CHAPTER II

IODINATION OF COUMARINS

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The work on the iodination of coumarins it was thought would be of interest for various reasons. Extensive work has been carried out on the bromination of coumarins and it would be of interest to see if the iodination of coumarins would follow the same pattern. Further, the pattern of substitution sometimes varies with the iodinating agents and it would be of interest to see if this is so in the iodination of coumarins and lastly the iodo derivatives are compounds of synthetic interest and they could be subjected to the Rosenmund-von Braun reaction to get the syanocoumarins and to Üllmann reaction to synthesise bicoumarinyl derivatives and to crossed Ullmann reaction to synthesise arylcoumarins. It was with these ends in view that the iodination of coumarins was undertaken.

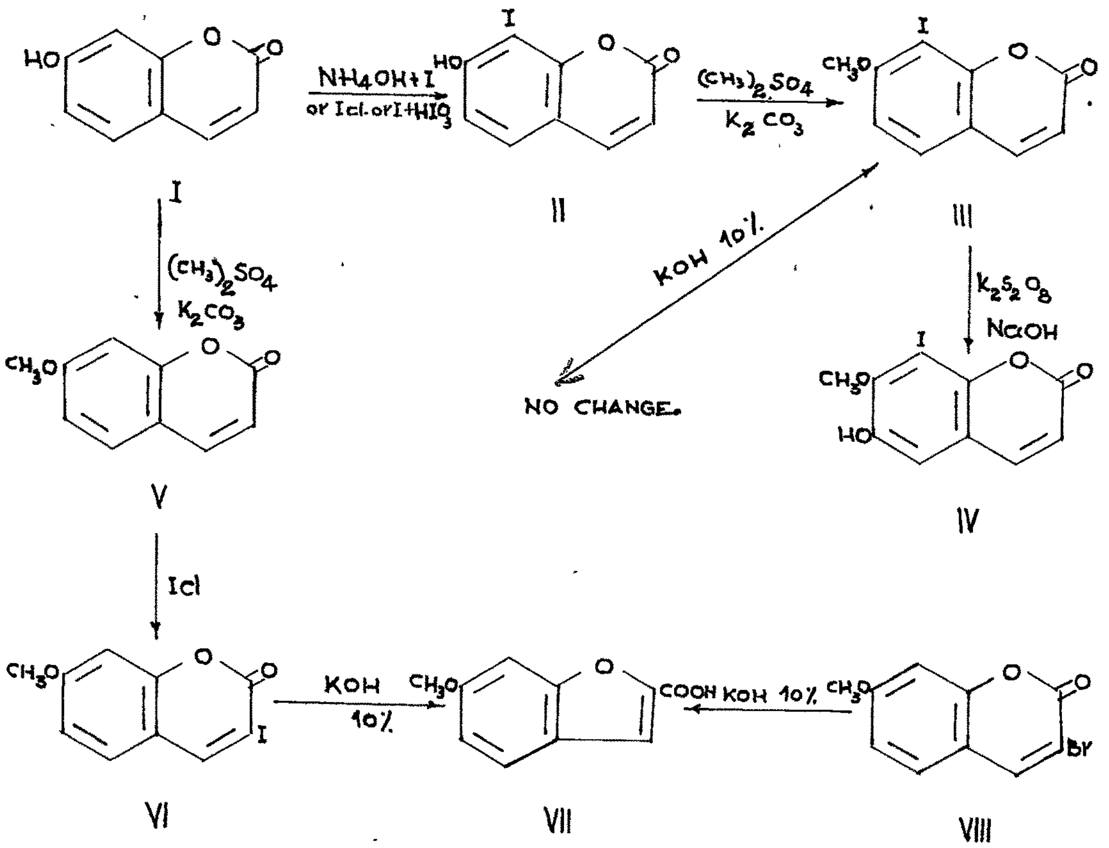
Three different iodinating agents were used : (i) iodine and ammonia (ii) iodine and iodic acid and (iii) iodine monochloride. Under second it is assumed that the reaction takes place according to the following equation.

$$5\ RH + 2\ I_2 + HIO_3 = 5\ RI + 3\ H_2O \ldots\ldots\ldots (1)$$

Iodination of 7-hydroxycoumarin and its methyl ether

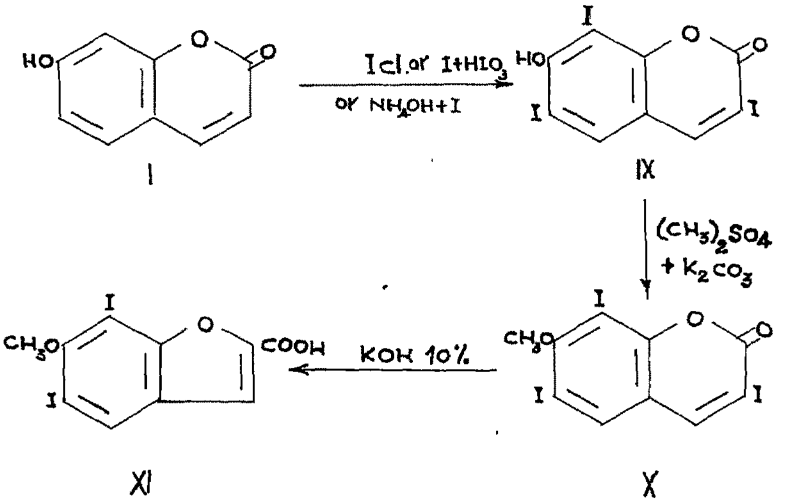
7-Hydroxycoumarin (I) on iodination with one mole of iodine monochloride gave a monoiodo derivative ; the methyl ether of which did not give a coumarilic acid derivative on heating with alkali indicating that the iodine atom had not entered the 3-position. The alternative positions are 6 and 8. The methyl ether of the monoiodo derivative was then subjected to Elbs Persulphate Oxidation in presence of alkali when a good yield of the oxidation product was obtained. This indicated that the 6-position in the methyl ether must be free. If the iodine atom had entered the 6-position and the 8-position had been free, the oxidation in this case would have been very difficult (cf. Da~~y~~lvi, Desai and Sethna, J. Indian Chem. Soc., 1951, 28, 366). Moreover the oxidation product gave an orange yellow colour with alkali which is characteristic of 6-hydroxycoumarin derivatives. The monoiodo derivative is therefore 7-hydroxy-8-iodocoumarin (II) and the Elbs Persulphate Oxidation product has the structure (IV). 7-Methoxycoumarin (V) on iodination with one mole of iodine monochloride gave a monoiodo derivative different from the 7-methoxy-8-iodocoumarin (III). On boiling with potassium hydroxide solution it gave a coumarilic acid derivative, which was found on direct comparison to be identical with 6-methoxycoumarilic acid (VII) prepared from 7-methoxy-3-bromocoumarin (VIII) by the action of alkali according to Seshadri and Varadrajan (J. Sci. Ind. Research, India, 1951, 11B, 39). The monoiodo product is therefore 7-methoxy-3-iodocoumarin (VI).

On iodination with two moles of iodine monochloride, (I) did not give a pure product but with excess of iodine monochloride it gave the 3,6,8-triiodo derivative. (IX). The methyl ether (X) on hydrolysis gave a diiodocoumarilic acid. The triiodocoumarin is therefore 7-hydroxy-3,6,8-triiodocoumarin (IX) and the coumarilic acid must be 6-methoxy-5,7-diiodocoumarilic acid (XI).



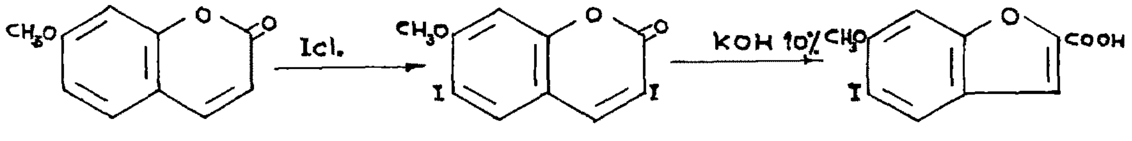
7-Methoxycoumarin on iodination with two moles of iodine monochloride gave a diiodo derivative. This gave a monoiodocoumarilic acid derivative different from the monoiodocoumarilic acid derivative obtained on hydrolysis of the diiodo derivative obtained on further iodination of 7-methoxy-8-iodocoumarin with iodine monochloride.

The diiodo derivative obtained from (V) therefore must have the 3,6-diiodo structure (XII) and the one obtained from 7-methoxy-8-iodocoumarin must have the 3,8-diiodo structure.(XIV), and the monoiodocoumarilic acids derived from them must be represented by (XIII) and (XV) respectively.

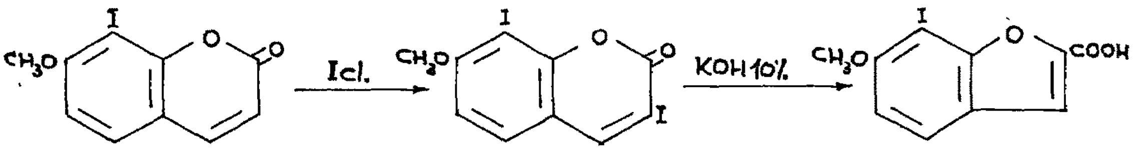


I IX X XI

7-Hydroxycoumarin (I) on iodination using molecular proportions of iodine and iodic acid as given in equation (1) gave a mixture from which only the 8-iodo derivative could be isolated in a pure form. When the proportions of iodine and



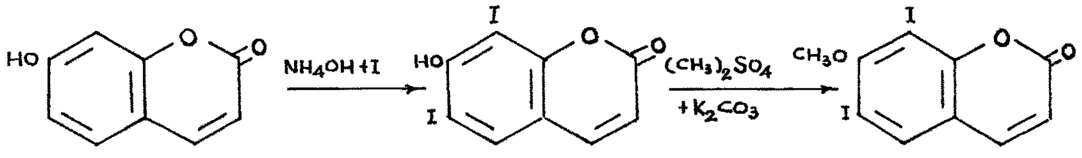
V XII XIII



III XIV XV

iodic acid were doubled it gave directly the 3,6,8-triiodo derivative (IX), no diiodo derivative could be isolated. 7-Methoxycoumarin could not be iodinated at all with iodine and iodic acid.

