CHAPTER II

IODINATION OF COUMARINS

CHAPTER II

Iodination of Coumarins

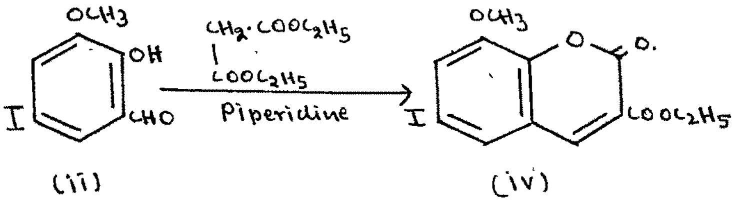
Chlorination and especially bromination of coumarin derivatives has been extensively studied and the work done has been reviewed in Chapter I. It has been seen that in the bromination of 7-hydroxycoumarin derivatives and their methyl ethers the first bromine atom in all cases enters the pyrone ring in the 3-position and the subsequent bromine atoms enter the benzene ring. In the 5-hydroxycoumarin derivatives however it has been observed that the first bromine atom enters the benzene ring in the 8-position. It was thought of interest to see whether the same pattern would follow in the iodination of these coumarin derivatives.

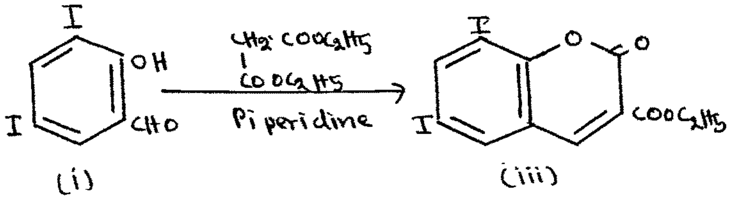
Direct iodination of coumarins has not been studied though some iodo derivatives ~~are~~ have been obtained by indirect methods. Dey and Row (J. Chem. Soc., 1924, 125, 554) obtained 6-iodocoumarin from 6-aminocoumarin by diazotisation and Sandmeyer reaction. They also obtained the same compound by the iodination of sodium bisulphite complex of coumarin in cold dilute alkali. They obtained 8-iodo-6-nitrocoumarin by the same method.

Subbarao and Sundaramurthy (Proc. Indian Acad. Sci., 1955, 42A, 249) obtained 7-iodo-4-methyl-3-phenylcoumarin from 7-amino-4-methyl-3-phenylcoumarin through diazotisation and Sandmeyer reaction.

Buu Hoi et al. (Compt. rend. 1956, 243, 1126 ; C.A., 1957, 51, 5058) condensed 3,5-diiodosalicylaldehyde (i) and

5-iodo-3-methoxysalicylaldehyde (ii) with diethyl malonate in presence of piperidine and obtained ethyl-6,8-diiodocoumarin-3-carboxylate (iii) and ethyl-6-iodo-8-methoxycoumarin-3-carboxylate (iv). The same aldehydes with ethyl acetoacetate gave the corresponding 3-acetyl derivatives and with ethyl benzoylacetate the 3-benzoyl derivatives.





Covello and Piscope (Gazz. Chim. ital., 1958, <u>88</u>, 101 ; C.A., 1959, <u>53</u>, 2216) obtained 6-iodo-4-hydroxycoumarin by the condensation of 5-iodo-2-acetoxybenzoic acid with sodium derivative of diethyl malonate and hydrolysis and decarboxylation of the compound formed.

The direct iodination of coumarin derivatives has now been studied with three different iodinating agents : (i) iodine monochloride, (ii) iodine and iodic acid and (iii) iodine and ammonia. Under (ii) it is assumed that the reaction takes place according to the following equation :

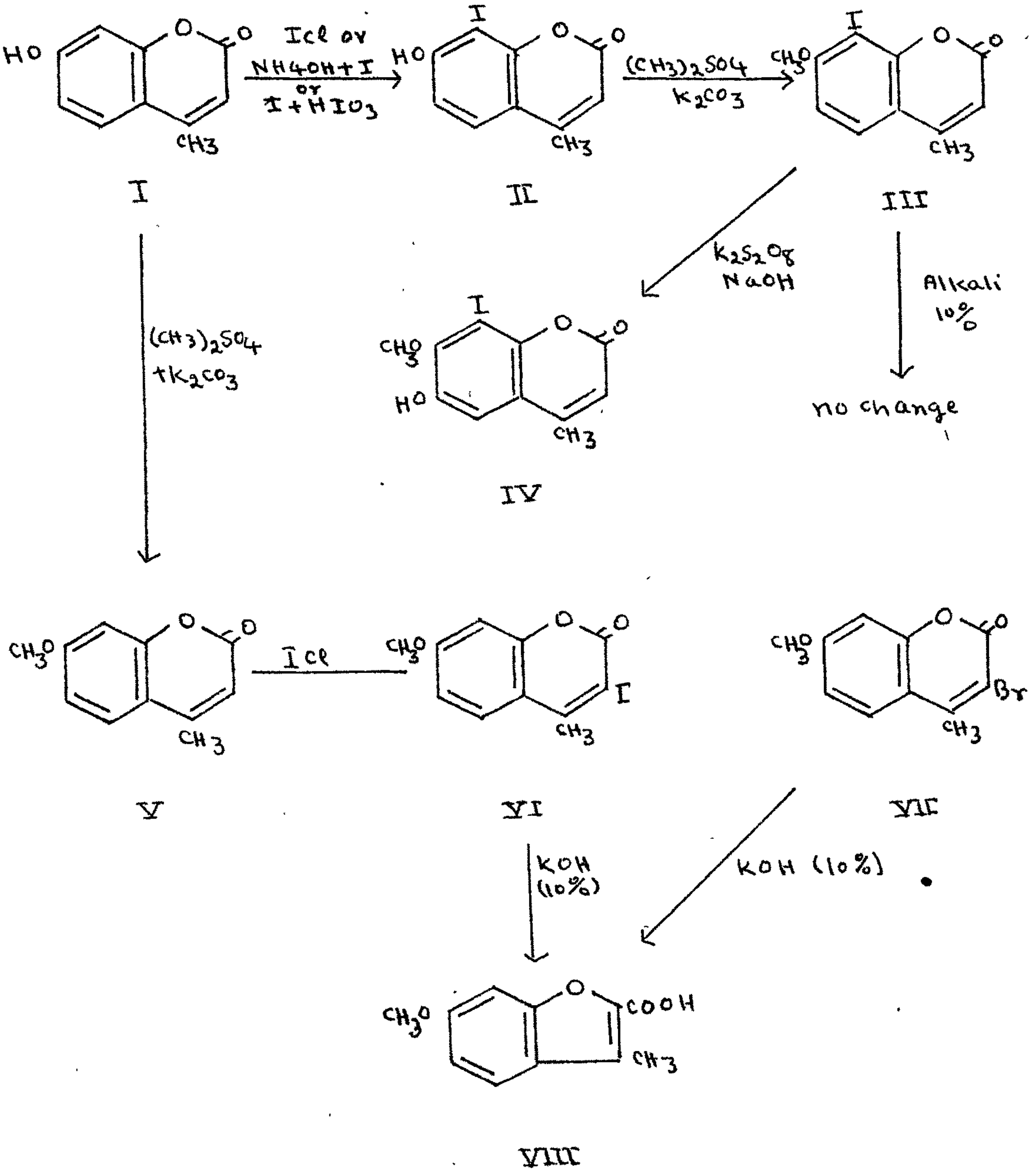
$$5\ RH + 2\ I_2 + HIO_3 = 5\ RI + 3\ H_2O.$$

Coumarin did not undergo iodination by any of the above three methods.

Iodination of 7-hydroxy-4-methylcoumarin and its methyl ether.

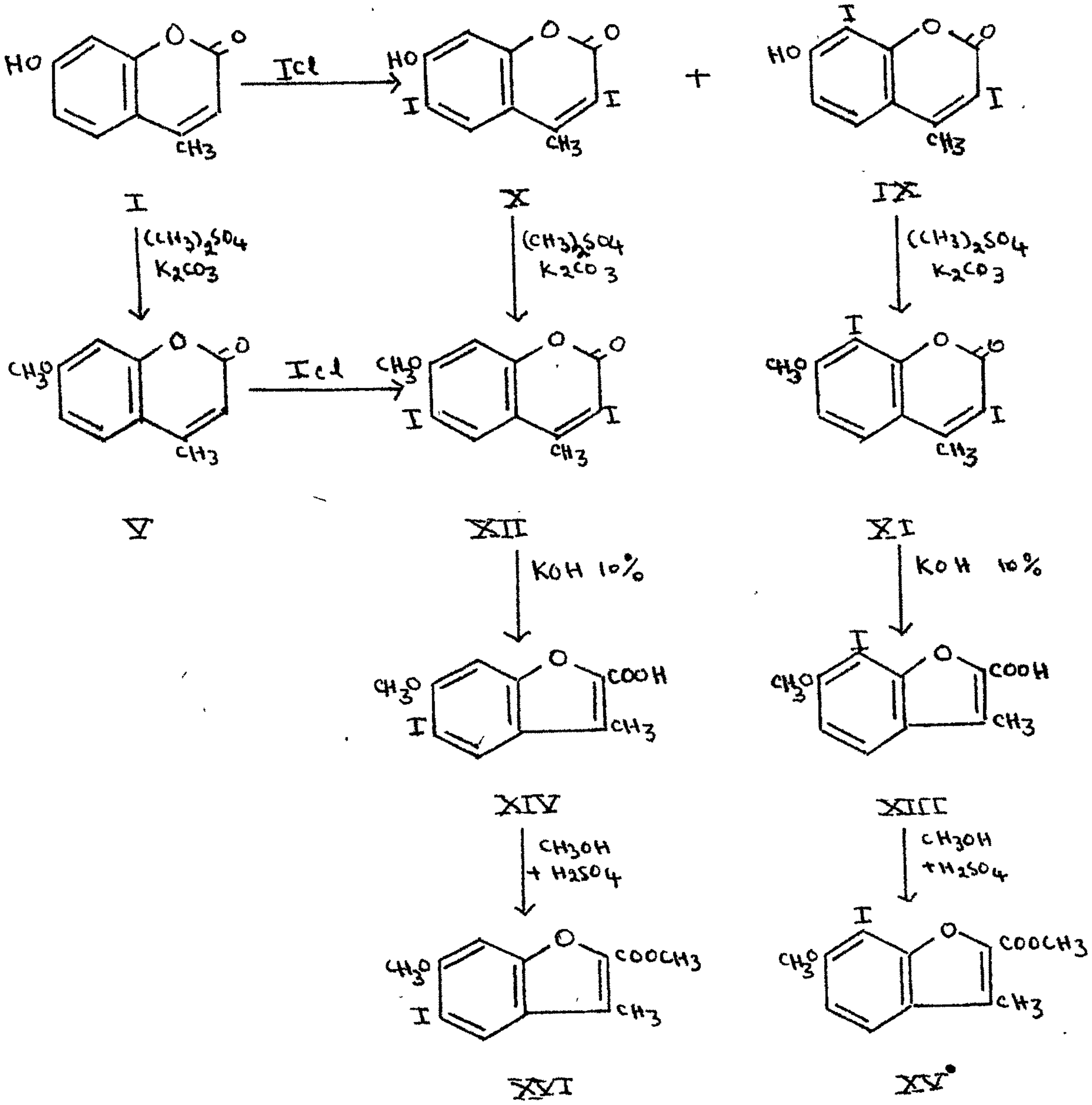
7-Hydroxy-4-methylcoumarin (I) on iodination with one mole of iodine monochloride gave a monoiodo derivative. The methyl ether of the monoiodo derivative did not give a coumarilic acid derivative on heating with alkali indicating that the first iodine atom had not entered the 3-position. The alternative 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, thus indicating that the 6-position in the methyl ether must be free. (Parikh and Sethna, J. Indian Chem. Soc., 1950, 27, 369). 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 as found by Dalvi, 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-hydroxycoumarins (Dalvi and Sethna, J. Indian Chem. Soc., 1949, 26, 359, 467). The monoiodo derivative is therefore 7-hydroxy-8-iodo-4-methylcoumarin (II) and the Elbs Persulphate Oxidation product is 6-hydroxy-7-methoxy-8-iodo-4-methylcoumarin (IV). The mother liquor from the crystallisation of the 8-iodo derivative left a mixture from which no other pure product could be isolated.

