C_{23}H_{15}O_4I$ requires : C = 57.27 % ; H = 3.11 % ; I = 26.35 %.

Hydrolysis of 7-methoxy-6-iodo-3-benzoylflavone : 2-Hydroxy-4-methoxy-5-iodo-acetophenone and 2-hydroxy-4-methoxy-5-iodobenzoic acid

7-Methoxy-6-iodo-3-benzoylflavone (1.5 g.) was refluxed with alcoholic potassium hydroxide (10 % ; 40 ml.) on a steam bath for 2 hours. 2-Hydroxy-4-methoxy-5-iodobenzoic acid and 2-hydroxy-4-methoxy-5-iodo-acetophenone described in section (i) were isolated on working up the reaction mixture as before. No debenzoylated flavone was obtained.

Kostanecki-Robinson acetylation of 2,4-dihydroxy-3,5-di-iodo-acetophenone : 7-Acetoxy-6,8-di-iodo-3-acetyl-2-methylchromone

2,4-Dihydroxy-3,5-di-iodo-acetophenone (2 g.)was mixed with fused sodium acetate (10 g.) and acetic anhydride (30 ml.). The reaction mixture was heated at 125-130° for half an hour and then at 155-160° for 5 hours as before. The product obtained on working up as before crystallised from ethyl alcohol (charcoal) in buff coloured needles, m.p. 230-231°. Yield 0.7 g.

Analysis :-

9.28 mg. of the substance gave 11.14 mg. of carbon dioxide and 1.48 mg. of water.

16.46 mg. of the same substance gave 15.10 mg. of silver iodide.

Found : C = 32.76 % ; H = 1.78 % ; I = 49.59 %.

$C_{14}H_{10}O_5I_2$ requires : C = 32.81 % ; H = 1.95 % ; I = 49.61 %.

7-Hydroxy-6,8-di-iodo-3-acetyl-2-methylchromone

The above chromone (1 g.) was dissolved in concentrated sulphuric acid (15 ml.) and stirred occasionally. It was kept at room temperature for 4 hours and then poured over crushed ice. The separated product crystallised from acetic acid in brown needles, m.p. 234°.

Analysis :

9.64 mg. of the substance gave 10.68 mg. of carbon dioxide and 1.72 mg. of water.

15.32 mg. of the same substance gave 15.20 mg. of silver iodide.

Found : C = 30.24 % ; H = 1.99 % ; I = 53.63 %.

$C_{12}H_8O_4I_2$ requires : C = 30.64 % ; H = 1.70 % ; I = 54.04 %.

The same di-iodo-3-acetylchromone was also obtained on iodination of 7-hydroxy-3-acetyl-2-methylchromone (1.09 g. ; 0.005 mole) in warm alcohol with iodine (1.51 g. ; 0.006 mole) and iodic acid (0.8 g.) in water with stirring for 2 hours. Yield 1.5 g.

Attempts to de-acetylate the above compound (1 g.) with aqueous alcoholic sodium carbonate solution (5 % ; 25 ml.)

by heating on a steam bath for 2 hours led to decomposition and no definite product could be isolated from the reaction mixture on acidification.

The hydroxy-di-iodochromone (2.3 g.) when refluxed in glacial acetic acid (120 ml.) for 10 hours underwent decomposition and the solution became violet in colour. It was concentrated by distillation and poured over sodium hydrogen sulphite solution. The separated shining product crystallised from ethyl alcohol in needles. M.P. and mixed m.p. with 7-hydroxy-6-iodo-3-acetyl-2-methylchromone was 253-254°.

The methyl ether, prepared by refluxing the hydroxy di-iodochromone (2 g.) in dry benzene with dimethyl sulphate (2 ml.) in presence of anhydrous potassium carbonate (4 g.) for 4 hours, crystallised from ethyl alcohol in colourless needles, m.p. 210-211°.

Analysis :

9.02 mg. of the substance gave 10.61 mg. of carbon dioxide and 1.94 mg. of water.

11.872 mg. of the same substance gave 11.588 mg. of silver iodide.

Found : C = 32.10 % ; H = 2.41 % ; I = 52.76 %.

$C_{13}H_{10}O_4I_2$ requires : C = 32.23 % ; H = 2.07 % ; I = 52.36 %.

Hydrolysis of 7-methoxy-6,8-di-iodo-3-acetyl-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-3-acetyl-2-methylchromone

(1 g.) was heated with aqueous alcoholic sodium carbonate solution (5 % ; 25 ml.) for 2 hours, on a steam bath. 2-Hydroxy-3,5-di-iodo-4-methoxybenzoic acid and 2-hydroxy-3,5-di-iodo-4-methoxyacetophenone described in section (i) were obtained on working up the reaction mixture.