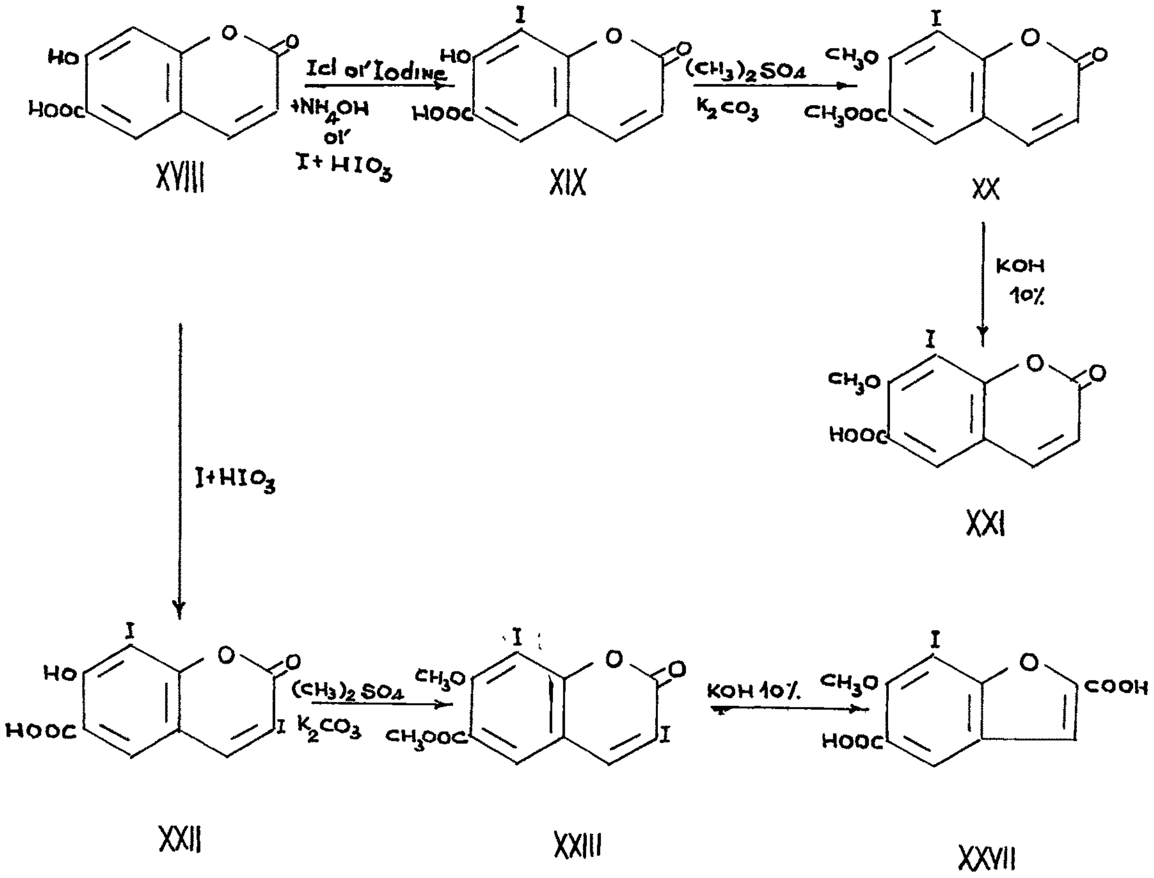
7-Hydroxycoumarin (I) on iodination with one mole of iodine in presence of ammonia gave the 8-iodo derivative. With two moles of iodine, (I) gave ~~the~~ a diiodo derivative when the reaction mixture was stirred for five minutes, but if it was allowed to react for fifteen minutes if yielded the 3,6,8-triiodo derivative (IX). (IX) was obtained in quantitative yield when four moles of iodine were used in the presence of ammonia. The diiodo derivative remained unchanged when boiled with alkali, and hence was assigned the 6,8-diiodo structure (XVII).



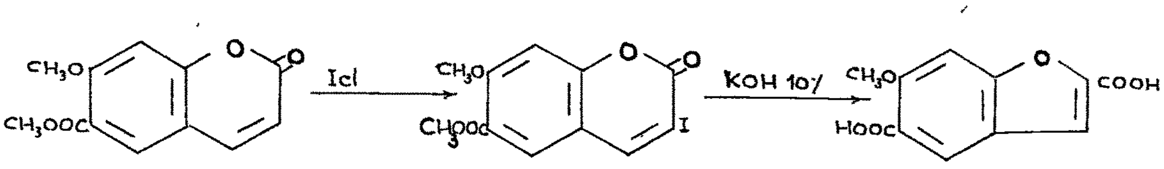
I XVI XVII

Iodination of 7-hydroxycoumarin-6-carboxylic acid and ~~the~~ methyl 7-methoxycoumarin-6-carboxylate

7-Hydroxycoumarin-6-carboxylic acid (XVIII) on iodination with one mole of iodine monochloride gave a monoiodo derivative in poor yield. Its methoxy ester did not give a coumarilic acid derivative on boiling with alkali but instead gave an iodocoumarin carboxylic acid. The ester is therefore methyl-7-methoxy-8-iodocoumarin-6-carboxylate (XX) and the acid is 7-~~hydroxy~~ methoxy-8-iodocoumarin-6-carboxylic acid (XXI).



The methoxy ester (XXV) on iodination with one mole of iodine monochloride gave a monoiodo derivative (~~XXVI~~) different from the iodo methoxy ester (XX) described above. On boiling with potassium hydroxide solution it gave an iodine free coumarilic acid derivative which must be 6-methoxy-5-carboxycoumarilic acid (XXVII). The monoiodo product is therefore methyl-7-methoxy-3-iodocoumarin-6-carboxylate (XXVI). The methoxy ester (XXV) on iodination with excess of iodine monochloride gave a better yield of the 3-iodo derivative but no diiodo compound was obtained.



XXV XXVI XXVII

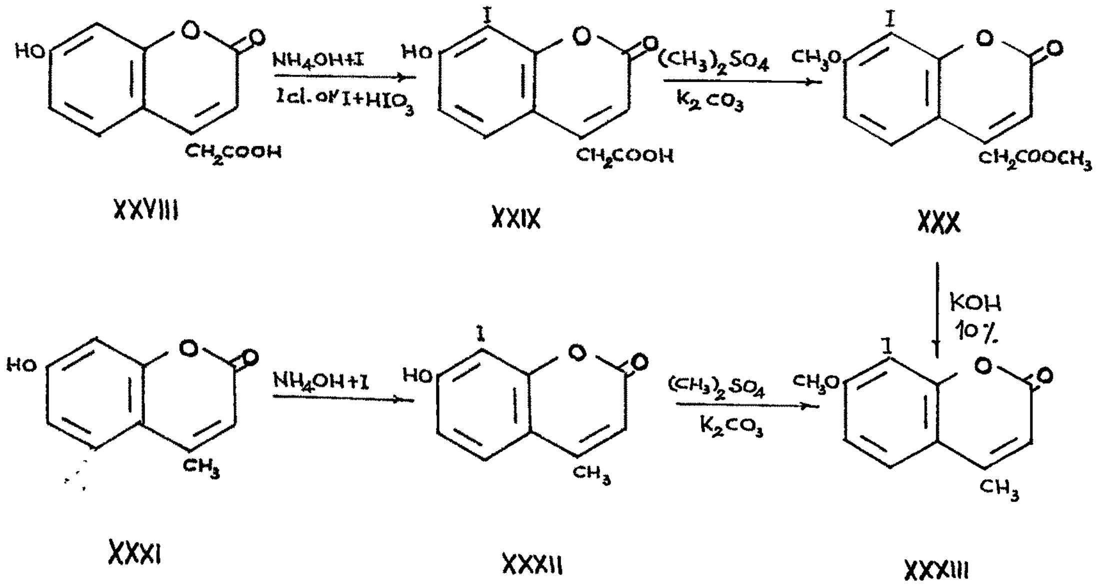
Iodination of 7-hydroxycoumarin-6-carboxylic acid by using molecular proportions of iodine and iodic acid as given in equation (1) yielded the 8-iodo derivative. With four times the amounts of iodine and iodic acid the same acid (XVIII) yielded ~~the~~ a diiodo derivative ~~([illegible])~~ which on methylation and hydrolysis with alkali gave an iodocoumarilic acid. Hence the diiodo derivative must be 7-hydroxy-3,8-diiodocoumarin-6-carboxylic acid (XXII) and the coumarilic acid:6-methoxy-5-carboxy-7-iodocoumarilic acid (XXVII). Iodination of the acid (XVIII) with one mole of iodine in presence of ammonia gave a mixture from which the 8-iodo derivative could be isolated in poor yield. No further iodination was possible even with excess of iodine. The methoxy methylester (XXV) could not be iodinated at all with iodine in presence of ammonia or by iodine and iodic acid.