7-Methoxy-4-methylcoumarin (V) on iodination with one mole of iodine monochloride gave a monoiodo derivative different from the 7-methoxy-8-iodo-4-methylcoumarin (III). On boiling with 10 % sodium hydroxide solution it gave a coumarilic acid derivative which was found, on direct comparison, to be the same as 6-methoxy-3-methylcoumarilic acid (VIII) obtained on hydrolysis of 7-methoxy-3-bromo-4-methylcoumarin (VII) according to Limaye and Bhide

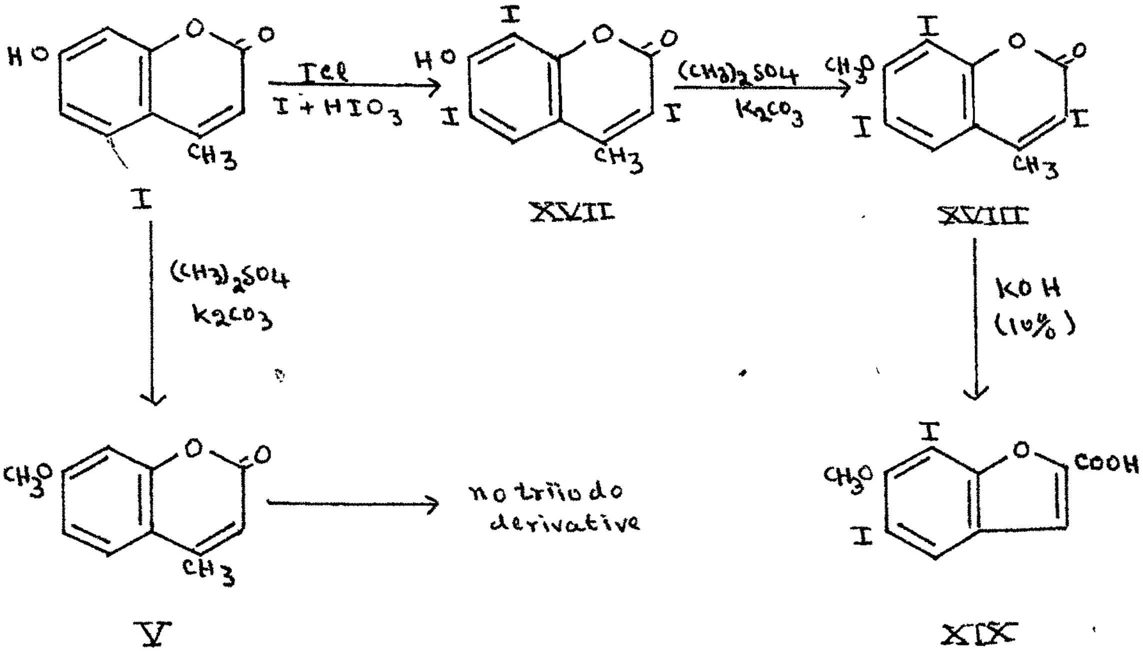


(Rasayanam, 1938, 1, 136); Chem. Abstr., 1939, 33, 1699). The monoiodo product is therefore 7-methoxy-3-iodo-4-methylcoumarin (VI). When 7-methoxy-8-iodo-4-methylcoumarin was heated with concentrated ammonia in a sealed tube the iodine was eliminated and (V) was obtained. No other product was detected.

On iodination of (I) with two moles of iodine monochloride no pure product was obtained. However, on iodination with 4 moles of iodine monochloride it gave two diiodo derivatives. (A) m.p.264° and (B) m.p.249°. The two diiodo derivatives were separated by fractional crystallisations from acetic acid. The product (A) being sparingly soluble came out first. The product (B) was isolated from the filtrate. The methyl ether of (A) gave a monoiodocoumarilic acid derivative on boiling with potassium hydroxide solution indicating that one of the two iodine atoms had entered the 3-position. Further, this methyl ether was found to be the same as the product obtained on further iodination of the 8-iodocoumarin derivative (III) with iodine monochloride. The product (A) is therefore 7-hydroxy-3,8-diiodo-4-methylcoumarin (IX). The methyl ether of product (B) was found to be identical with the product obtained on iodination of (V) with 6 moles of iodine monochloride. This methyl ether also gave a monoiodocoumarilic acid derivative on boiling with 10 % alkali indicating that one of the two iodine atoms had entered the 3-position. It has therefore been assigned the alternate structure : 7-hydroxy-3,6-diiodo-4-methylcoumarin (X).



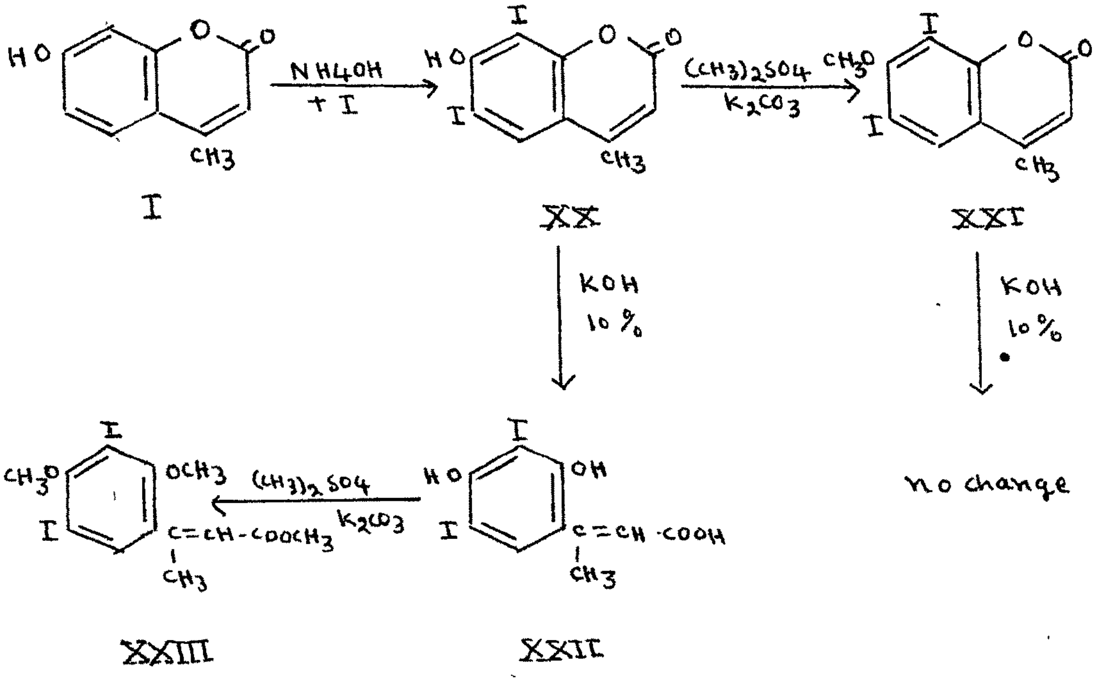
On iodination with excess of iodine monochloride (I) gave a triiodo derivative. The methyl ether of the triiodo derivative on hydrolysis gave a diiodocoumarilic acid which must be 6-methoxy-5,7-diiodo-3-methylcoumarilic acid (XIX). The triiodocoumarin is therefore 7-hydroxy-3,6,8-triiodo-4-methylcoumarin (XVII). 7-Methoxy-4-methylcoumarin did not give any triiodo derivative even with excess of iodine monochloride.



7-Hydroxy-4-methylcoumarin (I) on iodination using molecular proportions of iodine and iodic acid as given in equation (ii) gave a mixture of iodo derivatives from which only the 8-iodo derivative (II) could be isolated in a pure form. When the proportions of iodine and iodic acid were doubled it gave directly the 3,6,8-triiodo derivative (XVII), no diiodo derivative could be isolated. Under similar conditions 7-methoxy-4-methylcoumarin (V) could not be iodinated.