Kostanecki-Robinson benzoylation of 2,4-dihydroxy-3,5-di-iodo-acetophenone : 7-Hydroxy-6-iodo-3-benzoylflavone

2,4-Dihydroxy-3,5-di-iodo-acetophenone (4 g.) was mixed with fused sodium benzoate (1.50 g.) and benzoic anhydride (40 g.). The reaction mixture was heated in an oil bath first at 125-130° for half an hour and then at 155-160° for 5 hours as before. The reaction mixture became red coloured. It was then repeatedly treated with hot water and sodium hydrogen carbonate solution. The residue, reddish brown in colour, could not be purified and so was treated with concentrated sulphuric acid (15 ml.) and kept at room temperature for 24 hours. The reaction mixture was then poured over crushed ice and the product obtained was purified by sodium hydroxide treatment. It crystallised from nitrobenzene in buff coloured needles. M.P. and mixed m.p. with 7-hydroxy-6-iodo-3-benzoylflavone described before was 303° (decomp.). Yield 0.1 g.

Iodination of 7-hydroxy-3-benzoylflavone with iodine and iodic acid : 7-Hydroxy-6,8-di-iodo-3-benzoylflavone

7-Hydroxy-3-benzoylflavone (1.7 g. ; 0.005 mole) in warm alcohol was treated with iodine crystals (1.51 g. ; 0.006 mole) and iodic acid (0.7 g.) in water with stirring for 2 hours. The separated product crystallised in colourless cubes from ethyl alcohol, m.p. 208° (decomp.). Yield 1.9 g. It decomposed on boiling with acetic acid.

Analysis :

11.84 mg. of the substance gave 9.46 mg. of silver iodide.

Found : I = 43.19 %.

$C_{22}H_{12}O_4I_2$ requires : I = 42.76 %.

The methyl ether, prepared by refluxing the di-iodoflavone (1 g.) in dry benzene with dimethyl sulphate (1 ml.) in presence of anhydrous potassium carbonate (2 g.) on a steam bath for 8 hours crystallised in colourless needles, m.p. 238-239°.

Analysis :

9.16 mg. of the substance gave 15.36 mg. of carbon dioxide and 2.16 mg. of water.

10.12 mg. of the same substance gave 7.78 mg. of silver iodide.

Found : C = 45.76 % ; H = 2.64 % ; I = 41.56 %.

$C_{23}H_{14}O_4I_2$ requires : C = 45.39 % ; H = 2.30 % ; I = 41.68 %.

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

7-Methoxy-6,8-di-iodo-3-benzoylflavone (1 g.) was refluxed with alcoholic potassium hydroxide (10 % ; 20 ml.) on a steam bath for 2 hours. On working up the reaction mixture 2-hydroxy-3,5-di-iodo-4-methoxybenzoic acid and

2-hydroxy-3,5-di-iodo-4-methoxy-acetophenone described in section (i) were obtained. No debenzoylated flavone was obtained.

Kostanecki-Robinson acetylation of 2,6-dihydroxy-3,5-di-iodo-acetophenone : 5-Acetoxy-6,8-di-iodo-3-acetyl-2-methylchromone

2,6-Dihydroxy-3,5-di-iodo-acetophenone (2 g.) was mixed with fused sodium acetate (8 g.) and acetic anhydride (35 ml.). The reaction mixture was heated in an oil bath at 125-130° for half an hour and then at 155-160° for 5 hours. The product obtained on working up as before crystallised from ethyl alcohol (charcoal) in colourless needles, m.p. 175-176°. Yield 0.9 g.

Analysis :

9.28 mg. of the substance gave 11.02 mg. of carbon dioxide and 1.72 mg. of water.

10.378 mg. of the same substance gave 9.564 mg. of silver iodide.

Found : C = 32.41 % ; H = 2.07 % ; I = 49.81 %.

$C_{14}H_{10}O_5I_2$ requires : C = 32.81 % ; H = 1.95 % ; I = 49.61 %.

5-Hydroxy-6,8-di-iodo-3-acetyl-2-methylchromone

The above di-iodochromone (1 g.) was dissolved in concentrated sulphuric acid (15 ml.) and kept at room temperature for 4 hours. The product obtained on pouring the reaction mixture over crushed ice crystallised from acetic acid in yellow needles, m.p. 219°. Its alcoholic solution gave a red colouration with alcoholic ferric chloride and formed a yellow sodium salt with sodium hydroxide solution.

Analysis :

9.42 mg. of the substance gave 10.48 mg. of carbon dioxide and 1.14 mg. of water.

18.25 mg. of the same substance gave 18.44 mg. of silver iodide.

Found : C = 30.36 % ; H = 1.35 % ; I = 54.62 %.
$C_{12}H_8O_4I_2$ requires : C = 30.64 % ; H = 1.70 % ; I = 54.04 %.

The same di-iodochromone was obtained on iodination of 5-hydroxy-3-acetyl-2-methylchromone (1.09 g. ; 0.005 mole) in warm alcohol with iodine (1.01 g. ; 0.004 mole) and iodic acid (0.5 g.) in water. The separated product crystallised from acetic acid in yellow needles. Yield 1.6 g.