Iodination of 7-hydroxycoumarin-4-acetic acid

As has been mentioned in the general introduction bromination of 7-hydroxycoumarin-4-acetic acid was found to take place at the reactive methylene group(**Dey** and Radhabai

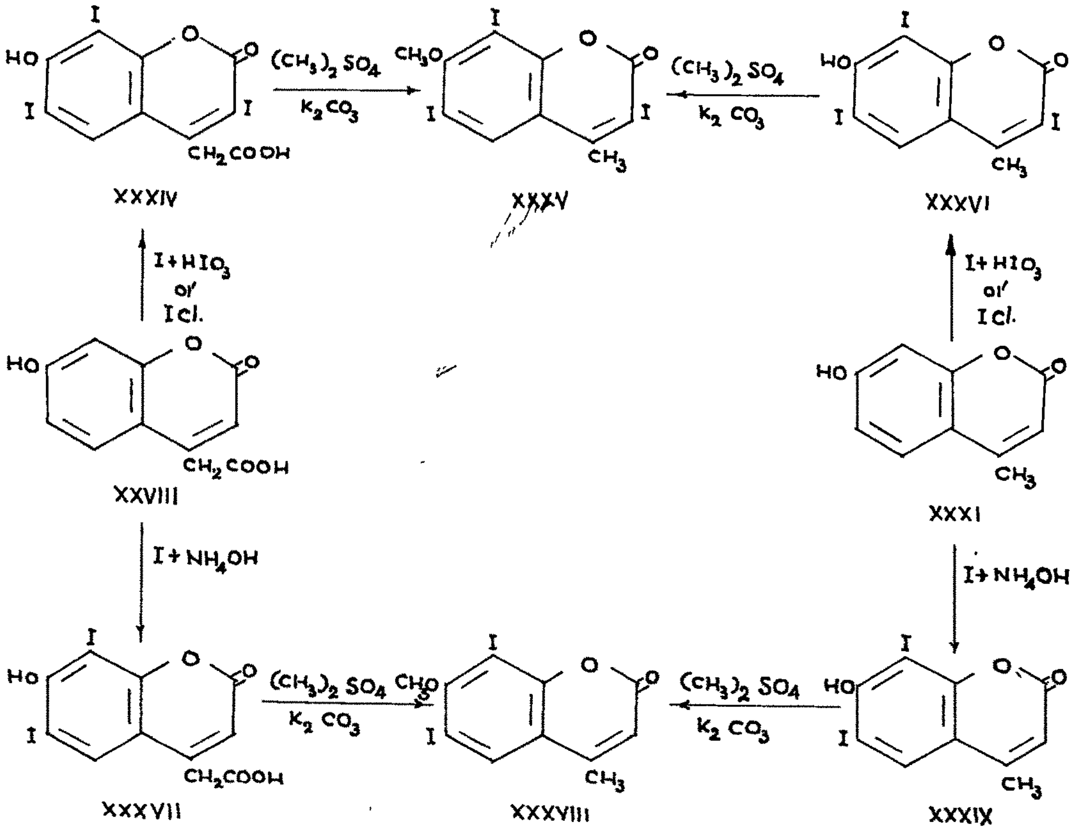
J. Indian Chem. Soc., 1934, 11, 635). In view of this it was thought of interest to see how the iodination would take place.

Iodination of 7-hydroxycoumarin-4-acetic acid (XXVIII) with one mole of iodine monochloride furnished a monoiodo derivative which on methylation and hydrolysis yielded 7-methoxy-8-iodo-4-methylcoumarin, as seen by direct comparison with a specimen prepared according to Lele and Sethna (J. Org. Chem., 1958, 23, 1731). In iodination with one mole of iodine in presence of ammonia and iodine and iodic acid the acid (XXVIII) yielded the same 8-iodo derivative as described above. With two moles of iodine monochloride it yielded a mixture of compounds from which no pure product could be isolated. However, excess of iodine monochloride gave a triiodo derivative. This triiodo derivative on methylation yielded 7-methoxy-3,6,8-triiodo-4-methylcoumarin



identical with the product described by Lele and Sethna (loc. cit.) decarboxylation having taken place during the methylation. The iodination of the hydroxy acid (XXVIII) with excess of iodine and iodic acid also gave the triiodo acid derivative (XXXIV).

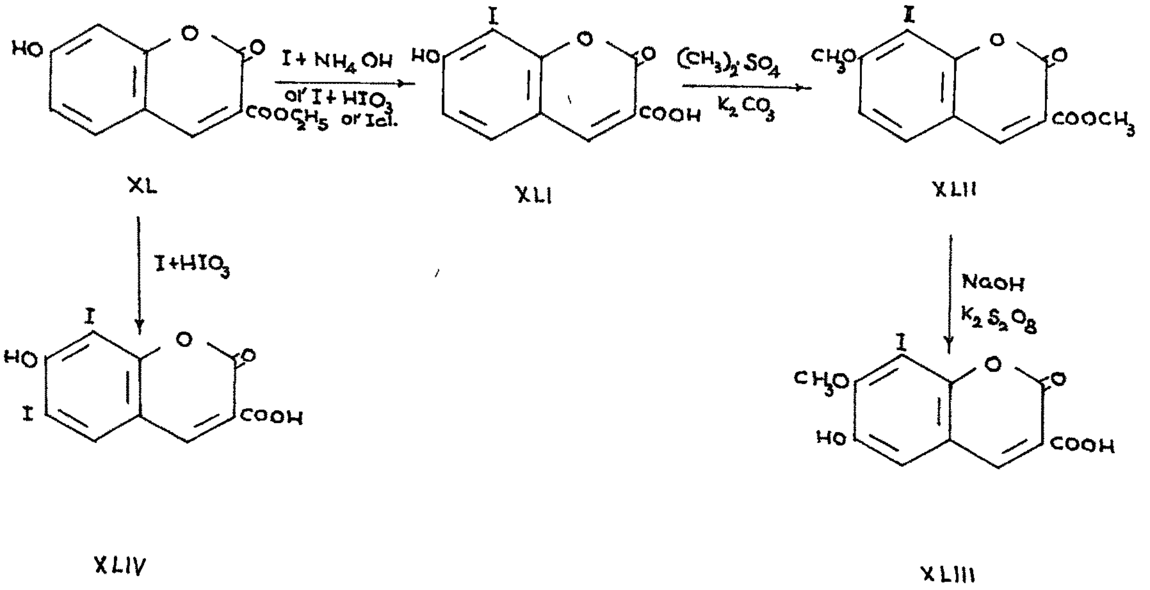
Iodination of (XXVIII) with two moles of iodine in presence of ammonia yielded a diiodo acid ~~(XXXVII)~~ which on methylation gave the 6,8-diiodo derivative (XXXVIII) identical with the product described by Lele and



Sethna (loc. cit.) hence the original diiodo derivative must be 7-hydroxy-6,8-diiodocoumarin-4-acetic acid. (XXXVII) No triiodo derivative could be ~~isolated~~ obtained by this method even when iodine was taken in excess.

Iodination of ethyl 7-hydroxycoumarin-3-carboxylate

Ethyl 7-hydroxycoumarin-3-carboxylate (XL) on iodination with one mole of iodine in presence of ammonia gave a mono iodo acid. This iodo acid was methylated and esterified and subjected to Elbs Persulphate Oxidation when a hydroxy iodo derivative was obtained. It was therefore presumed that the product obtained on iodination was the 8-iodo derivative (XLI) and the Elbs Persulphate Oxidation product was 6-hydroxy-7-methoxy-8-iodo-3-carboxylic acid (XLIII)



Ethyl 7-hydroxycoumarin-3-carboxylate (XL) on iodination with iodine monochloride and with molecular proportions of iodine and iodic acid gave the same mono iodo derivative (XLI). On iodination with two moles of iodine and iodic acid it gave a diiodo acid to which the 6,8-diiodo structure (XLIV) has been assigned.

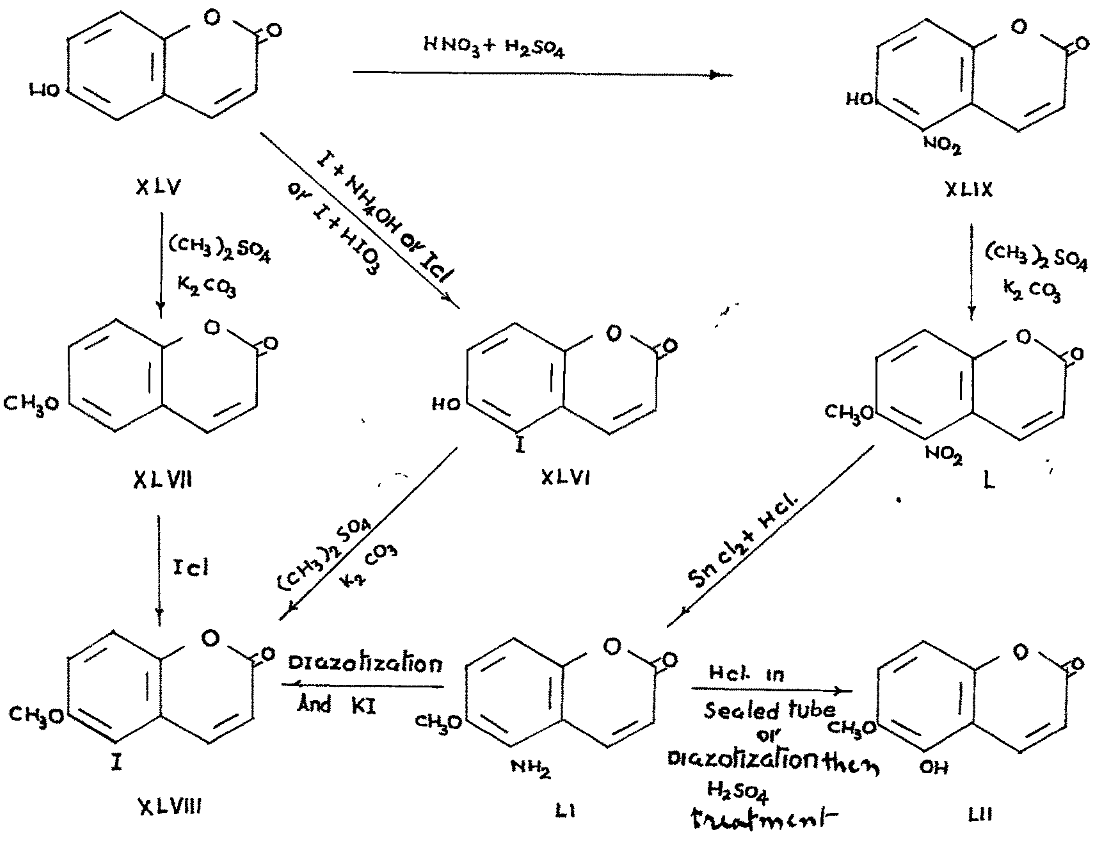
Iodination of 6-hydroxycoumarin and its methyl ether

With one mole of iodine monochloride 6-hydroxycoumarin (XLV) gave a monoiodo derivative. Its methyl ether remained unchanged on heating with alkali indicating that the iodine atom had not entered the 3-position. Of the alternate structures 5- or 7-iodo the monoiodo derivative has been assigned the 5-iodo structure (XLVI) for the following reasons :

6-Hydroxycoumarin (XLV) on nitration gave a mononitro derivative. Its methyl ether remained unchanged on boiling with liquor ammonia. On reduction with stannous chloride and hydrochloric acid the nitro derivative gave the amino derivative. This was hydrolysed with dilute hydrochloric acid in a sealed tube to the corresponding hydroxycoumarin, m.p. 240°. This was also obtained by diazotization of the amino compound and boiling with sulphuric acid. The product gave a yellow colour with sodium hydroxide. It was different from 7-hydroxy-6-methoxycoumarin synthesised as given below and hence was assigned 5-hydroxy-6-methoxycoumarins structure (LII). The nitro derivative is therefore 6-hydroxy-5-nitrocoumarin (XLIX) and the amino derivative is 6-methoxy-5-aminocoumarin (LI).