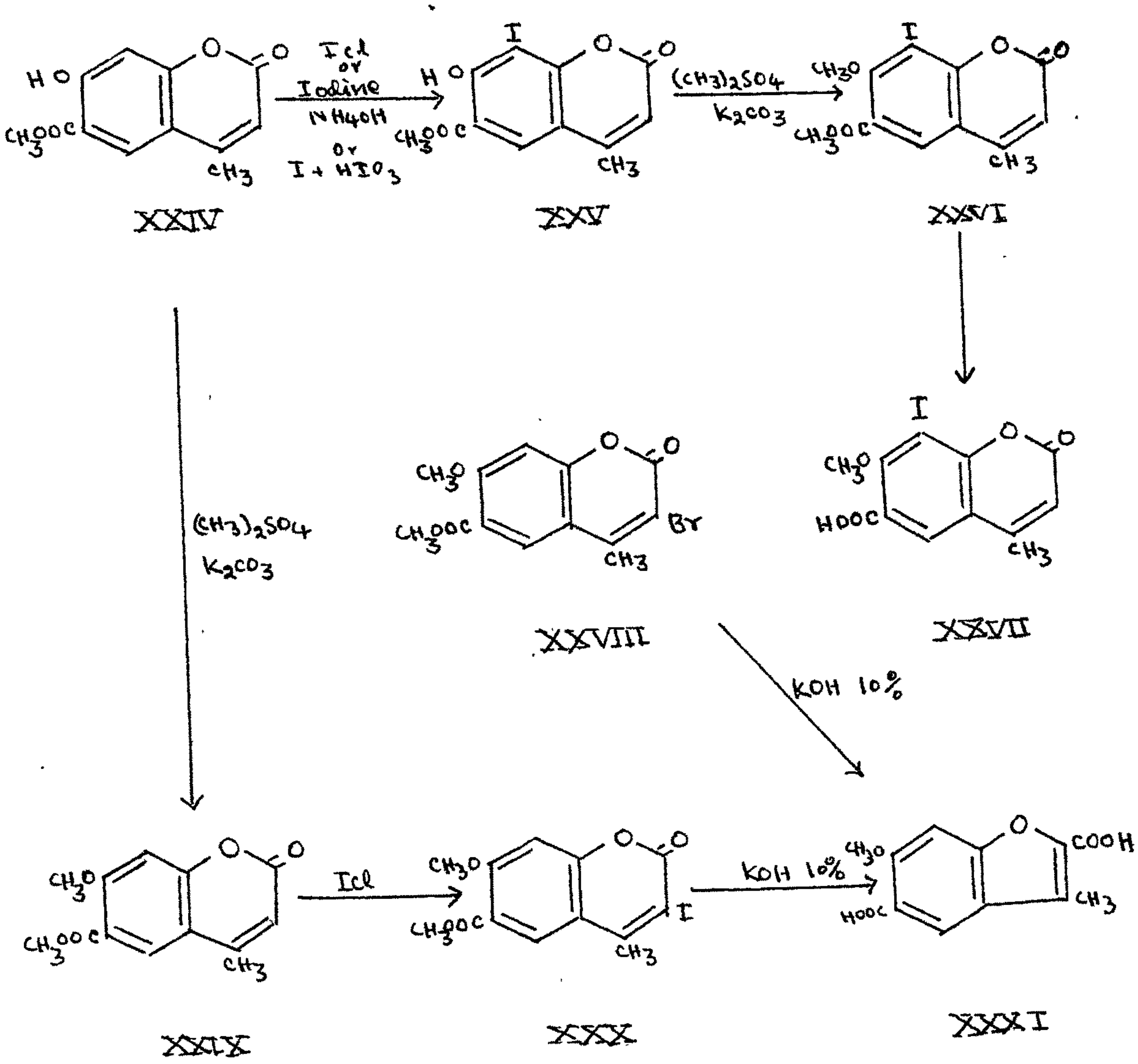
On iodination with one mole of iodine in presence of ammonia 7-hydroxy-4-methylcoumarin (I) gave the 8-iodo derivative (II) described above. With two moles of iodine

(I) gave the diiodo derivative not obtained by the other two methods. The methyl ether of this compound remained unchanged on boiling with alkali indicating that even the second iodine atom had not entered the pyrone ring. Further iodination of this compound using iodine and iodic acid gave the 3,6,8-triiodo derivative (XVII). The diiodo derivative is therefore 7-hydroxy-6,8-diiodo-4-methylcoumarin (XX). On refluxing it with 10 % sodium hydroxide solution the pyrone ring opened up and a diiodo acid was obtained to which the β-methyl-2,4-dihydroxy-3,5-diiodocinnamic acid (XXII) structure has been assigned. Attempts to close the α-pyrone ring again did not succeed as with concentrated or dilute hydrochloric acid iodine was liberated. Its dimethoxy ester (XXIII) has also been prepared. 7-Methoxy-4-methylcoumarin (V) could not be iodinated at all by this method.



2. Iodination of methyl-7-hydroxy-4-methylcoumarin-6-carboxylate and its methyl ether.

Methyl-7-hydroxy-4-methylcoumarin-6-carboxylate (XXIV) on iodination with one mole of iodine monochloride gave a monoiodo derivative in poor yield. The methoxy ester of this compound did not give ~~a~~ an iodine free coumarilic acid derivative on boiling with alkali but instead gave an iodocoumarin carboxylic acid. The iodoester is therefore methyl-7-hydroxy-8-iodo-4-methylcoumarin-6-carboxylate (XXV). The methyl ether of the coumarin ester (XXIX) on iodination with one mole of iodine monochloride gave a monoiodo derivative which ~~is~~ was different from the methyl ether of (XXV) described above. On boiling with 10 % alkali this iodo derivative gave a coumarilic acid derivative which was found, on direct comparison, to be the same as 6-methoxy-3-methyl-5-carboxycoumarilic acid (XXXI) obtained on hydrolysis of methyl-7-methoxy-3-bromo-4-methylcoumarin-6-carboxylate (XXVIII) (Dalvi, and Sethna J. Indian Chem. Soc., 1949, 26, 359). The monoiodo product is therefore methyl-7-methoxy-3-iodo-4-methylcoumarin-6-carboxylate (XXX). The hydroxy ester (XXIV) on iodination with excess of iodine monochloride gave a chloro-iodo derivative which was not investigated further. The methyl ether (XXIX) on iodination with excess of iodine monochloride gave a better yield of the 3-iodo derivative but no diiodo compound could be isolated.

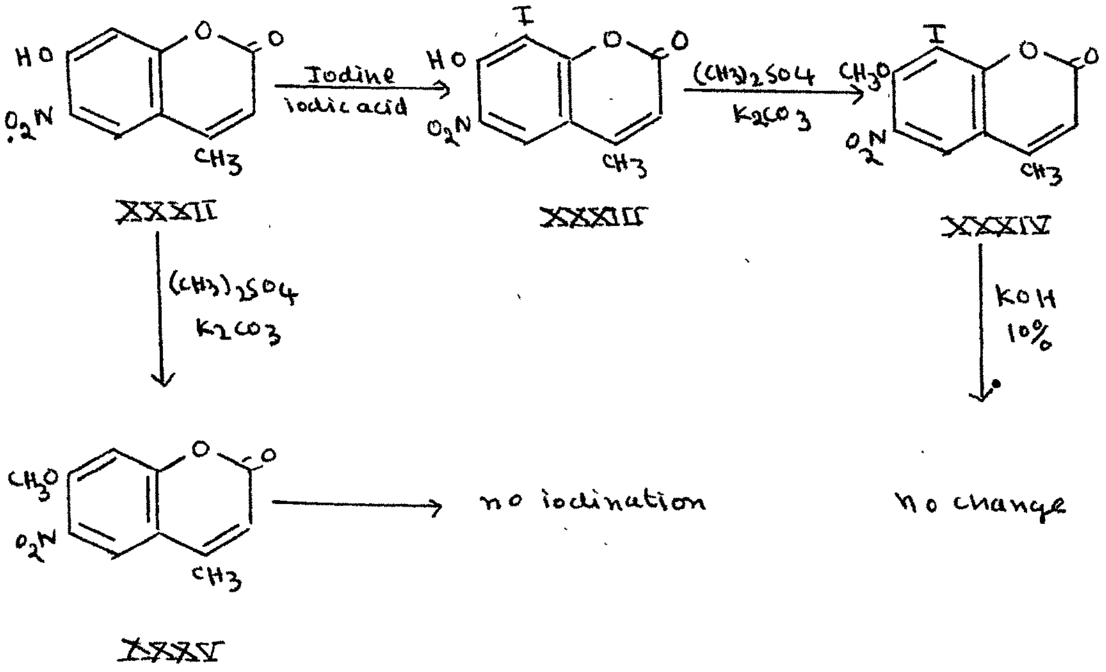


The hydroxy ester (XXIV) on iodination with molecular proportions of iodine and iodic acid as given in equation (II) yielded the 8-iodo derivative (XXV). No further iodination was found possible even with excess of iodine and iodic acid. The methyl ether (XXIX) could not be iodinated at all with iodine and iodic acid.

The hydroxy ester (XXIV) and the corresponding acid on iodination with one mole of iodine in presence of ammonia yielded the corresponding 8-iodo derivatives in excellent yield. No further iodination was possible even with excess of iodine by this method. The methyl ether (XXIX) could not be iodinated at all by this method.

3. <u>Iodination of 7-hydroxy-6-nitro-4-methylcoumarin and its methyl ether</u>.

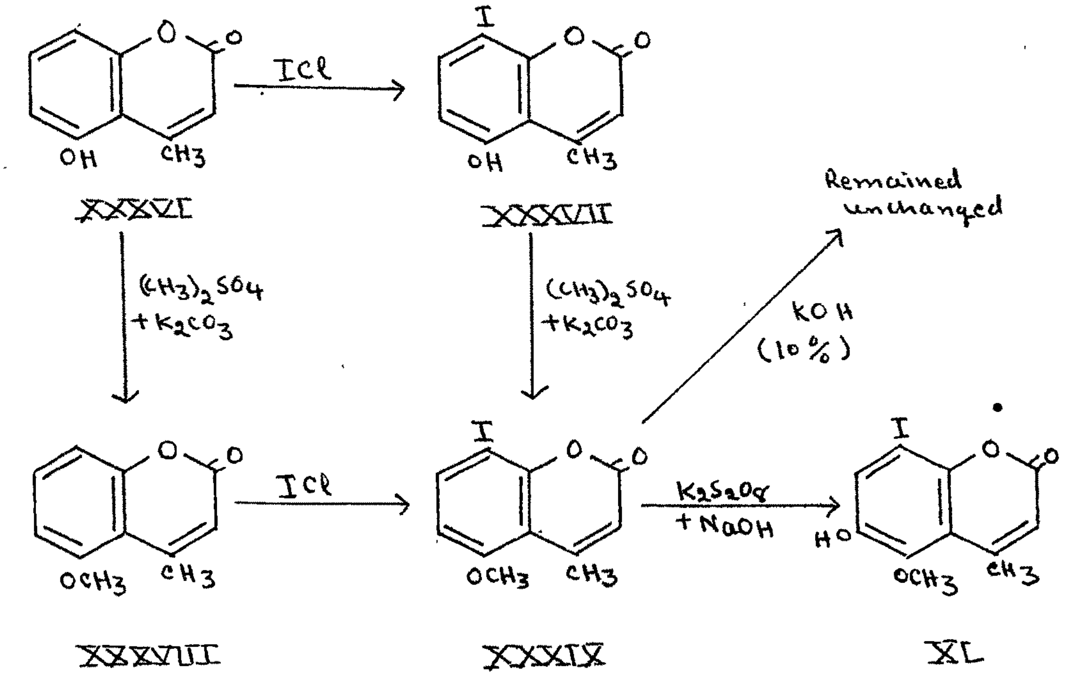
7-Hydroxy-6-nitro-4-methylcoumarin (XXXII) on iodination with one mole of iodine monochloride yielded a chloro-iodo derivative which was not investigated further. 7-Methoxy-6-nitro-4-methylcoumarin (XXXV) could not be iodinated at all by iodine monochloride. On iodination using molecular proportions of iodine and iodic acid as given in equation (ii) (XXXII) yielded a monoiodo derivatice. The methyl ether of this compound did not give any coumarilic acid derivative on heating with alkali.