Attempts to de-acetylate the above compound (1 g.) with aqueous alcoholic sodium carbonate solution (5 % ; 20 ml.)by heating on a steam bath for 2 hours led to decomposition and no definite product could be isolated.

The methyl ether, prepared by refluxing the above hydroxychromone (1.5 g.) in dry benzene with dimethyl sulphate (2 ml.) and anhydrous potassium carbonate on a steam bath for 18 hours, crystallised from ethyl alcohol in colourless needles, m.p. 213-214°.

Analysis :

9.22 mg. of the substance gave 10.85 mg. of carbon dioxide and 1.99 mg. of water.

9.988 mg. of the same substance gave 9.652 mg. of silver iodide.

Found : C = 32.11 % ; H = 2.41 % ; I = 52.23 %.
$C_{13}H_{10}O_4I_2$ requires : C = 32.23 % ; H = 2.07 % ; I = 52.36 %.

Hydrolysis of 5-methoxy-6,8-di-iodo-3-acetyl-2-methylchromone : 2-Hydroxy-6-methoxy-3,5-di-iodo-acetophenone

5-Methoxy-6,8-di-iodo-3-acetyl-2-methylchromone (1 g.) was refluxed with aqueous alcoholic sodium carbonate solution (5 % ; 25 ml.) for 2 hours on a steam bath. The product obtained on acidification after purification through sodium hydroxide solution treatment, crystallised from aqueous ethyl alcohol in yellow needles. M.P. and mixed m.p. with 2-hydroxy-3,5-di-iodo-6-methoxyacetophenone described in section (i).was 111°.

Kostanecki-Robinson benzoylation of 2,6-dihydroxy-3,5-di-iodo-acetophenone : 5-Benzoyloxy-6,8-di-iodo-3-benzoylflavone

2,6-Dihydroxy-3,5-di-iodo-acetophenone (2 g.) was mixed with fused sodium benzoate (2 g.) and benzoic anhydride (20 g.) and the reaction mixture was heated in an oil bath at 125-130° for half an hour and then at 155-160° for 5 hours. The reaction mixture was treated repeatedly with hot water to remove sodium benzoate and benzoic anhydride and finally washed with sodium hydrogen carbonate solution and the residue crystallised from acetic acid (charcoal) in colourless cubes, m.p. 235°. Yield 0.6.g.

Analysis :

9.56 mg. of the substance gave 17.38 mg. of carbon dioxide and 1.67 mg. of water.

17.42 mg. of the same substance gave 11.88 mg. of silver iodide.

Found : C = 49.61 % ; H = 1.96 % ; I = 36.87 %.
$C_{29}H_{16}O_5I_2$ requires : C = 49.85 % ; H = 2.29 % ; I = 36.39 %.

5-Hydroxy-6,8-di-iodo-3-benzoylflavone

The above di-iodoflavone (1 g.) was dissolved in concentrated sulphuric acid (15 ml.) by stirring and the reaction mixture kept at room temperature over-night. The product obtained on pouring it on crushed ice crystallised in yellow needles from acetic acid, m.p. 228°. Its alcoholic solution gave a deep red colouration with alcoholic ferric chloride. It gave a yellow sodium salt with sodium hydroxide solution.

Analysis :

8.54 mg. of the substance gave 14.06 mg. of carbon dioxide and 1.68 mg. of water.

9.812 mg. of the same substance gave 7.774 mg. of silver iodide.

Found : C = 44.92 % ; H = 2.20 % ; I = 42.83 %.
$C_{22}H_{12}O_4I_2$ requires : C = 44.44 % ; H = 2.02 % ; I = 42.76 %.

The above di-iodoflavone was also obtained on iodination of 5-hydroxy-3-benzoylflavone (1.71 g. ; 0.005 mole) dissolved in warm alcohol with iodine (1.01 g.; 0.004 mole) and iodic acid (0.5 g.) in water. Yield 1.9 g.

Attempts to de-~~acetylate~~ benzoylate the above compound (1 g.) with alcoholic potash (10 % ; 20 ml.) by heating on a steam bath for 2 hours did not succeed.

The methyl ether, prepared by refluxing the hydroxyflavone (2 g.) in dry benzene with dimethyl sulphate (2.5 ml.) in presence of anhydrous potassium carbonate (5 g.) for 18 hours, crystallised from aqueous ethyl alcohol in colourless needles, m.p. 198-199°.

Analysis :

9.70 mg. of the substance gave 16.20 mg. of carbon dioxide and 2.04 mg. of water.

10.224 mg. of the same substance gave 7.822 mg. of silver iodide.

	Found	: $C = 45.58\ \%$; $H = 2.35\ \%$; $I = 41.36\ \%$.
$C_{23}H_{14}O_4I_2$	requires	: $C = 45.39\ \%$; $H = 2.30\ \%$; $I = 41.68\ \%$.

5-Methoxy-6,8-di-iodo-3-benzoylflavone (1 g.) remained unchanged when refluxed with alcoholic potash (10 % ; 20 ml.) on a steam bath for 4 hours.