6-Methoxy-5-aminocoumarin (LI) on diazotization and treatment with potassium iodide gave an iodo derivative which was found on direct comparison to be the same as the methyl ether of the iodo derivative (XLVI) described above which proved that the monoiodo derivative was the 5-iodo compound.

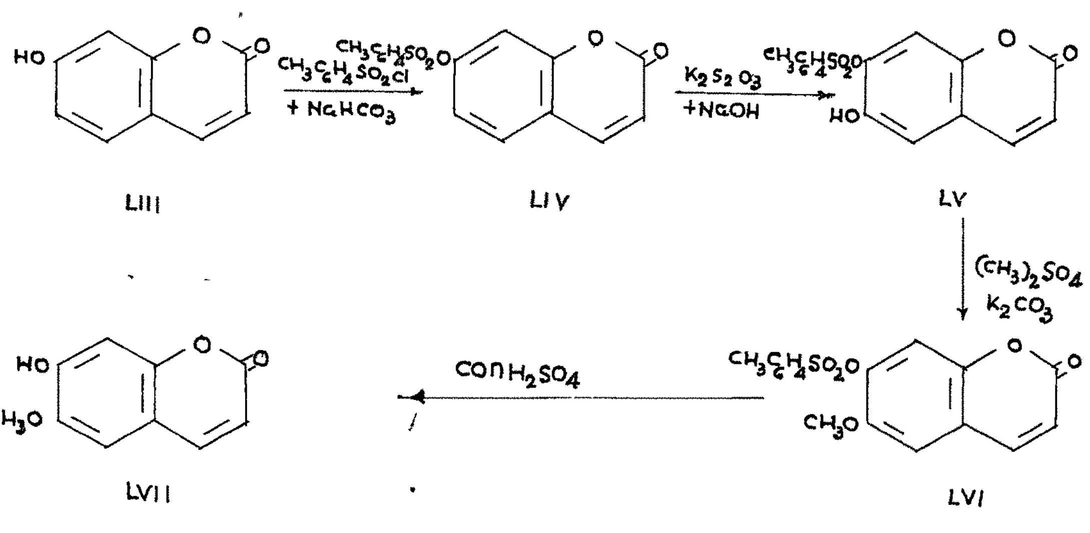
Iodination of (XLV) with one mole of iodine in presence of ammonia or with iodine and iodic acid gave the same monoiodo derivative (XLVI) . 6-Methoxycoumarin (XLVII) on iodination with iodine monochloride gave the same 5-iodo derivative (XLVIII) described above. No higher iodination product was obtained even with excess of iodine monochloride or iodine and iodic acid.



7-Hydroxy-6-methoxycoumarin (Scopoletin) has been synthesised previously by various methods. (E.Glaser. Arch.

Pharm, 1928, 266, 537 ; A. Robertson, J. Chem. Soc., 1931, 1241 ; Soka and Kallir., Ber., 1931, 64B, 909 ; W.Baker and Evans, J. Chem. Soc., 1938, 372 ; Chaudhari and Robertson, J. Chem. Soc., 1948, 1671 ; Amrard and Vollus., Bull. Soc. Chim. France 1948, 1109 ; K.Aghoramurthy and Seshadri, J. Sci. Ind. Research (India) 1952, 11B, 411 ; Donald, J. Org. Chem., 1961, 1217). In the present work it was synthesised as follows :

7-Hydroxycoumarin (LIII) on treatment with p-toluene sulphonyl chloride gave 7-tosyloxycoumarin (LIV) which on Elbs Persulphate Oxidation in pyridine solution gave the corresponding 6-hydroxycoumarin derivative (LV). This was methylated to yield (LVI) which was hydrolysed with concentrated sulphuric acid to 7-hydroxy-6-methoxycoumarin (LVII), m.p. 203-204°. It gave a deep blue fluorescence in alkaline and sulphuric acid solutions.

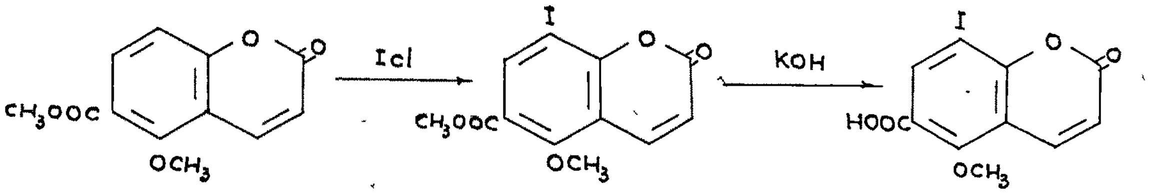


Iodination of methyl 5-methoxycoumarin-6-carboxylate

Methyl 5-methoxycoumarin-6-carboxylate (LVIII) on iodination with one mole of iodine monochloride gave a monoiodo derivative which on hydrolysis with alkali did not give any iodine free coumarilic acid but it gave an iodocoumarin carboxylic acid (LX) hence the monoiodo derivative was methyl 5-methoxy-8-iodocoumarin-6-carboxylate (LIX).

Methyl 5-methoxycoumarin-6-carboxylate could not be iodinated by the other two methods viz. (1) iodine and iodic acid and (2) iodine and ammonia. No higher iodination product was obtained when the iodine monochloride was taken in excess.

Iodination of 5-hydroxycoumarin has not been studied as the yields in the decarboxylation and in the demethylation were poor.



LVIII LIX LX

Some attempted iodinations

Iodination of 7-methylcoumarin, 7,8-dihydroxycoumarin and naphtha 1,2-α-pyrone was attempted using the different iodinating agents but neither of these coumarins gave an iodo derivative; the original coumarin was obtained in all cases.

EXPERIMENTAL

Iodination of 7-hydroxycoumarin and its methyl ether : 7-Hydroxy-8-iodocoumarin

(a) With iodine and ammonia.

7-Hydroxycoumarin (1.62 g. ; 0.01 mole) dissolved in ammonia (22 % ; 10 ml.) and water (35 ml.) was treated drop-wise with iodine (2.54 g. ; 0.01 mole) in potassium iodide (5 g.) solution with vigorous stirring of the reaction mixture. It was then poured in ice cold dilute sulphuric acid. The separated solid was filtered and crystallised from acetic acid in needles, m.p. 228-230°. Yield 1.2 g.

Analysis :

17.22 mg. of the substance gave 14.04 mg. of silver iodide.

Found : I = 44.07 %.

$C_9H_5O_3I$ requires : I = 44.10 %.

(b) With iodine and iodic acid.

7-Hydroxycoumarin (1.62 g. ; 0.01 mole) was dissolved in warm alcohol (10 ml.) and iodine crystals (1.01 g. ; 0.004 mole) were added. To this clear warm solution iodic acid (0.35 g.) dissolved in minimum quantity of water was then added and the mixture stirred for 3 hours. The product which separated crystallised from acetic acid in needles. Melting point and mixed m.p. with the above product was 228-230°. Yield 0.8 g.

(c) With iodine monochloride.

A mixture of 7-hydroxycoumarin (1.62 g. ; 0.01 mole) in acetic acid (10 ml.) and hydrochloric acid (10 ml. ; d. 1.11) was treated with iodine monochloride (1.62 g. ; 0.01 mole) and the reaction mixture left over-night at 60° in an oven. It was then diluted with water and the product which separated crystallised from acetic acid in needles, m.p. 228-230°. The mixed m.p. with the above product was not depressed. Yield 0.03 g.

7-Methoxy-8-iodocoumarin

The above iodocoumarin (2.8 g.) in acetone (100 ml.) was refluxed with dimethyl sulphate (2 ml.) and anhydrous potassium carbonate (4 g.) for 10 hours. The product obtained was washed with sodium hydroxide solution and then crystallised from dilute alcohol in needles, m.p. 158-160°.

Analysis :

10.18 mg. of the substance gave 14.94 mg. of carbon dioxide and 2.32 mg. of water.

19.34 mg. of the same substance gave 15.00 mg. of silver iodide.

Found : C = 40.06 % ; H = 2.55 % ; I = 41.93 %.

$C_{10}H_7O_3I$ requires : C = 39.74 % ; H = 2.32 % ; I = 42.07 %.

The methyl ether on refluxing with alcoholic potassium hydroxide solution (10 % ; 20 ml.) for 2 hours remained unchanged.

Elbs Persulphate Oxidation of 7-methoxy-8-iodocoumarin : 6-Hydroxy-7-methoxy-8-iodocoumarin

7-Methoxy-8-iodocoumarin (2 g.) was dissolved in sodium hydroxide solution (10 % ; 50 ml.) by warming on a steam bath. The solution was then cooled and potassium persulphate (1.8 g. ; 40 ml. water) was 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 kept over-night. The following day it was just acidified with hydrochloric acid when the original 7-methoxy-8-iodocoumarin (0.4 g.) was obtained. This was filtered and the filtrate extracted with ether twice. The aqueous layer was then heated on a boiling water bath with concentrated hydrochloric acid (40 ml.) for about an hour. The product which separated on cooling crystallised from dilute alcohol in needles, m.p. 217°. Yield 0.4 g.

It dissolved in sodium hydroxide solution to give a deep yellow solution.