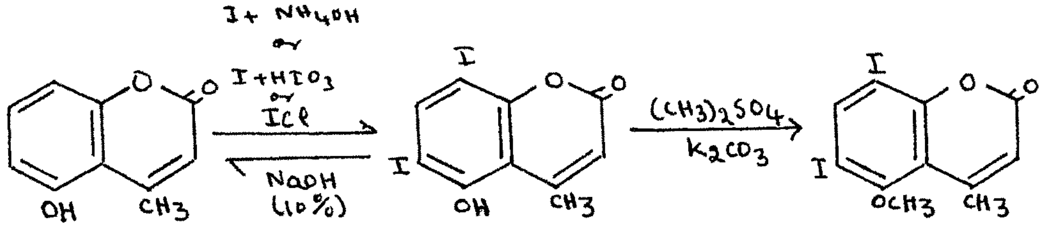
The iodination product must therefore be 7-hydroxy-8-iodo-6-nitro-4-methylcoumarin (XXXIII). The methyl ether (XXXV) could not be iodinated at all by this method. Using iodine in presence of ammonia (XXXII) could not be iodinated as it is insoluble in ammonia solution.

4. Iodination of 5-hydroxy-4-methylcoumarin and its methyl ether.

5-Hydroxy-4-methylcoumarin (XXXVI) obtained according to Sethna and Shah (J. Chem. Soc., 1938, 228), on iodination with one mole of iodine monochloride gave a monoiodo derivative. The methyl ether of this product was found to be identical with the compound obtained on iodination of 5-methoxy-4-methylcoumarin (XXXVIII) with one mole of iodine monochloride. The methyl ether did not give any coumarilic acid derivative on boiling with alkali



which indicated that the iodine atom had not entered the 3-position. Further, on Elbs Persulphate Oxidation it gave an oxidation product in good yield which indicated that the 6-position in the methyl ether was free. 5-Hydroxy-8-iodo-4-methylcoumarin (XXXVII) and 5-methoxy-8-iodo-4-methylcoumarin (XXXIX) structures have therefore been assigned to the iodination products. On iodination with 4 moles of iodine monochloride, (XXXVI) gave only the monoiodo derivative in a better yield. However, with a large excess of iodine monochloride (16 moles) it gave a diiodo derivative. The methyl ether of this did not give any coumarilic acid derivative indicating that even the second iodine atom had not entered the 3-position. The diiodo derivative was therefore assigned the 5-hydroxy-6,8-diiodo-4-methylcoumarin (XLI) structure.

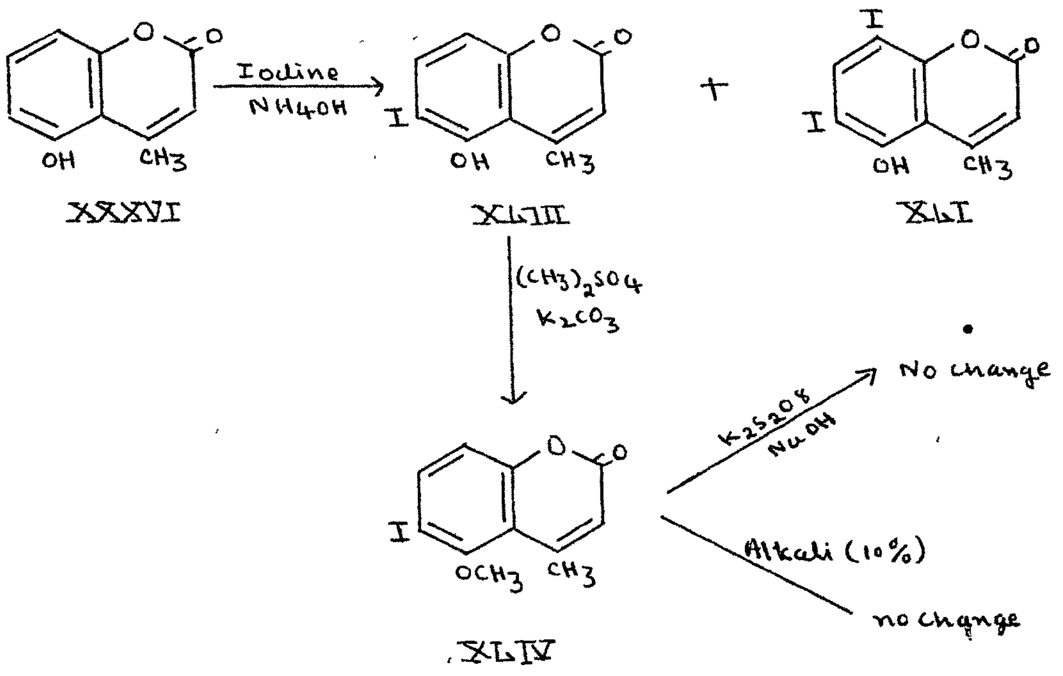


XXXVI XLI XLII

On boiling with 10 % alkali it yielded 5-hydroxy-4-methylcoumarin both the iodine atoms being eliminated. Even with large excess of iodine monochloride (XXXVI) did not give any triiodo derivative. 5-Methoxy-4-methylcoumarin (XXXVIII) did not give the diiodo derivative even with large excess of iodine monochloride.

5-Hydroxy-4-methylcoumarin (XXXVI) on iodination using molecular proportions of iodine and iodic acid as given in equation (ii) gave directly the 6,8-diiodo derivative (XLI). The monoiodo derivative could not be isolated. On iodination with double the quantity of iodine and iodic acid only the 6,8-diiodo product in excellent yield was obtained. No triiodo derivative was obtained with excess of iodine. The diiodo derivative was found to be unstable and on prolonged stirring of the reaction mixture iodine was liberated. 5-Methoxy-4-methylcoumarin could not be iodinated at all under similar conditions.

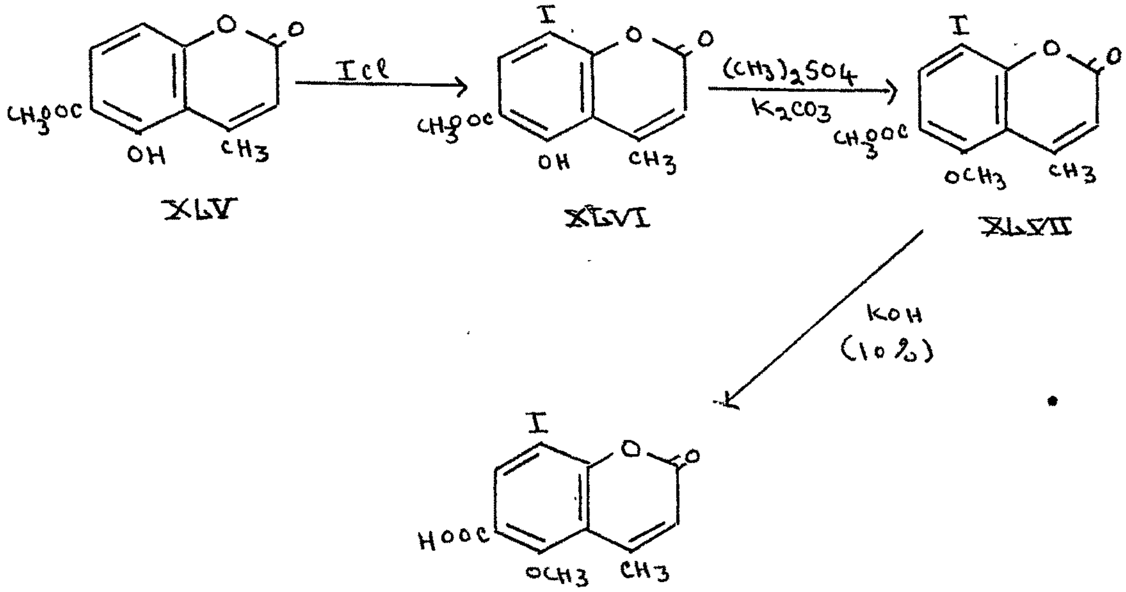
On iodination with one mole of iodine in presence of ammonia (XXXVI) gave a mixture of a monoiodo derivative and a diiodo derivative. The monoiodo derivative was found to be different from 5-hydroxy-8-iodo-4-methylcoumarin



(XXXVII) described earlier. The methyl ether of this compound did not give any coumarilic acid derivative on boiling with alkali nor did it undergo Elbs Persulphate Oxidation. The monoiodo derivative is therefore 5-hydroxy-6-iodo-4-methylcoumarin (XLIII). The diiodo compound was found, on direct comparison, to be the 6,8-diiodo derivative (XLI). This was obtained in excellent yield on iodination with two moles of iodine by this method. No triiodo derivative could be prepared by this method. 5-Methoxy-4-methylcoumarin could not be iodinated at all by this method.

5. <u>Iodination of methyl-5-hydroxy-4-methylcoumarin-6-carboxylate and its methyl ether</u>.

Methyl-5-hydroxy-4-methylcoumarin-6-carboxylate (XLV) on iodination with one mole of iodine monochloride



XLVIII

gave a monoiodo derivative. The methyl ether of this compound did not give any iodine free coumarilic acid derivative on boiling with alkali but gave an iodocoumarin carboxylic acid. The iodination product is therefore methyl-5-hydroxy-8-iodo-4-methylcoumarin-6-carboxylate (XLVI) and the acid is 5-methoxy-8-iodo-4-methylcoumarin-6-carboxylic acid (XLVIII). The 5-hydroxyester (XLV) did not give any higher iodination product with excess of iodine monochloride. The ester (XLV) could not be iodinated by iodine in presence of ammonia as it was insoluble in ammonia solution.

The results obtained in the iodination of coumarins are summarised in the Table I. The products obtained in the bromination of the same coumarins are also given for comparison.

From the results given in Table I it will be seen that whereas the first bromine atom enters the 3-position in the coumarin ring system in the case of the simple and 7-hydroxycoumarins, in the case of iodination simple coumarin did not iodinate at all and the 7-hydroxycoumarins gave the 8-iodo derivatives. In the case of 7-methoxycoumarins the iodine atom enters first the 3-position. In the case of 5-hydroxycoumarin derivatives, however both the bromine and the iodine atoms enter the 8-position.