Analysis :

10.48 mg. of the substance gave 14.46 mg. of carbon dioxide and 2.32 mg. of water.

18.46 mg. of the same substance gave 13.62 mg. of silver iodide.

Found : C = 37.66 % ; H = 2.48 % ; I = 39.88 %.

$C_{10}H_7O_4I$ requires : C = 37.74 % ; H = 2.20 % ; I = 39.94 %.

7-Methoxy-3-iodocoumarin

7-Methoxycoumarin (1.76 g. ; 0.01 mole) in acetic acid (5 ml.) was treated with iodine monochloride (1.62 g. ; 0.01 mole) and the mixture kept at 60° over-night. The next day it was diluted with water and the paste obtained treated with cold alcohol. The white residue crystallised from alcohol in fine needles, m.p. 155-156°. Yield 0.4 g.

Analysis :

16.48 mg. of the substance gave 12.86 mg. of silver iodide.

Found : I = 42.18 %.

$C_{10}H_7O_3I$ requires : I = 42.07 %.

6-Methoxycoumarilic acid

The above iodocoumarin (0.4 g.) was refluxed with alcoholic potassium hydroxide solution (10 % ; 10 ml.) for 2 hours on a steam bath. The product which separated on acidification was purified through sodium bicarbonate solution and crystallised from dilute alcohol in needles, m.p. 205-206°. Mixed m.p. with the product obtained on hydrolysis of 7-methoxy-3-bromocoumarin according to Seshadri and Varadrajan (J. Sci. and Ind. Research, 1951, 11B, 39) was not depressed.

7-Hydroxy-6,8-diiodocoumarin

7-Hydroxycoumarin (1.62 g. ; 0.01 mole) in liquor ammonia (22 % ; 10 ml.) and water (25 ml.) was treated with iodine (5.08 g. ; 0.02 mole) in potassium iodide (10 g.) solution with vigorous stirring of the mixture. As soon as all the iodine was absorbed it was immediately acidified with cold dilute sulphuric acid. The separated product crystallised from acetic acid in needles, m.p. 232°. Yield 0.5 g.

Analysis :

17.02 mg. of the substance gave 19.44 mg. of silver iodide.

Found : I = 61.74 %.

$C_9H_4O_3I_2$ requires : I = 61.30 %.

7-Methoxy-6,8-diiodocoumarin

The above diiodocoumarin (0.5 g.) was methylated by refluxing its acetone solution with dimethyl sulphate (0.5 ml.) in presence of anhydrous potassium carbonate (1.5 g.) as usual. It crystallised from acetic acid in needles, m.p. 168-170°.

Analysis :

10.46 mg. of the substance gave 10.58 mg. of carbon dioxide and 1.42 mg. of water.

19.14 mg. of the same substance gave 20.9 mg. of silver iodide.

Found : C = 27.59 % ; H = 1.52 % ; I = 59.01 %.

$C_{10}H_6O_3I_2$ requires : C = 28.04 % ; H = 1.41 % ; I = 59.30 %.

The methyl ether on heating with 10 % alcoholic potassium hydroxide solution (15 ml.) under reflux remained unchanged.

7-Hydroxy-3,6,8-triiodocoumarin

7-Hydroxycoumarin (1.62 g. ; 0.01 mole) was dissolved in ammonia (20 % ; 10 ml.) and water (30 ml.)

and iodine (5.08 g. ; 0.02 mole) in potassium iodide (10 g.) solution was added. The solution was stirred for 10 minutes and then acidified with dilute sulphuric acid and the separated product crystallised from dilute alcohol in needles, m.p. 234-235°. Yield 2 g.

Analysis :

15.26 mg. of the substance gave 19.9 mg. of silver iodide.

Found : I = 70.49 %.

$C_9H_3O_3I_3$ requires : I = 70.55 %.

The same product was obtained when 7-hydroxycoumarin (1.62 g. ; 0.01 mole) in warm alcohol (20 ml.) was treated with iodine (5.08 g. ; 0.02 mole) and iodic acid (1.8 g.) in water. Yield 2 g.

The same product was also obtained when 7-hydroxycoumarin (1.62 g. ; 0.01 mole) in acetic acid (10 ml.) and hydrochloric acid (10 ml.) was treated with iodine monochloride (12.96 g. ; 0.08 mole) and the reaction mixture was kept for 48 hours at 60°. The needles which separated crystallised from acetic acid. Yield 0.2 g.

7-Methoxy-3,6,8-triiodocoumarin

The above triiodocoumarin (1 g.) was methylated by refluxing its acetone solution with dimethyl sulphate (0.8 ml.) in presence of anhydrous potassium carbonate (2 g.) as usual. M.p. 208-210°.

Analysis :

10.36 mg. of the substance gave 8.32 mg. of carbon dioxide and 1.16 mg. of water.

18.12 mg. of the same substance gave 22.86 mg. of silver iodide.

Found : C = 21.92 % ; H = 1.25 % ; I = 68.19 %.

$C_{10}H_5O_3I_3$ requires : C = 21.66 % ; H = 0.90 % ; I = 68.77 %.

6-Methoxy-5,7-diiodocoumarilic acid

7-Methoxy-3,6,8-triiodocoumarin (0.5 g.) was refluxed with alcoholic potassium hydroxide solution (10 % ; 20 ml.) for 2 hours. The product obtained on acidification was purified through sodium bicarbonate solution. It crystallised from acetic acid in needles, m.p. 240-242°.

Analysis :

10.58 mg. of the substance gave 10.62 mg. of carbon dioxide and 1.72 mg. of water.

16.24 mg. of the same substance gave 17.20 mg. of silver iodide.

Found : C = 27.37 % ; H = 1.81 % ; I = 57.24 %.

$C_{10}H_6O_4I_2$ requires : C = 27.03 % ; H = 1.35 % ; I = 57.20 %.

7-Methoxy-3,6-diiodocoumarin

7-Methoxycoumarin (1.8 g. ; 0.01 mole) in acetic acid (5 ml.) was treated with iodine monochloride (3.24 g. ; 0.02 mole) and the mixture left over-night at 60°. Next day the needles obtained were recrystallised from acetic acid, m.p. 246-247°. Yield 1.2 g.

Analysis :

19.28 mg. of the substance gave 21.18 mg. of silver iodide.

Found : I = 59.37 %.

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

6-Methoxy-5-iodocoumarilic acid

7-Methoxy-3,6-diiodocoumarin (0.5 g.) was refluxed with alcoholic potassium hydroxide solution (10 % ; 20 ml.) for 2 hours on a steam bath. The product obtained on acidification with hydrochloric acid was purified through sodium bicarbonate solution. It crystallised from dilute alcohol, m.p. 258-260°.

Analysis :

10.18 mg. of the substance gave 13.98 mg. of the carbon dioxide and 1.94 mg. of water.

18.82 mg. of the same substance gave 13.86 mg. of silver iodide.

Found : C = 37.48 % ; H = 2.18 % ; I = 39.80 %.

$C_{10}H_7O_4I$ requires : C = 37.74 % ; H = 2.20 % ; I = 39.94 %.

7-Methoxy-3,8-diiodocoumarin

7-Methoxy-8-iodocoumarin (3.02 g. ; 0.01 mole) was dissolved in acetic acid (50 ml.) and treated with iodine monochloride (1.62 g. ; 0.01 mole) and the mixture kept at 60° for 48 hours in an oven. The product which separated crystallised from acetic acid in needles, m.p. 238-240°. Yield 2 g. The mixed m.p. with 7-methoxy-3,6-diiodo-coumarin was depressed by over 20°.

Analysis :

19.14 mg. of the substance gave 21.08 mg. of silver iodide.

Found : I = 59.50 %.

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

6-Methoxy-7-iodocoumarilic acid

The above diiodocoumarin (0.5 g.) was refluxed with alcoholic potassium hydroxide solution (10 % ; 20 ml.) for 2 hours on a steam bath. The product obtained on acidification was purified through sodium bicarbonate solution. It crystallised from acetic acid in needles, m.p. 270-280°.

Analysis :

10.48 mg. of the substance gave 14.40 mg. of carbon dioxide and 2.42 mg. of water.

19.20 mg. of the same substance gave 14.36 mg. of silver iodide.

Found : C = 37.50 % ; H = 2.58 % ; I = 40.43 %.

$C_{10}H_7O_4I$ requires : C = 37.78 % ; H = 2.20 % ; I = 39.94 %.

Iodination of 7-hydroxycoumarin-6-carboxylic acid and its methyl ether and methyl ester

7-Hydroxy-8-iodocoumarin-6-carboxylic acid

7-Hydroxycoumarin-6-carboxylic acid (1.03 g. ; 0.005 mole) was dissolved in alcohol (40 ml.) and treated with iodine (0.508 g. ; 0.002 mole) and iodic acid (0.2 g.) in water with continuous stirring. The separated product crystallised from acetic acid in needles, m.p. 258-260° (efferv.). Yield 1.8 g.

Analysis :

15.36 mg. of the substance gave 10.90 mg. of silver iodide.

Found : I = 38.36 %.

$C_{10}H_5O_5I$ requires : I = 38.25 %.

The same product was ~~also~~ obtained when 7-hydroxycoumarin-6-carboxylic acid (2.06 g. ; 0.01 mole) in acetic acid (40 ml.) was treated with iodine monochloride (3.24 g. ; 0.02 mole) and the mixture left at 60-70° for 24 hours.

The same product was also obtained when 7-hydroxycoumarin-6-carboxylic acid (2.06 g. ; 0.01 mole) was dissolved in liquor ammonia (25 ml.) and water (25 ml.) and then treated with a solution of iodine (2.54 g. ; 0.01 mole) in potassium iodide (5 g.). The mixture was stirred machanically for 15 minutes. The clear solution was acidified with cold dilute sulphuric acid. The separated product after repeated crystallisation from alcohol and acetic acid gave ~~a~~ the iodo product in very poor yield, m.p. 258-260°. (efferv.)

Methyl-7-methoxy-8-idocoumarin-6-carboxylate

The acetone solution of the above iodo acid (2 g.) was treated with dimethyl sulphate (1 ml.) in presence of anhydrous potassium carbonate (2 g.). The product crystallised from acetic acid in fine silky needles, m.p. 162°.

Analysis :

10.44 mg. of the substance gave 15.14 mg. of carbon dioxide and 2.66 mg. of water.

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

Found : C = 39.57 % ; H = 2.85 % ; I = 35.59 %.
$C_{12}H_9O_5I$ requires : C = 40.00 % ; H = 2.50 % ; I = 35.30 %.

7-Methoxy-8-iodocoumarin-6-carboxylic acid

The above ester (0.5 g.) was refluxed with alcoholic potassium hydroxide solution (10 % ; 20 ml.) on a steam bath for 2 hours. The product obtained on acidification crystallised from acetic acid in needles, m.p. 235-237°.

Analysis :

10.36 mg. of the substance gave 14.60 mg. of carbon dioxide and 2.10 mg. of water.

13.82 mg. of the same substance gave 9.42 mg. of silver iodide.

Found : C = 38.46 % ; H = 2.27 % ; I = 36.84 %.
$C_{11}H_7O_5I$ requires : C = 38.15 % ; H = 2.02 % ; I = 36.70 %.

7-Hydroxy-3,8-diiodocoumarin-6-carboxylic acid

7-Hydroxycoumarin-6-carboxylic acid (1.03 g. ; 0.005 mole) in warm alcohol (40 ml.) was treated with iodine (2.03 g. ; 0.008 mole) and iodic acid (1 g.). The solution was stirred for 4 hours and then diluted with large volume of water. The separated product crystallised from alcohol in needles, m.p. 272°. Yield 0.2 g.

Analysis :

19.36 mg. of the substance gave 19.0 mg of silver iodide.

Found : I = 53.05 %.
$C_{10}H_4O_5I_2, H_2O$ requires : I = 53.35 %.

Methyl-7-methoxy-3,8-diiodocoumarin-6-carboxylate

The methoxy ester of the above diiodocoumarin was prepared by refluxing its (1 g.) acetone solution with dimethyl sulphate (1 ml.) in presence of anhydrous potassium carbonate (2 g.). It crystallised from benzene petroleum ether (b.p. 40-60°) in buds, m.p. 205-206°.

Analysis :

9.12 mg. of the substance gave 9.86 mg. of carbon dioxide and 1.72 mg. of water.

19.40 mg. of the same substance gave 18.76 mg. of silver iodide.

Found : C = 29.52 % ; H = 2.10 % ; I = 52.25 %.
$C_{12}H_8O_5I_2$ requires : C = 29.63 % ; H = 1.64 % ; I = 52.26 %.

6-Methoxy-7-iodo-5-carboxycoumarilic acid

The above diiodo ester (0.5 g.) in alcoholic potassium hydroxide solution (10 % ; 20 ml.) was refluxed on a water bath for 2 hours. The product obtained was purified through sodium bicarbonate solution. It crystallised from acetic acid in needles, m.p. 272°.

Analysis :

10.22 mg. of the substance gave 13.82 mg. of carbon dioxide and 2.06 mg. of water.

19.18 mg. of the same substance gave 12.32 mg. of silver iodide.

Found : C = 36.91 % ; H = 2.26 % ; I = 34.70 %.

$C_{11}H_7O_6I$ requires : C = 36.47 % ; H = 1.93 % ; I = 35.09 %.

Methyl 7-methoxy-3-iodocoumarin-6-carboxylate

Methyl 7-methoxycoumarin-6-carboxylate (2.34 g. ; 0.01 mole) in acetic acid (20 ml.) was treated with iodine monochloride (1.62 g. ; 0.01 mole) and the mixture was kept at 60° for 24 hours. Next day the needles which separated were recrystallised from acetic acid, m.p. 245°. Yield 1.5 g. The same product was obtained in a better yield when iodine monochloride was taken in excess (0.04 moles)

Analysis :

14.44 mg. of the substance gave 6.92 mg. of silver iodide.

Found : I = 35.15 %.

$C_{12}H_9O_5I$ requires : I = 35.30 %.

6-Methoxy-5-carboxycoumarilic acid

The above methoxy iodo ester (0.5 g.) was treated with alcoholic potassium hydroxide solution (10 % ; 20 ml.) on a steam bath for 2 hours. The product obtained on working up as usual crystallised from dilute acetic acid in needles, m.p. 285-286°.

Analysis :

10.94 mg. of the substance gave 22.52 mg. of carbon dioxide and 3.34 mg. of water.

Found : C = 56.18 % ; H = 3.41 %.

$C_{11}H_8O_6$ requires : C = 55.94 % ; H = 3.41 %.

Iodination of 7-hydroxycoumarin-4-acetic acid : 7-Hydroxy-8-iodocoumarin-4-acetic acid

7-Hydroxycoumarin-4-acetic acid (2.24 g. ; 0.01 mole) was dissolved in liquor ammonia (22 % ; 10 ml.) and water (25 ml.) and was treated with iodine (2.54 g. ; 0.01 mole) in potassium iodide (5 g.) solution. The clear solution was acidified with dilute sulphuric acid. The separated product was purified through sodium bicarbonate solution. It crystallised from acetic acid, in which it was sparingly soluble, in needles, m.p. 227-228°. (efferv.) Yield 2.5 g.

Analysis :

15.88 mg. of the substance gave 10.76 mg. of silver iodide.

Found : I = 36.63 %.

$C_{11}H_7O_5I$ requires : I = 36.70 %.

The same product was obtained when 7-hydroxycoumarin-4-acetic acid (1.1 g. ; 0.005 mole) in warm alcohol (10 ml.) was treated with iodine (0.508 g. ; 0.002 mole) and iodic acid (0.2 g.). Yield 2 g.

The same product was also obtained when a mixture of 7-hydroxycoumarin-4-acetic acid (2.24 g. ; 0.01 mole) in acetic acid (15 ml.) and hydrochloric acid (15 ml.) was treated with iodine monochloride (1.6 g. ; 0.01 mole) and the reaction mixture left over-night at 60° in an oven and then ~~reaction mixture~~ worked up as usual. Yield 0.2 g.

Methyl-7-methoxy-8-iodocoumarin-4-acetate

The acetone solution of the above iodo coumarin (2 g.) was refluxed with dimethyl sulphate (2 ml.) in presence of anhydrous potassium carbonate (6 g.). The product obtained was purified by washing with sodium hydroxide solution. It crystallised from benzene-petroleum ether (b.p. 40-60°) mixture in silky needles, m.p. 140-142°.

Analysis :

9.82 mg. of the substance gave 15.20 mg. of carbon dioxide and 2.9 mg. of water.

16.28 mg. of the same substance gave 10.28 mg. of silver iodide.

	Found	: C = 42.24 % ; H = 3.30 % ; I = 34.13 %.
$C_{13}H_{11}O_5I$	requires	: C = 41.70 % ; H = 2.94 % ; I = 33.95 %.

7-Methoxy-8-iodo-4-methylcoumarin

The above iodocoumarin ester (0.4 g.) was refluxed with alcoholic potassium hydroxide solution (10 % ; 10 ml.) for 2 hours on a steam bath. The product which separated on acidification was insoluble in sodium bicarbonate solution. It crystallised from rectified spirit in needles, m.p. 199°. Mixed m.p. with an authentic specimen of 7-methoxy-8-iodo-4-methylcoumarin prepared according to Lele and Sethna, (J. Org. Chem., 1958, 23, 1731) was not depressed. Decarboxylation took place during the hydrolysis.

7-Hydroxy-6,8-diiodocoumarin-4-acetic acid

7-Hydroxycoumarin-4-acetic acid (2.24 g. ; 0.01 mole) was dissolved in liquor ammonia (22 % ; 10 ml.) and water (25 ml.)and treated drop-wise with iodine crystals (5.08 g. ; 0.02 mole) in potassium iodide solution with stirring. The clear solution was acidified with dilute ice cold sulphuric acid and the product obtained purified through potassium bicarbonate solution. It crystallised from acetic acid in needles, m.p. 235-236°. Yield 3.5 g.

Analysis :

20.34 mg. of the substance gave 19.50 mg. of silver iodide.

Found : I = 51.82 %.

$C_{11}H_6O_5I_2.H_2O$ requires: I = 51.83 %.

7-Methoxy-6,8-diiodo-4-methylcoumarin

The above diiodocoumarin (2 g.) was refluxed in acetone (250 ml.) with dimethyl sulphate (2 ml.) in presence of anhydrous potassium carbonate (6 g.) for 8 hours. The product obtained on working up the reaction mixture as usual crystallised from acetic acid in needles, m.p. 212°. Mixed m.p. with an authentic specimen of 7- methoxy-6,8-diiodo-4-methylcoumarin prepared according to Lele and Sethna (loc.cit.) was not depressed. Decarboxylation took place during the methylation.

7-Hydroxy~~coumarin~~-3,6-8-triiodocoumarin-4-acetic acid

7-Hydroxycoumarin-4-acetic acid (1.12 g. ; 0.005 mole) dissolved in alcohol (10 ml.) was treated with iodine (2.03 g. ; 0.008 mole) and iodic acid (0.8 g.) in water. The product obtained was purified through sodium bicarbonate solution. It crystallised from acetic acid in thin plates, m.p. 238-240°. Yield 2 g.

Analysis :

18.18 mg. of the substance gave 21.58 mg. of silver iodide.

Found : I = 64.20 %.

$C_{11}H_5O_5I_3$ requires : I = 63.70 %.

The same product was also obtained when 7-hydroxycoumarin-4-acetic acid (2.24 g. ; 0.01 mole) was dissolved in a mixture of acetic acid and concentrated hydrochloric acid (10 ml. each) and the solution was treated with iodine monochloride (6.4 g. ; 0.04 mole). Yield 1.2 g.

7-Methoxy-3,6,8-triiodo-4-methylcoumarin

The above triiodocoumarin (2.0 g.) was dissolved in acetone (250 ml.) and refluxed with dimethyl sulphate (2 ml.) and anhydrous potassium carbonate (6 g.). The product obtained crystallised from acetic acid in needles, m.p. 217°. Mixed m.p. with an authentic specimen of 7-methoxy-3,6,8-triiodo-4-methylcoumarin prepared according to Lele and Sethna (loc.cit.) was not depressed.