In this connection the results obtained by other workers and the ideas put forward regarding the reactivity of different positions in the coumarin ring system may be briefly mentioned.

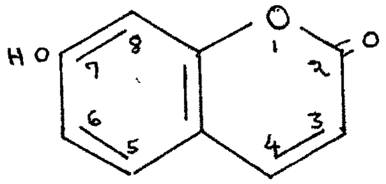
Table I

No.	Substance	Iodinating* agents and their molecular proportions	Product obtained
1.	Coumarin	A, B, C	No iodination
2.	7-Hydroxy-4-methylcoumarin	A (1 : 1)	8-Iodo-
		B (5 : 2 : 1)	"
		C (1 : 1)	"
		A (1 : 4)	3,8-Diiodo- 3,6-Diiodo-
		A (1 : 16)	3,6,8-Triiodo-
		B (5 : 4 : 2)	"
		C (1 : 2)	6,8-Diiodo-
3.	7-Methoxy-4-methylcoumarin	A (1 : 1)	3-Iodo-
		A (1 : 6)	3,6-Diiodo-
4.	7-Hydroxy-4-methylcoumarin-6-carboxylic acid	C (1 : 1)	8-Iodo-
5.	Methyl-7-hydroxy-4-methylcoumarin-6-carboxylate	A (1 : 1)	8-Iodo-
		B (5 : 2 : 1)	"
		C (1 : 1)	"
6.	Methyl-7-methoxy-4-methylcoumarin-6-carboxylate	A (1 : 1)	3-Iodo-
7.	7-Hydroxy-6-nitro-4-methylcoumarin	B (5 : 2 : 1)	8-Iodo-

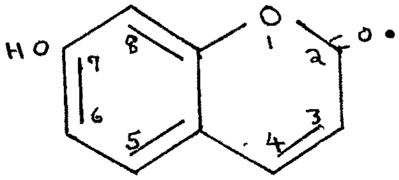
Yield %	Bromo ** derivative	References for brominations of coumarins
-	3-Bromo-	Perkin (J.Chem.Soc., 1870,23, 368 ; 1871, 24, 37)
	6-Bromo-	Read and Reid (J.Chem.Soc., 1928, 745)
25	3-Bromo-	Dalvi and Sethna (J.Indian chem. Soc., 1949, 26, 359, 467)
40		
82		
22	3,8-Dibromo-	"
40	3,6-Dibromo-	"
36	3,6,8-Tribromo-	"
59		
66		
42	3-Bromo-	Limaye and Bhide (Rasayanam, 1938, 1, 136)
75	3,6-Dibromo-	Dalvi and Sethna (J. Indian Chem. Soc., 1949, 26, 359, 467)
66	3-Bromo-	"
13	3-Bromo-	"
53	3,8-Dibromo-	"
76		
66	3-Bromo-	"
62	-	

8.	5-Hydroxy-4-methylcoumarin	A (1 : 1)	8-Iodo-	38	8-Bromo-
		A (1 : 8)	6,8-Diiodo-	42	6,8-Dibromo-
		B (5 : 2 ; 1)	"	68	
		C (1 : 2)	"	73	
		C (1 : 1)	6-Iodo-	30	
					3,6,8-Tribromo-
9.	5-Methoxy-4-methylcoumarin	A (1 : 1)	8-Iodo-	42	8-Bromo-
					3,8-Dibromo-
					3,6,8-Tribromo-
10.	Methyl-5-hydroxy-4-methylcoumarin-6-carboxylate	A (1 : 1)	8-Iodo-	21	8-Bromo-
		B (5 : 2 : 1)	"	48	
11.	Methyl-5-methoxy-4-methylcoumarin-6-carboxylate	A (1 : 1)	8-Iodo-	54	-

Rangaswami and Seshadri (Proc. Ind. Acad. Sci., 1941, 14A, 547) have attempted to explain the reactivity of the 7-hydroxycoumarin derivatives on the theory of the fixation of the double bond (Mills and Nixon, J. Chem. Soc. 1930, 2510), and have discussed at length the fixation of the aromatic double bonds in the coumarin ring system. They state that though in coumarin itself substitution invariably takes place in the 6-position, in the 7-hydroxycoumarin it is exclusively in the 8-position. When attempts are made to build up fresh ring starting with 7-hydroxycoumarins, it is the 8-position that is involved in the ring formation. Thus, employing 7-hydroxycoumarin and bromoacetal Spath and Pailer (Ber., 1934, 67, 1212) obtained the angular compound, angelicin. Rangaswami and Seshadri (Porc. Indian Acad.Sci., 1937, 6A, 112) similarly found that the Pechmann condensation between 7-hydroxycoumarins and malic acid or acetoacetic ester gave mostly the angular coumarino-a-pyrones. Again attempts to introduce a formyl group into 7-hydroxycoumarins gave the 8-formylcoumarins. All these show that 7-hydroxycoumarins react in the form (A).



A



B

The most reliable evidence for this structure however comes from the work of Baker and Lothian (J. Chem.

Soc., 1935, 628, 1936, 275) who found that 7-allyloxy-4-methylcoumarin undergoes Claisen transormation to 7-hydroxy-8-allyl-4-methylcoumarin thus proving conclusively that there exists a double bond between the 7 and 8 positions.

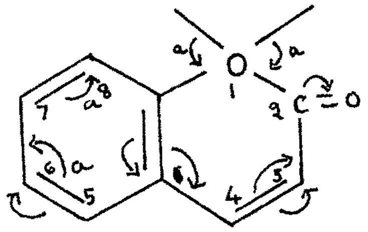
Evidence which does not fall into line with the above was first obtained by Limaye (Limaye and Gangal, Rasayanam, 1936, 15). He found that when 7-acetoxy-4-methylcoumarin was subjected to Fries migration, the 8-acetyl-7-hydroxy compound was the major product but it was accompanied by a small quantity of the 6-acetylisomer. The simultaneous formation of the angular coumarino-α-pyrone and the linear isomer from the Pechmann condensation using 7-hydroxycoumarin and malic acid (Rangaswami and Seshadri, Proc. Indian Acad. Sci., 1937, 6A, 112) corroborates the above observation and shows the slight but significant reactivity of the 6-position in this compound. These authors applied Fieser's technique to the coumarin ring system and obtained unequivocal evidence on the distribution of the single and double bonds. They found that 7-hydroxy-4,8-dimethylcoumarin coupled with diazotised p-nitraniline and formed with mercuric acetate a mercury derivative which contained 2-acetoxymercuri groups replacable by bromine atoms. The allyl ether and the acetyl derivative also smoothly underwent the Claisen transformation and Fries migration respectively. In structure (A) the carbon atom 7 which carries the hydroxyl group is attached by means of a double bond to the carbon atom 8. Therefore, the position 8 will be more reactive than the position 6. In structure (B) for the same reason the position 6 will be more reactive than the position 8. All these reactions can be explained only on the assumption of a reactive 6-position which is possible only if the bonds can take up positions as depicted in structure (B). Thus in coumarins while the normal structure corresponds to (A) the other is not precluded. Thus the fixation theory does not satisfactorily account for all the recorded observations, if this fixation is taken to be rigid.

The theory of resonance (Pauling and Sherman, J. Chem. Phys., 1933, 1, 605 ; Pauling, Brockway and Beach, J. Am. Chem. Soc., 1935, 57, 2705) seems to eliminate this difficulty. According to this theory, the actual structure of coumarin can neither be (A) nor (B), but some intermediate between the two. If (A) is of materially lower energy than (B), the actual structure will resemble more closely to the structure of the lower energy (A). Since the structure with a double bond common to both the rings possesses lower energy (due to less distortion of valency bonds) the actual structure will resemble more ~~to~~ the structure (A) and hence the reactivity will be manifested according to the structure (A) and the 6-position will be less reactive than the 8-position.

An obvious exception to the above is the bromination of coumarin, which is found to occur in many cases in the 3-position of the coumarin nucleus as already stated. Perkin

(J. Chem. Soc., 1870, 23, 368 ; 1871, 24, 37) suggested that bromination of coumarin is essentially an addition reaction. It produces the 3,4-dibromo product, which then loses hydrobromic acid, giving 3-bromocoumarin. In some cases however, this is not the case and the first bromine atom enters the benzene ring.

Thakor and Shah (J. Univ. Bombay, 1947, 16, 38 ; C.A., 1948, 42, 4171) gave the explanation of the reactivity of various positions and also the influence of various substituents in the coumarin ring in terms of the electron theory. According to them, in coumarin there are several systems at work simultaneously : the anionoid O at 1 ; the cationoid C : O at 2 and the system of conjugated double bonds, which helps electron drifts considerably. The O of C : O, being cationoid, will cause electron displacement toward itself from the anionoid O at 1 and from position 3, which having a double bond, is anionoid. Consequently, the reactivity of C : O will be nullified, while both the O (at 1) and the double bond between 3 and 4 partly lo~~o~~se their anionoid character. The O at 1, being anionoid, will cause electron drifts as shown by the arrows marked (a) in the figure. Thus positions 6 and 8 will be the most reactive, with position 6 the more reactive



because position 8 is closer to the O at 1. In hydroxycoumarins the O of the OH exerts a dominating influence. In 8-hydroxycoumarin, the anionoid O causes electron displacement and renders position 7 reactive, position 5 also becomes reactive, while the reactivity of position 6 is subdued. In 7-hydroxycoumarins the 8 position is made most reactive, while position 6 will also show some reactivity. In 5-hydroxy-4-methylcoumarin the OH increases the reactivity of both the 6, and 8-positions. Masking of the OH group by methylation, acetylation etc., makes the production of a para isomer predominant. Groups like Me, NH_2, OH etc., by exerting a negative inductive effect, increase the electron availability in all parts of the molecule. Such groups increase the speed of substitution. Groups such as NO_2, CN, COOH etc., which exert a positive inductive effect, decrease the electron availability of the molecule making substitution more difficult.

From the foregoing discussion it will be clear that there is no single factor which determines the position of the incoming group but it is governed by several factors : the influence of the double bond, the ortho and para directing influence of the hydroxyl groups and the steric effect of the groups present.

EXPERIMENTAL

Iodination of 7-hydroxy-4-methylcoumarin with (a) one mole of iodine monochloride (b) molecular proportions of iodine and iodic acid as given in equation (ii) (c) one mole of iodine and ammonia : 7-Hydroxy-8-iodo-4-methylcoumarin.

(a) A mixture of 7-hydroxy-4-methylcoumarin (1.76 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 overnight in a well stoppered flask at 60° in an oven. Next day it was stirred vigorously for 2 hours and the separated solid filtered and washed with water. It crystallised from acetic acid in needles, m.p. 268°. Yield 0.75 g.