Iodination of ethyl 7-hydroxycoumarin-3-carboxylate : 7-Hydroxy-8-iodocoumarin-3-carboxylic acid

Ethyl 7-hydroxycoumarin-3-carboxylate (2.34 g. ; 0.01 mole) dissolved in ammonia (22 % ; 10 ml.) and water (35 ml.) was treated drop-wise with iodine (2.54 g. ; 0.01 mole) in potassium iodide (5 g.) solution with vigorous stirring of the reaction mixture for 10 minutes. It was then added to ice cold dilute sulphuric acid. The separated product was taken up in sodium bicarbonate ~~and the filtrate acidified~~. The product obtained from the bicarbonate solution on acidification. crystallised from acetic acid in cubes. m.p. 265-266° (efferv.). It was sparingly soluble in organic solvents.

Analysis :

4.250 mg. of the substance gave 5.048 mg. of carbon dioxide and 0.972 mg. of water.

14.476 mg. of the same substance gave 9.398 mg. of silver iodide.

Found : C = 32.41 % ; H = 2.56 % ; I = 35.09 %.

$C_{10}H_5O_5I.2H_2O$ requires : C = 32.61 % ; H = 2.44 % ; I = 34.51 %.

The same compound was obtained when ethyl 7-hydroxycoumarin-3-carboxylate (1.2 g. ; 0.005 mole) was dissolved in warm alcohol (20 ml.) and treated with iodine (0.508 g. ; 0.002 mole) and iodic acid (0.2 g.) in minimum quantity of water, and also when ethyl 7-hydroxycoumarin-3-carboxylate (2.3 g. ; 0.01 mole) was dissolved in acetic acid (10 ml.) and hydrochloric acid (10 ml.) and the solution treated with iodine monochloride (1.62 g. ; 0.01 mole),

Methyl 7-methoxy-8-iodocoumarin-3-carboxylate

The above iodo acid (1.0 g.) was taken up in a soxhlet thimble and potassium carbonate (2 g.) and acetone (250 ml.) ~~was~~ were taken in a flask and the reaction mixture was refluxed for 10 hours. The product obtained on removal of acetone was washed with dilute alkali and crystallised from acetic acid in needles, m.p. 206-207°.

Analysis :

4.914 mg. of the substance gave 7.188 mg. of carbon dioxide and 1.168 mg. of water.

9.884 mg. of the same substance gave 6.392 mg. of silver iodide.

Found : C = 39.92 % ; H = 2.66 % ; I = 34.96 %.

$C_{12}H_9O_5I$ requires : C = 40.00 % ; H = 2.50 % ; I = 35.28 %.

6-Hydroxy-7-methoxy-8-iodocoumarin-3-carboxylic acid

Methyl 7-methoxy-8-iodo-3-carboxylate (1 g.) was warmed on a steam bath with sodium hydroxide solution (10 % ; 20 ml.) ~~with~~ and pyridine (3 ml.). The clear solution was oxidised with potassium persulphate (1 g.) in water (20 ml.) as usual. The product obtained on working up the reaction mixture crystallised from dilute alcohol in needles, m.p. 255-256°. Yield 0.2 g.

Analysis :

4.018 mg. of the substance gave 5.122 mg. of carbon dioxide and 0.828 mg. of water.

10.744 mg. of the same substance gave 6.730 mg. of silver iodide.

Found : C = 34.79 % ; H = 2.30 % ; I = 33.86 %.

$C_{11}H_7O_6I\ H_2O$ requires : C = 34.73 % ; H = 2.37 % ; I = 33.42 %.

7-Hydroxy-6,8-diiodocoumarin-3-carboxylic acid

Ethyl 7-hydroxycoumarin-3-carboxylate (1.2 g. ; 0.005 mole) was dissolved in warm alcohol (20 ml.) and treated with iodine (1.02 g. ; 0.004 mole) and iodic acid (0.4 g.) in minimum quantity of water, and the reaction mixture stirred vigorously for 3 hours. The product obtained on dilution of the reaction mixture was purified through sodium bicarbonate solution. It crystallised from acetic acid in needles, m.p. 220-222°. (efferv.)

Analysis :

4.918 mg. of the substance gave 4.402 mg. of carbon dioxide and 0.878 mg. of water.

17.140 mg. of the same substance gave 16.324 mg. of silver iodide.

Found : C = 24.42 % ; H = 1.99 % ; I = 51.48 %.

$C_{10}H_4O_5I_2.2H_2O$ requires : C = 24.30 % ; H = 1.63 % ; I = 51.42 %.

The same compound was obtained when ethyl 7-hydroxycoumarin-3-carboxylate (2.3 g. ; 0.01 mole) was dissolved in acetic acid (20 ml.) and hydrochloric acid (20 ml.) and the solution treated with iodine monochloride (6.4 g. ; 0.04 mole)

Attempt to methylate the above diiodo derivative (2.3 g.) with dimethyl sulphate (1 ml.) or methyl iodide (1 ml.) in acetone solution in presence of anhydrous potassium carbonate (3 g.) by refluxing for 12 hours did not succeed. Original diiodo acid was recovered.

Iodination of 6-hydroxycoumarin and its methyl ether

6-Hydroxy-5-iodocoumarin.

6-Hydroxycoumarin (1.62 g. ; 0.01 mole) was dissolved in liquor ammonia (22 % ; 5 ml.) and water (250 ml.) and treated with iodine (2.54 g. ; 0.01 mole) and potassium iodide (5 g.) solution. The clear solution on acidification with cold dilute sulphuric acid gave a product which crystallised from alcohol in needles, m.p. 244-245° (decomp.). Yield 2.5 g.

Analysis :

18.94 mg. of the substance gave 15.46 mg. of silver iodide.

Found : I = 44.12 %.

$C_9H_5O_3I$ requires : I = 44.10 %.

The same product was obtained when 6-hydroxycoumarin (1.62 g. ; 0.01 mole) dissolved in warm alcohol (20 ml.) was treated with iodine crystals (1.01 g. ; 0.004 mole) and iodic acid (0.4 g.) in water. The mixture was stirred for 3 hours and diluted with water. The separated product crystallised from alcohol in needles, m.p. 244-245°. Yield 2.3 g.

The same product was also obtained when 6-hydroxycoumarin (1.62 g. ; 0.01 mole) was dissolved in acetic acid (25 ml.) and hydrochloric acid (25 ml.) and treated with iodine monochloride (1.62 g. ; 0.01 mole). The mixture was left over-night at 60° in an oven. On the next day it was stirred vigorously for 2 hours. The product which separated on dilution with water crystallised as above. Yield 2 g.

6-Methoxy-5-iodocoumarin

Obtained as usual by refluxing an acetone solution of the iodo compound (1 g.) with dimethyl sulphate (1 ml.) and anhydrous potassium carbonate (3 g.) for 8 hours. It crystallised from acetic acid in needles, m.p. 148-149°.

Analysis :

10.36 mg. of the substance gave 15.04 mg. of carbon dioxide and 2.46 mg. of water.

16.44 mg. of the same substance gave 12.92 mg. of silver iodide.

Found : C = 39.52 % ; H = 2.66 % ; I = 42.48 %.
$C_{10}H_7O_3I$ requires : C = 39.74 % ; H = 2.33 % ; I = 42.07 %.

The same product was also obtained when 6-methoxycoumarin (1.8 g. ; 0.01 mole) in acetic acid (5 ml.) was treated with iodine monochloride (1.6 g. ; 0.01 mole) and the reaction mixture worked up as usual. Yield 1.2 g.

The iodo derivative remained unchanged when refluxed with potassium hydroxide solution (10 % ; 20 ml.) for 2 hours on a steam bath.

6-Hydroxy-5-nitrocoumarin

6-Hydroxycoumarin (2.2 g.) in concentrated sulphuric acid (10 ml.) was slowly treated with a mixture of nitric acid and sulphuric acid (1 : 3 ; 4 ml.) at 0°. After one hour the reaction mixture was added to crushed ice when a yellow solid separated. It was crystallised first from acetic acid and then from benzene, yellow needles, m.p. 208-210°. It decomposed on keeping.

Analysis :

9.634 mg. of the substance gave 0.653 ml. of nitrogen at 41° and 753 mm.

Found : N = 7.30 %.

$C_9H_5O_5N$ requires : N = 6.80 %.

6-Methoxy-5-nitrocoumarin

The above nitrocoumarin (1 g.) was dissolved in acetone (100 ml.) and refluxed with potassium carbonate (2 g.) and dimethyl sulphate (1 ml.) for 12 hours. The product obtained on removal of acetone was washed with dilute sodium hydroxide solution. It crystallised from dilute alcohol in needles, m.p. 151-152°.

Analysis :

4.346 mg. of the substance gave 8.660 mg. of carbon dioxide and 1.302 mg. of water.

4.910 mg. of the substance gave 0.263 ml. of nitrogen at 30° and 750 mm.

Found : C = 54.38 % ; H = 3.35 % ; N = 5.95 %.

$C_{10}H_7O_5N$ requires : C = 54.30 % ; H = 3.19 % ; N = 6.33 %.

The above compound (0.3 g.) when refluxed with liquor ammonia (22 % ; 20 ml.) on a steam bath for 3 hr. did not undergo any change.

6-Methoxy-5-aminocoumarin

6-Methoxy-5-nitrocoumarin (1 g.) in alcohol (5 ml.) was treated with stannous chloride (2 g.) and hydrochloric acid (14 ml.). The solution was refluxed on a sand bath for 2 hours. It was then cooled and made alkaline with 22 % ammonium hydroxide solution. The white emulsion was extracted repeatedly with ether. The yellow product obtained on removal of ether crystallised from benzene-petroleum ether mixture in shining yellow needles, m.p. 157-158°. It was soluble in hydrochloric acid.

Analysis :

4.412 mg. of the substance gave 10.168 mg. of carbon dioxide and 1.808 mg. of water.

6.182 mg. of the same substance gave 0.422 ml. of nitrogen at 31° and 750 mm.