Analysis :

17.974 mg. of the substance gave 13.936 mg. of AgI.

Found : I = 41.91 %.

$C_{10}H_7O_3I$ requires : I = 42.06 %.

(b) 7-Hydroxy-4-methylcoumarin (4.4 g.) was dissolved in warm alcohol (60 ml.) and iodine crystals (2.54 g.) were added. To this clear warm solution, iodic acid (0.88 g.) dissolved in water (2 ml.) was added and the mixture stirred for 2 hours and left overnight. Next day the precipitated solid was filtered and dried. The crude mixture was boiled for 20 minutes with toluene (50 ml.) and filtered. The insoluble residue was crystallised from acetic acid when the above product was obtained. Yield 3.0 g. No other pure product could be isolated.

(c) A mixture of 7-hydroxy-4-methylcoumarin (1.76 g. ; 0.01 mole) in ammonia (10 ml.) and water (30 ml.) was treated drop-wise with iodine (2.54 g. ; 0.01 mole) in potassium iodide (5 g.) solution while the mixture was stirred vigorously. It was then poured in cold dilute sulphuric acid. The separated solid was filtered, washed with water and crystallised from acetic acid when the above iodocoumarin was obtained. Yield 2.5 g.

7-Methoxy-8-iodo-4-methylcoumarin.

The above iodocoumarin (0.5 g.) in acetone (50 ml.) was refluxed with dimethyl sulphate (0.5 ml.) and anhydrous potassium carbonate (1 g.) for 8 hours. The potassium carbonate was filtered and the acetone removed. The residue obtained was washed with dilute sodium hydroxide solution (4 %) to remove the original coumarin and crystallised from rectified spirit in needles, m.p.199°.

Analysis :

3.64 mg. of the substance gave 5.582 mg. of carbon dioxide and 0.876 mg. of water.

16.69 mg. of the same substance gave 12.492 mg. of silver iodide.

Found : C = 41.85 % ; H = 2.69 % ; I = 40.46 %.

$C_{11}H_9O_3I$ requires : C = 41.77 % ; H = 2.84 % ; I = 40.19 %.

The methyl ether on refluxing with alcoholic potassium hydroxide solution (10 %) remained unchanged. On heating it with liquor ammonia in a sealed tube iodine was eliminated and 7-methoxy-4-methylcoumarin was obtained.

Elbs Persulphate Oxidation of 7-methoxy-8-iodo-4-methylcoumarin : 6-Hydroxy-7-methoxy-8-iodo-4-methylcoumarin.

7-Methoxy-8-iodo-4-methylcoumarin (1 g.) was dissolved in sodium hydroxide solution (10 % ; 40 ml.) by warming on a steam bath. The solution was then cooled and potassium persulphate (0.9 g. in 40 ml. water) was added gradually from a separating funnel during two hours. The solution was mechanically stirred and the temperature was not allowed to rise above 10°. The reaction mixture was then kept overnight. The next day it was acidified with concentrated hydrochloric acid till it was just acidic when the original substance (0.1 g.) was obtained. This was filtered and the filtrate extracted twice with ether. The aqueous layer was then heated on a boiling water bath with concentrated hydrochloric acid (25 ml.) for about an hour. The product which separated on cooling crystallised from acetic acid in plates, m.p. 234°. Yield 0.2 g.

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

Analysis :

3.238 mg. of the substance gave 4.772 mg. of carbon dioxide and 0.776 mg. of water.

11.704 mg. of the same substance gave 8.234 mg. of silver iodide.

Found : C = 40.22 % ; H = 2.68 % ; I = 38.03 %.
$C_{11}H_9O_4I$ requires : C = 39.77 % ; H = 2.70 % ; I = 38.30 %.

Iodination of 7-methoxy-4-methylcoumarin with one mole of iodine monochloride : 7-Methoxy-3-iodo-4-methylcoumarin.

7-Methoxy-4-methylcoumarin (1.90 g. ; 0.01 mole) in acetic acid (25 ml.) was treated with iodine monochloride (1.62 g. ; 0.01 mole) and the mixture kept at 60° overnight. The next day it was stirred vigorously for 2 hours and the separated product filtered and washed with acetic acid. It crystallised from acetic acid in needles, m.p.162°. Yield 1.3 g.

Analysis :

7.568 mg. of the substance gave 5.580 mg. of silver iodide.

Found : I = 39.85 %.
$C_{11}H_9O_3I$ requires : I = 39.85 %.

6-Methoxy-3-methylcoumarilic acid.

The above iodocoumarin (0.5 g.) was refluxed with alcoholic potassium hydroxide solution (10 % ; 20 ml.) for 2 hours on a steam bath. The product which separated on acidification was purified through sodium bicarbonate solution. It crystallised from acetic acid, m.p.186° (effer.). Mixed melting point with the product obtained on hydrolysis of 7-methoxy-3-bromo-4-methylcoumarin according to Limaye and Bhide (loc.cit.) was not depressed.

Iodination of 7-hydroxy-4-methylcoumarin with 4 moles of iodine monochloride : 7-Hydroxy-3,8-diiodo- and 7-hydroxy-3,6-diiodo-4-methylcoumarin.

(i) 7-Hydroxy-3,8-diiodo-4-methylcoumarin :

7-Hydroxy-4-methylcoumarin (3.5 g. ; 0.02 mole) in acetic acid (25 ml.) and hydrochloric acid (40 ml.) was treated with iodine monochloride (12.80 g. ; 0.08 mole) and the reaction mixture was kept for 48 hours at 60°. ~~The next day~~ It was then stirred vigorously for 2 hours and the separated solid filtered and washed with more of acetic acid. It was then dissolved completely in glacial acetic acid and kept in a refrigerator overnight. The separated solid was filtered and recrystallised from acetic acid in needles, m.p. 264°. Yield 1.9 g.

The filtrate was treated as described under (ii) later.

Analysis :

12.604 mg. of the substance gave 13.70 mg. of silver iodide.

Found : I = 58.76 %.

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

7-Methoxy-3,8-diiodo-4-methylcoumarin.

The above diiodocoumarin was methylated by refluxing its acetone solution with dimethyl sulphate in presence of anhydrous potassium carbonate as before. M.p. 262°.

Analysis :

5.921 mg. of the substance gave 6.405 mg. of carbon dioxide and 1.143 mg. of water.

20.168 mg. of the same substance gave 21.65 mg. of silver iodide.

Found : C = 29.52 % ; H = 2.16 % ; I = 58.03 %.

$C_{11}H_8O_3I_2$ requires : C = 29.86 % ; H = 1.81 % ; I = 57.46 %.

The same product was obtained when 7-methoxy-8-iodo-4-methylcoumarin (0.63 g.) in acetic acid (40 ml.) was treated with iodine monochloride (0.32 g.).

6-Methoxy-7-iodo-3-methylcoumarilic acid.

7-Methoxy-3,8-diiodo-4-methylcoumarin (0.5 g.) was refluxed with alcoholic potassium hydroxide solution (10 % ; 40 ml.) for 2 hours.The product obtained on acidification was purified through sodium bicarbonate solution. It crystallised from acetic acid in needles,m.p. 222° (effer.).

Analysis :

5.762 mg. of the substance gave 8.471 mg. of carbon dioxide and 1.606 mg. of water.

14.122 mg. of the same substance gave 10.008 mg. of silver iodide.

Found : C = 40.11 % ; H = 3.12 % ; I = 38.31 %.

$C_{11}H_9O_4I$ requires : C = 39.70 % ; H = 2.70 % ; I = 38.30 %.

The methyl ester. Prepared by refluxing the above coumarilic acid (0.3 g.) in methyl alcohol (25 ml.) with concentrated sulphuric acid (5 ml.) on a steam bath for 8 hours was crystallised from dilute alcohol in colourless needles, m.p. 180°.

Analysis :

6.082 mg. of the substance gave 9.298 mg. of carbon dioxide and 1.914 mg. of water.

10.300 mg. of the same substance gave 7.018 mg. of silver iodide.

Found :C = 41.72 % ; H = 3.52 % ; I = 36.83 %.

$C_{12}H_{11}O_4I$ requires:C = 41.62 % ; H = 3.18 % ; I = 36.70 %.

(ii) 7-Hydroxy-3,6-diiodo-4-methylcoumarin.

Filtrate from (i) (p.65) was diluted with water when a product separated. It crystallised from acetic acid in colourless needles,m.p.249°. Yield 3.4 g.

Analysis :

13.176 mg. of the substance gave 14.412 mg. of silver iodide.

Found : I = 59.12 %.

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

7-Methoxy-3,6-diiodo-4-methylcoumarin.

The methyl ether of the diiodocoumarin was prepared by refluxing its acetone solution with dimethyl sulphate in the presence of anhydrous potassium carbonate. The methyl ether crystallised from rectified spirit in needles,m.p.248°.

Analysis :

7.820 mg. of the substance gave 8.545 mg. of carbon dioxide and 1.608 mg. of water.

13.672 mg. of the same substance gave 14.504 mg. of silver iodide.

Found : C = 29.82 % ; H = 2.30 % ; I = 57.34 %.

$C_{11}H_8O_3I_2$ requires :C = 29.86 % ; H = 1.81 % ; I = 57.46 %.

The same product was obtained when 7-methoxy-4-methylcoumarin (1.9 g. ; 0.01 mole) in glacial acetic acid (30 ml.) was treated with iodine monochloride (9.6 g. ; 0.06 mole). Yield 3.2 g.

6-Methoxy-5-iodo-3-methylcoumarilic acid.

7-Methoxy-3,6-diiodo-4-methylcoumarin (0.5 g.) was refluxed with alcoholic potassium hydroxide solution (10 % ; 40 ml.) for 2 hours. The product obtained on acidification was purified through sodium bicarbonate washings. It crystallised from dilute acetic acid in colourless needles, m.p. 218° (effer.). It gave a violet colour with sulphuric acid.

Analysis :

8.414 mg. of the substance gave 12.27 mg. of carbon dioxide and 2.07 mg. of water.

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

Found : C = 39.81 % ; H = 2.75 % ; I = 38.01 %.

$C_{11}H_9O_4I$ requires : C = 39.77 % ; H = 2.70 % ; I = 38.30 %.

The methyl ester. Prepared by refluxing the above coumarilic acid (0.3 g.) in methyl alcohol (25 ml.) with concentrated sulphuric acid (5 ml.) on a steam bath for 8 hours was crystallised from petroleum ether (60-80°) in needles, m.p.160°.

Analysis :

5.428 mg. of the substance gave 8.352 mg. of carbon dioxide and 1.320 mg. of water.

10.138 mg. of the same substance gave 6.904 mg. of silver iodide.