Found : C = 62.89 % ; H = 4.60 % ; N = 7.56 %.

$C_{10}H_9O_3N$ requires : C = 62.84 % ; H = 4.82 % ; N = 7.33 %.

6-Methoxy-5-hydroxycoumarin

The above aminocoumarin (0.2 g.) was heated in a carius tube with hydrochloric acid (4 ml.) and water (24 ml.) at 150-160° for 3 hours. The product obtained on extraction with ether crystallised from benzene-alcohol-petroleum ether mixture in shining yellow needles, m.p. 240°. It dissolved in sodium hydroxide to give a yellow solution.

The same product was also obtained when the aminocoumarin (0.1 g.) was diazotized and the diazonium solution was heated with sulphuric acid (30 % ; 20 ml.).

Analysis :

4.650 mg. of the substance gave 10.704 mg. of carbon dioxide and 1.770 mg. of water.

Found : C = 62.82 % ; H = 4.26 %.

$C_{10}H_8O_4$ requires : C = 62.50 % ; H = 4.20 %.

6-Methoxy-5-iodocoumarin

6-Methoxy-5-aminocoumarin (0.3 g.) was dissolved in concentrated hydrochloric acid (6 ml.) at 0° and treated with sodium nitrite (0.35 g.) solution at 0° during 15 minutes. This solution was then added drop-wise to potassium iodide (0.5 g.) solution at 0° during 15 minutes, and the reaction mixture then kept at room temperature for 3 hr. The separated product was washed with water and treated with sodium bisulphite solution. It was crystallised first from dilute alcohol and then from benzene-petroleum mixture. Needles, m.p. 148-150°. Mixed m.p. with 6-methoxy-5-iodocoumarin described before was not depressed.

7-Tosyloxycoumarin

To a mechanically stirred solution of 7-hydroxycoumarin (4.9 g. ; 0.03 mole) and p-toluene sulphonylchloride (6 g. ; 0.03 mole) in acetone (100 ml.), a solution of sodium bicarbonate (4 g.) in water (30 ml.) was added in four lots. After vigorous stirring for 4 hrs. the reaction mixture was poured in water when shining plates seperated. The product after washing with sodium hydroxide solution was crystallised from dilute alcohol. Thin plates, m.p. 152-153°. Yield 4.5 g.

Analysis :

4.652 mg. of the substance gave 10.344 mg. of carbon dioxide and 1.680 mg. of water.

Found : C = 60.68 % ; H = 4.04 %.

$C_{16}H_{12}O_5S$ requires : C = 60.75 % ; H = 3.79 %.

6-Hydroxy-7-tosyloxycoumarin

7-Tosyloxycoumarin (3.3 g.) dissolved in pyridine

(75 ml.) was mechanically stirred and potassium hydroxide (8 g.) in water (100 ml.) was added. The solution was externally cooled and potassium persulphate (8 g.) in water (200 ml.) was then gradually added during 3 hrs. Next day the solution was just acidified and the separated paste filtered. The clear solution was washed with ether and then treated with sodium sulphite (8 g.) and hydrochloric acid (100 ml.), warmed on a steam bath for 45 minutes and cooled. The separated solid crystallised from dilute alcohol in thin plates, m.p. 204-205°. Yield 0.2 g. The paste on working up gave the original product.

Analysis :

4.412 mg. of the substance gave 9.338 mg. of carbon dioxide and 1.420 mg. of water.

Found : C = 57.76 % ; H = 3.60 %.

$C_{16}H_{12}O_6S$ requires : C = 57.89 % ; H = 3.61 %.

6-Methoxy-7-tosyloxycoumarin

The above coumarin (0.5 g.) in acetone (100 ml.) was refluxed with anhydrous potassium carbonate (1 g.) and dimethyl sulphate (0.3 ml.) for 8 hours. The product obtained on working up as usual crystallised from acetic acid in cubes, m.p. 208-210°.

Analysis :

4.434 mg. of the substance gave 9.608 mg. of carbon dioxide and 1.598 mg. of water.

Found : C = 59.13 % ; H = 4.03 %.

$C_{17}H_{14}O_6S$ requires : C = 58.95 % ; H = 4.04 %.

7-Hydroxy-6-methoxycoumarin (Scopoletin)

The above methyl ether (0.3 g.) was dissolved in concentrated sulphuric acid (10 ml.) and kept for 24 hours. Next day it was poured over crushed ice. The solid obtained was purified through sodium hydroxide treatment. It crystallised from water in needles, m.p. 203-204°. The same m.p. has been given in the literature. Its alcoholic, sulphuric acid and alkaline solution showed brilliant blue fluoresence.

Analysis :

3.972 mg. of the substance gave 9.112 mg. of carbon dioxide and 1.508 mg. of water.

Found : C = 62.60 % ; H = 4.25 %.

$C_{10}H_8O_4$ requires : C = 62.50 % ; H = 4.25 %.

Iodination of methyl 5-methoxycoumarin-6-carboxylate :

Methyl 5-methoxy-8-iodocoumarin-6-carboxylate

Methyl 5-methoxycoumarin-6-carboxylate (1.2 g. ; 0.005 mole) in acetic acid (20 ml.) was treated with iodine monochloride (0.8 g. ; 0.005 mole) and the reaction mixture was kept at 60° for 24 hours. Next day it was stirred ~~with a magnetic stirrer~~ for 3 hours and then diluted with water. The precipitated product crystallised from dilute alcohol in needles, m.p. 157-158°. Yield 0.8 g.

Analysis :

19.24 mg. of the substance gave 12.36 mg. of silver iodide.

Found : I = 34.70 %.

$C_{12}H_9O_5I$ requires : I = 35.30 %.

5-Methoxy-8-iodocoumarin-6-carboxylic acid

The above ester (0.3 g.) was refluxed with alcoholic potassium hydroxide solution (10 % ; 25 ml.) on a steam bath for 2 hours. The product obtained on acidification was purified through sodium bicarbonate solution. It crystallised from acetic acid in needles, m.p. 238-240° (efferv.).

Analysis :

10.22 mg. of the substance gave 14.20 mg. of carbon dioxide and 2.16 mg. of water.

20.00 mg. of the same substance gave 13.68 mg. of silver iodide.

Found : C = 37.92 % ; H = 2.37 % ; I = 36.97 %.

$C_{11}H_7O_5I$ requires : C = 38.15 % ; H = 2.02 % ; I = 36.70 %.

Attempted iodination of 7,8-dihydroxycoumarin

(a) with Iodine and ammonia

7,8-Dihydroxycoumarin (1.78 g. ; 0.01 mole) was dissolved in ammonia (22 % ; 10 ml.) and treated with iodine (2.54 g. ; 0.01 mole) in potassium iodide (5 g.) solution. The colour of the solution became dark brown. The reaction mixture was vigorously stirred and acidified with ice cold dilute sulphuric acid solution. No product could be isolated from the solution.

(b) With iodine and iodic acid

7,8-Dihydroxycoumarin (0.9 g. ; 0.005 mole) was dissolved in alcohol (5 ml.) and treated with iodine (0.508 g. ; 0.002 mole) and iodic acid (0.2 g.) in minimum quantity of water. The solution was stirred for 2 hours and added to water. No product was obtained as such or after extraction of the clear solution with ether.

(c) Iodine monochloride

7,8-Dihydroxycoumarin (1.78 g. ; 0.01 mole) dissolved in acetic acid (8 ml.) and hydrochloric acid (8 ml.) was treated with iodine monochloride (1.62 g. ; 0.01 mole) and the reaction mixture was kept at 60° for 24 hours. Next day it was stirred for 2 hours and then diluted with water. No product could be isolated from the reaction mixture.

Attempted iodination of naphtha-1:2-α-pyrone

(a) With iodine and ammonia

Naphtha-1:2-α-pyrone (1.96 g. ; 0.01 mole) prepared according to Koelsch and Masley (J. Am. Chem. Soc., 1953, 75, 3596) was dissolved in dioxan (10 ml.) and treated with ammonia (22 % ; 20 ml.) followed by iodine (2.54 g. ; 0.01 mole) in potassium iodide (5 g.) solution with vigorous stirring. After one hour it was acidified with dilute ice cold sulphuric acid. The product which separated was the original coumarin.

(b) Iodine and iodic acid

Naphtha-1:2-α-pyrone (1.96 g. ; 0.01 mole) was dissolved in alcohol (10 ml.) and treated with iodine (1 g. ; 0.004 mole) and iodic acid (0.2 g.) in minimum quantity of water. The reaction mixture was stirred for 6 hours, and then diluted with water . The product obtained was found to be original coumarin.

(c) With iodine monochloride

Naphtha-1:2-a-pyrone (1.96 g. ; 0.01 mole) was dissolved in acetic acid (10 ml.) and hydrochloric acid (10 ml.) was treated with iodine monochloride (1.62 g. ; 0.01 mole) and the reaction mixture was kept at 60° for 24 hours. Next day it was stirred for 3 hours and then diluted with water. The product obtained was found to be the original coumarin.

Attempted iodination of 7-methylcoumarin

(a) With iodine and iodic acid

7-Methylcoumarin (1.6 g. ; 0.01 mole) was dissolved in alcohol (10 ml.) and iodine (4.04 g. ; 0.004 mole) was added. Then it was treated with iodic acid (1.6 g.) in minimum quantity of water. The solution was stirred for 6 hours and kept over-night. Next day it was diluted with water and the excess of iodine was removed by washing with sodium bisulphite. The brownish liquid which separated was taken in ether and washed with alkali. The residue obtained on evaporation of ether gave a brown paste from which the original coumarin was obtained in a small quantity.

(b) With iodine monochloride

7-Methylcoumarin (1.6 g. ; 0.01 mole) dissolved in acetic acid (5 ml.) was added to iodine monochloride (6.48 g. ; 0.04 mole). The solution was stirred for 3 hours and kept at 60° for 48 hours. It was then further stirred and diluted with water. The solid was treated with sodium bisulphite. The product obtained ~~was~~ when crystallised from alcohol ~~which~~ was found to be the original 7-methylcoumarin.