Found : C = 41.99 % ; H = 2.72 % ; I = 36.81 %.

$C_{12}H_{11}O_4I$ requires : C = 41.62 % ; H = 3.18 % ; I = 36.70 %.

Iodination of 7-hydroxy-4-methylcoumarin with two moles of iodine in presence of ammonia : 7-Hydroxy-6,8-diiodo-4-methylcoumarin.

7-Hydroxy-4-methylcoumarin (1.76 g. ; 0.01 mole) in liquor ammonia (10 ml.) and water (30 ml.) was treated drop-wise with iodine (5.08 g. ; 0.02 mole) in potassium iodide (10 g.) solution with vigorous stirring of the reaction mixture. The separated ammonium salt was filtered. On crystallisation from acetic acid,needles,m.p.230° of the hydroxydiiodo coumarin were obtained. Yield 2.8 g.

Analysis :

10.112 mg. of the substance gave 11.20 mg. of silver iodide.

Found : I = 59.87 %.

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

β-Methyl-2,4-dihydroxy-3,5-diiodocinnamic acid.

The above diiodo coumarin (1 g.) was refluxed with alcoholic potassium hydroxide solution (10 % ; 50 ml.) for

2 hours. The product obtained on acidification with concentrated hydrochloric acid crystallised from glacial acetic acid in needles,m.p.242° (effer.). Attempts to cyclize it to the original coumarin did not succeed as on boiling with concentrated hydrochloric acid iodine was liberated.

Analysis :

5.676 mg. of the substance gave 5.644 mg. of carbon dioxide and 0.700 mg. of water.

10.116 mg. of the same substance gave 10.662 mg. of silver iodide.

Found : C = 27.13 % ; H = 1.38 % ; I = 56.97 %.

$C_{10}H_8O_4I_2$ requires : C = 26.90 % ; H = 1.79 % ; I = 56.95 %.

Methyl-β-methyl-2,4-dimethoxy-3,5-diiodocinnamate.

Simultaneous methylation and esterification of the above acid was carried out by refluxing its acetone solution with excess of dimethyl sulphate in presence of anhydrous potassium carbonate. It crystallised from rectified spirit in needles,m.p.169°. It decolourised dilute potassium permanganate solution and bromine in acetic acid.

Analysis :

8.782 mg. of the substance gave 10.26 mg. of carbon dioxide and 2.504 mg. of water.

9.350 mg. of the same substance gave 8.93 mg. of silver iodide.

Found : C = 31.89 % ; H = 3.19 % ; I = 51.63 %.

$C_{13}H_{14}O_4I_2$ requires : C = 31.96 % ; H = 2.86 % ; I = 52.04 %.

7-Metho~~d~~xy-6,8-diiodo-4-methylcoumarin.

The methyl ether of the 7-hydroxy-6,8-diiodo-4-methylcoumarin was prepared by refluxing its acetone solution with dimethyl sulphate in presence of anhydrous potassium carbonate as before. It crystallised from rectified spirit in needles, m.p. 212°.

Analysis :

6.529 mg. of the substance gave 7.159 mg. of carbon dioxide and 1.103 mg. of water.

14.940 mg. of the same substance gave 15.802 mg. of silver iodide.

Found : C = 29.92 % ; H = 1.89 % ; I = 57.18 %.
$C_{11}H_8O_3I_2$ requires : C = 29.86 % ; H = 1.81 % ; I = 57.46 %.

It remained unchanged on boiling with alcoholic potassium hydroxide solution (10 %).

Iodination of 7-hydroxy-4-methylcoumarin with excess of iodine monochloride : 7-Hydroxy-3,6,8-triiodo-4-methylcoumarin.

A mixture of 7-hydroxy-4-methylcoumarin (1.76 g. ; 0.01 mole) in acetic acid (30 ml.) and hydrochloric acid (30 ml.) was treated with iodine monochloride (9.6 g. ; 0.16 mole) and the reaction mixture left overnight at 60°. The separated solid was filtered and washed with more of acetic acid. It crystallised from acetic acid in needles, m.p. 254°. Yield 2.0 g.

Analysis :

15.576 mg. of the substance gave 19.794 mg. of silver iodide.

Found : I = 68.69 %.

$C_{10}H_5O_3I_3$ requires : I = 68.77 %.

The same product was obtained when 7-hydroxy-4-methylcoumarin (4.4 g.) in warm alcohol (100 ml.) was treated with iodine (5.08 g.) and iodic acid (1.76 g. in 5 ml. water). Yield 8.2 g.

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

The above triiodocoumarin was methylated by refluxing its acetone solution with dimethyl sulphate in presence of anhydrous potassium carbonate as before. It crystallised from rectified spirit in needles, m.p. 217°.

Analysis :

5.891 mg. of the substance gave 4.982 mg. of carbon dioxide and 0.537 mg. of water.

11.56 mg. of the same substance gave 14.43 mg. of silver iodide.

Found : C = 23.08 % ; H = 1.02 % ; I = 67.48 %.

$C_{11}H_7O_3I_3$ requires : C = 23.25 % ; H = 1.23 % ; I = 67.08 %.

6-Methoxy-5,7-diiodo-3-methylcoumarilic acid.

7-Methoxy-3,6,8-triiodo-4-methylcoumarin (1 g.) was refluxed with alcoholic potassium hydroxide solution (10 % in 50 % alcohol) for 2 hours. The solution was diluted with water and acidified. The separated product was purified through sodium bicarbonate solution. It crystallised from glacial acetic acid in colourless needles, m.p. 270° (effer.).

Analysis :

7.038 mg. of the substance gave 7.416 mg. of carbon dioxide and 1.16 mg. of water.

6.624 mg. of the substance gave 6.851 mg. of silver iodide.

Found : C = 28.76 % ; H = 1.84 % ; I = 55.91 %.

$C_{11}H_8O_4I_2$ requires : C = 28.82 % ; H = 1.74 % ; I = 55.46 %.

The methyl ester. Prepared by refluxing the above coumarilic acid (0.3 g.) in methyl alcohol (25 ml.) with concentrated sulphuric acid (5 ml.) on a steam bath for 8 hours was crystallised from dilute alcohol in colourless needles, m.p. 160°.

Analysis :

5.126 mg. of the substance gave 5.672 mg. of carbon dioxide and 1.197 mg. of water.

9.727 mg. of the same substance gave 9.679 mg. of silver iodide.

Found : C = 30.20 % ; H = 2.61 % ; I = 53.79 %.

$C_{12}H_{10}O_4I_2$ requires : C = 30.52 % ; H = 2.12 % ; I = 53.81 %.

Iodination of (a) 7-hydroxy-4-methylcoumarin-6-carboxylic acid and (b) its methyl ester with one mole of iodine in presence of ammonia.

(a) 7-Hydroxy-8-iodo-4-methylcoumarin-6-carboxylic acid.

A suspension of 7-hydroxy-4-methylcoumarin-6-carboxylic acid (2.2 g. ; 0.01 mole) in ammonia (50 ml.)

was treated with iodine (2.54 g. ; 0.01 mole) in potassium iodide (5 g.) and the mixture well stirred till a clear solution was obtained. The mixture was then poured over cold dilute sulphuric acid. The separated product crystallised from acetic acid, m.p. 237° (effer.).

Analysis :

10.798 mg. of the substance gave 7.323 mg. of silver iodide.

Found : I = 36.67 %.

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

(b) Methyl-7-hydroxy-8-iodo-4-methylcoumarin-6-carboxylate.

A mixture of methyl-7-hydroxy-4-methylcoumarin-6-carboxylate (2.34 g. ; 0.01 mole) in ammonia (20 ml.) and water (200 ml.) was treated with iodine (2.54 g. ; 0.01 mole) in potassium iodide (5 g.) solution and the mixture stirred for half an hour. The product obtained on pouring the mixture over dilute cold sulphuric acid crystallised from large volumes of acetic acid in needles, m.p. 285°. Yield 2.8 g.

Analysis :

8.818 mg. of the substance gave 5.712 mg. of silver iodide.

Found : I = 35.02 %.

$C_{12}H_9O_5I$ requires : I = 35.28 %.

The same product was obtained when methyl-7-hydroxy-4-methylcoumarin-6-carboxylate (1.17 g.) in alcohol (100 ml.) was treated with iodine (0.508 g.) and iodic acid (0.176 g.). Yield 0.95 g.

The same product was also obtained when the ester (0.83 g.) in acetic acid (60 ml.) was treated with iodine monochloride (2.3 g.) and the mixture left at 60-70° for 24 hours. Yield 0.2 g.

Methyl-7-methoxy-8-iodo-4-methylcoumarin-6-carboxylate.

The methyl ether of the above iodo-ester was prepared by refluxing its acetone solution with dimethyl sulphate in presence of anhydrous potassium carbonate. It crystallised from rectified spirit in needles,m.p.223°.

Analysis :

10.22 mg. of the substance gave 15.60 mg. of carbon dioxide and 2.62 mg. of water.

9.516 mg. of the same substance gave 5.964 mg. of silver iodide.

Found : C = ~~3~~41.65 % ; H = 2.87 % ; I = 33.88 %.
$C_{13}H_{11}O_5I$ requires : C = 41.71 % ; H = 2.94 % ; I = 33.90 %.

7-Methoxy-8-iodo-4-methylcoumarin-6-carboxylic acid.

The above methoxy ester (0.5 g.) was heated on a steam bath for 2 hours with alcoholic potassium hydroxide solution (10 % ; 40 ml.). The mixture was then cooled, diluted with water and acidified. The separated product was purified through sodium bicarbonate solution. It crystallised from dilute acetic acid in needles,m.p.237° (effer.).

Analysis :

10.34 mg. of the substance gave 15.30 mg. of carbon dioxide and 2.24 mg. of water.

10.812 mg. of the same substance gave 7.030 mg. of silver iodide.

Found : C = 40.38 % ; H = 2.42 % ; I = 35.15 %.

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

Iodination of methyl-7-methoxy-4-methylcoumarin-6-carboxylate with one mole of iodine monochloride : Methyl-7-methoxy-3-iodo-4-methylcoumarin-6-carboxylate.

Methyl-7-methoxy-4-methylcoumarin-6-carboxylate (2.48 g. ; 0.01 mole) in acetic acid (30 ml.) was treated with iodine monochloride (1.62 g. ; 0.01 mole) and the mixture kept at 60° overnight. The next day the separated product was filtered and washed with acetic acid. It crystallised from acetic acid in silky colourless needles, m.p.234°. Yield 2.5 g.

Analysis :

9.62 mg. of the substance gave 6.07 mg. of silver iodide.

Found : I = 34.1 %.

$C_{13}H_{11}O_5I$ requires : I = 33.9 %.

6-Methoxy-5-carboxy-3-methylcoumarilic acid.

The above iodocoumarin (0.5 g.) was refluxed with alcoholic potassium hydroxide solution (10 % ; 20 ml.) for 2 hours on a steam bath. The product which separated on acidification was purified through sodium bicarbonate solution. It crystallised from acetic acid in needles, m.p. 288° (effer.). Mixed melting point with the product obtained on hydrolysis of methyl-7-methoxy-3-bromo-4-methylcoumarin-6-carboxylate according to Dalvi and Sethna (loc.cit.) was not depressed.

Iodination of 7-hydroxy-6-nitro-4-methylcoumarin with iodine in presence of iodic acid : 7-Hydroxy-8-iodo-6-nitro-4-methylcoumarin.

7-Hydroxy-6-nitro-4-methylcoumarin (1.1 g. ; 0.005 mole) in alcohol (300 ml.) was treated with iodine (0.508 g.) and iodic acid (0.176 g. in 7 ml. water) and the mixture stirred for 2 hours. The separated product crystallised from acetic acid as yellow amorphous powder, m.p.273°. Yield 1.1 g.

Analysis :

15.264 mg. of the substance gave 10.194 mg. of silver iodide.

Found : I = 36.10 %.
$C_{10}H_6O_5NI$ requires : I = 36.60 %.

7-Methoxy-8-iodo-6-nitro-4-methylcoumarin.

The methyl ether of the above iodocoumarin was prepared by refluxing its acetone solution with dimethyl sulphate in presence of anhydrous potassium carbonate. It crystallised from acetic acid in needles, m.p.242°.

Analysis :

10.32 mg. of the substance gave 13.70 mg. of carbon dioxide and 1.92 mg. of water.

15.434 mg. of the same substance gave 9.938 mg. of Silver iodide

Found : c = 36.22 %, H = 2.08 %; I = 34.81 %.
$C_{11}H_8O_5NI$ requires: c = 36.56 %; H = 2.21 %; I = 35.18 %.

Iodination of 5-hydroxy-4-methylcoumarin with one mole of iodine monochloride : 5-Hydroxy-8-iodo-4-methylcoumarin.

A mixture of 5-hydroxy-4-methylcoumarin (1.76 g. ; 0.01 mole) in acetic acid (40 ml.) and hydrochloric acid (40 ml.) was treated with iodine monochloride (1.6 g. ; 0.01 mole) and the mixture left overnight at 60°. The next day it was stirred vigorously for 2 hours and the separated product filtered. It crystallised from acetic acid in needles, m.p.242°. Yield 1.2 g.

Analysis :

8.284 mg. of the substance gave 6.500 mg. of silver iodide.

Found : I = 42.41 %.

$C_{10}H_7O_3I$ requires : I = 42.06 %.

5-Methoxy-8-iodo-4-methylcoumarin.

The methyl ether of the above iodo coumarin was prepared by refluxing its acetone solution with dimethyl sulphate in presence of anhydrous potassium carbonate for 20 hours. It crystallised from rectified spirit in needles, m.p.254°.

Analysis :

4.231 mg. of the substance gave 6.481 mg. of carbon dioxide and 1.226 mg. of water.

6.220 mg. of the same substance gave 4.600 mg. of silver iodide.

Found : C = 41.80 % ; H = 3.24 % ; I = 39.98 %.

$C_{11}H_9O_3I$ requires : C = 41.77 % ; H = 2.84 % ; I = 40.19 %.

The same product was obtained when 5-methoxy-4-

methylcoumarin (1.90 g.) in acetic acid (20 ml.) was treated with iodine monochloride (1.6 g. ; 0.01 mole). Yield 1.4 g.

It remained unchanged on boiling with alcoholic potassium hydroxide solution (10 %).

Elbs Persulphate Oxidation of 5-methoxy-8-iodo-4-methylcoumarin : 6-Hydroxy-5-methoxy-8-iodo-4-methylcoumarin.

5-Methoxy-8-iodo-4-methylcoumarin (1 g.) was dissolved in sodium hydroxide solution (10 % ; 40 ml.) by warming on a steam bath and by adding a little pyridine. It was then oxidised with potassium persulphate (0.9 g. in 40 ml. water) as described before. The product obtained on working up the reaction mixture as before crystallised from acetic acid in needles,m.p.270°. It dissolved in sodium hydroxide solution to give a deep yellow solution.

Analysis :

7.392 mg. of the substance gave 10.780 mg. of carbon dioxide and 1.933 mg. of water.

11.446 mg. of the same substance gave 8.150 mg. of silver iodide.

Found : C = 39.81 % ; H = 2.93 % ; I = 38.49 %.

$C_{11}H_9O_4I$ requires : C = 39.77 % ; H = 2.70 % ; I = 38.30 %.

Iodination of 5-hydroxy-4-methylcoumarin with one mole of iodine in presence of ammonia : 5-Hydroxy-6-iodo- and 5-hydroxy-6,8-diiodo-4-methylcoumarin.

(a) 5-Hydroxy-6-iodo-4-methylcoumarin.

5-Hydroxy-4-methylcoumarin (1.76 g. ; 0.01 mole) in ammonia (10 ml.) and water (30 ml.) was treated with a solution of iodine (2.54 g. ; 0.01 mole) in potassium iodide (5 g.) while the mixture was stirred vigorously for 10 minutes only. The separated product was filtered and the filtrate poured over dilute cold sulphuric acid. The product obtained on acidification was the monoiodo derivative. It crystallised from acetic acid,m.p.175°.

The residue was treated as described under (b) later.

Analysis :

10.560 mg. of the substance gave 8.199 mg. of silver iodide.

Found : I = 41.97 %.

$C_{10}H_7O_3I$ requires : I = 42.06 %.

5-Methoxy-6-iodo-4-methylcoumarin.

The methyl ether was prepared by refluxing the acetone solution of the 6-iodo derivative,described above, with dimethyl sulphate in presence of anhydrous potassium carbonate as before. It crystallised from rectified spirit in needles,m.p.155°.

Analysis :

8.68 mg. of the substance gave 13.32 mg. of carbon dioxide and 2.26 mg. of water.

14.52 mg. of the same substance gave 10.72 mg. of silver iodide.

Found : C = 41.90 % ; H = 2.91 % ; I = 39.90 %.

$C_{11}H_9O_3I$ requires : C = 41.77 % ; H = 2.84 % ; I = 40.19 %.

It remained unchanged on boiling with alcoholic sodium hydroxide solution (10 %) nor did it undergo Elbs Persulphate Oxidation.

(b) 5-Hydroxy-6,8-diiodo-4-methylcoumarin.

Residue from (a) (p. 80) on crystallisation from acetic acid gave the diiodo derivative, M.p.230°. This was obtained in excellent yield on iodination with two moles of iodine by this method.

Analysis :

10.440 mg. of the substance gave 11.448 mg. of silver iodide.

Found : I = 59.28 %.

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

The diiodo product was found to be unstable. On boiling with acetic acid the compound decompose~~s~~d with the liberation of iodine. On refluxing the diiodo derivative with sodium hydroxide solution (10 %) iodine was eliminated and 5-hydroxy-4-methylcoumarin was obtained.

The same diiodo derivative was obtained when 5-hydroxy-4-methylcoumarin (1.1 g.) in alcohol (50 ml.) was treated with iodine (0.64 g.) and iodic acid (0.25 g.) Yield 1.8 g.

The same diiodo derivative was also obtained when

5-hydroxy-4-methylcoumarin (0.557 g.) in acetic acid (20 ml.) and hydrochloric acid (30 ml.) was treated with iodine monochloride (4.1 g.). Yield 0.6 g.

5-Methoxy-6,8-diiodo-4-methylcoumarin.

The methyl ether of the above diiodo coumarin was prepared by refluxing its acetone solution with dimethyl sulphate in presence of anhydrous potassium carbonate as before, m.p.224°.

Analysis :

3.580 mg. of the substance gave 3.962 mg. of carbon dioxide and 0.508 mg. of water.

9.796 mg. of the same substance gave 10.386 mg. of silver iodide.

Found : C = 30.20 % ; H = 1.59 % ; I = 57.31 %.

$C_{11}H_8O_3I_2$ requires : C = 29.86 % ; H = 1.81 % ; I = 57.46 %.

It remained unchanged on boiling with alcoholic potassium hydroxide solution (10 %).

Iodination of methyl-5-hydroxy-4-methylcoumarin-6-carboxylate with 4 moles of iodine monochloride : Methyl-5-hydroxy-8-iodo-4-methylcoumarin-6-carboxylate.

A mixture of methyl-5-hydroxy-4-methylcoumarin-6-carboxylate (0.83 g.) in acetic acid (30 ml.) was treated with iodine monochloride (2.3 g.) and the reaction mixture left overnight at 60°. The next day it was stirred vigorously and the separated solid was filtered and washed with more of acetic acid. It crystallised from acetic acid in needles, m.p.254°. Yield 0.3 g.

Analysis :

15.54 mg. of the substance gave 10.18 mg. of silver iodide.

Found : I = 35.41 %.

$C_{12}H_9O_5I$ requires : I = 35.28 %.

The same product was obtained when methyl-5-hydroxy-4-methylcoumarin-6-carboxylate (1.17 g.) in alcohol (50 ml.) was treated with iodine (0.508 g.) and iodic acid (0.176 g.). Yield 0.86 g.

Methyl-5-methoxy-8-iodo-4-methylcoumarin-6-carboxylate.

The methyl ether of the 8-iodo ester was prepared by refluxing its acetone solution with dimethyl sulphate in presence of anhydrous potassium carbonate as before. It crystallised from rectified spirit in needles, m.p.153-155°.

Analysis :

10.38 mg. of the substance gave 15.80 mg. of carbon dioxide and 2.48 mg. of water.

16.22 mg. of the same substance gave 10.26 mg. of silver iodide.

Found : C = 41.55 % ; H = 2.67 % ; I = 34.19 %.

$C_{13}H_{11}O_5I$ requires : C = 41.71 % ; H = 2.94 % ; I = 33.90 %.

5-Methoxy-8-iodo-4-methylcoumarin-6-carboxylic acid.

The above ester (0.5 g.) was refluxed with alcoholic potassium hydroxide solution (10 % ; 40 ml.) for

2 hours on a steam bath. The product which separated on acidification was purified through sodium bicarbonate solution. It crystallised from dilute acetic acid in needles, m.p. 245° (effer.).

Analysis :

9.92 mg. of the substance gave 14.60 mg. of carbon dioxide and 2.16 mg. of water.

9.24 mg. of the same substance gave 6.08 mg. of silver iodide.

Found : C = 40.17 % ; H = 2.43 % ; I = 35.57 %.

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