CHAPTER IV

ROSENMUND-VON BRAUN REACTION ON IODOCOUMARINS : SYNTHESIS OF CYANOCOUMARINS.

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Rosenmund-von Braun reaction on iodocoumarins : Synthesis of cyanocoumarins.

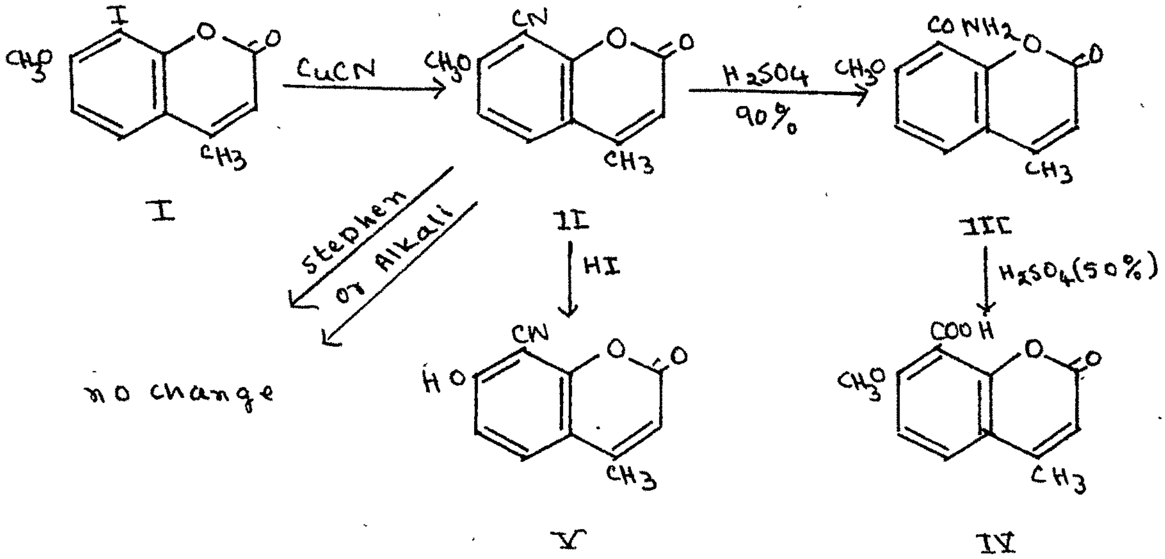
Aryl nitriles can be obtained by many methods. A survey of all methods has been made by Mowry (Chem. Revs., 1948, 42, 189). The reaction between an organic halide and a metallic cyanide was first investigated by Wohler and Liebig (Ann., 1832, 3, 249, 267) who obtained benzoyl cyanide by distillation of benzoyl chloride over mercuric cyanide. In 18~~8~~77 Merz and Weith (Ber., 1877, 10, 746) obtained α-naphtho-nitrile from α-bromonaphthalene by treatment with potassium ferrocyanide. They also synthesised benzonitrile from iodobenzene and silver cyanide. Rosenmund et al. (1919, 52B, 1749) found that the replacement of an aryl halogen atom by the cyano group can also be accomplished by the action of anhydrous cuprous cyanide. Diesbach et al. (Helv. Chim. Acta., 1923, 6, 548) extended this reaction and obtained dinitriles from dibromoxylenes in 88 % yield. The technique adopted was to add the aryl bromide and a slight excess of dry cuprous cyanide to sufficient dry pyridine or quinoline to form homogeneous complex at reaction temperatures. Aryl chlorides undergo the reaction satisfactorily if sufficiently activated by appropriate substituents. Another technique involves the use of cuprous cyanide in the absence of basic solvents. It was observed by von Braun (Ann., 1931, 488, 111) that the bromo derivatives of high boiling aromatic hydrocarbons are smoothly converted into nitriles in a very high yield by treatment with a slight excess of cuprous cyanide at 260° without using any solvent or promoter. Koelsch and Whitney (J. Am. Chem. Soc., 1936, 58, 1328) studied the Rosenmund-von Braun reaction in detail and they found that the reaction is autocatalytic, that addition of a small amount of nitrile shortens the reaction time and copper sulphate in small amounts has a marked catalytic effect. They recommended the addition of 0.01 mole of copper sulphate per 0.1 mole of iodo derivative and gradual addition of the halide to the mixture of cuprous cyanide and catalysts.

Though various chloro and bromocoumarins are known this reaction has not been applied to such compounds. Some cyanocoumarins have been synthesised but by other methods. For example, Dey and Kutti (Proc. Natl. Inst. Sci., India, 1940, 6, 641) obtained 5-cyano-8-methoxycoumarin from 5-amino-8-methoxycoumarin by diazotisation and treatment with potassium cyanide. Link et al. (J. Am. Chem. Soc., 1953, 75, 1886) obtained 3-cyano-4-methylcoumarin by sodium ethoxide catalysed aldol condensation of o-hydroxy acetophenone and ethyl cyanoacetate. Baker and Howes (J. Chem. Soc., 1953, 119) obtained 3-cyanocoumarin and 7-methoxy-3-cyanocoumarin by condensing malononitrile with salicylaldehyde and 2-hydroxy-~~2~~4-methoxybenzaldehyde respectively in presence of piperidine. Crawford and Rasburn (J. Chem. Soc., 1956, 2155) obtained 8-cyanocoumarin from 8-aminocoumarin by diazotisation and treatment with potassium cuprocyanide. Link et al. (J. Am. Chem. Soc., 1957, 79, 5301) obtained various 3-cyano-4-

alkylcoumarins by condensing ethyl cyanoacetate with o-hydroxyacylphenones in the presence of acetic acid and ammonium acetate. Various cyanocoumarins have now been prepared from the corresponding iodocoumarins, by the Rosenmund-von Braun reactions and their hydrolysis with alkali and sulphuric acid studied.

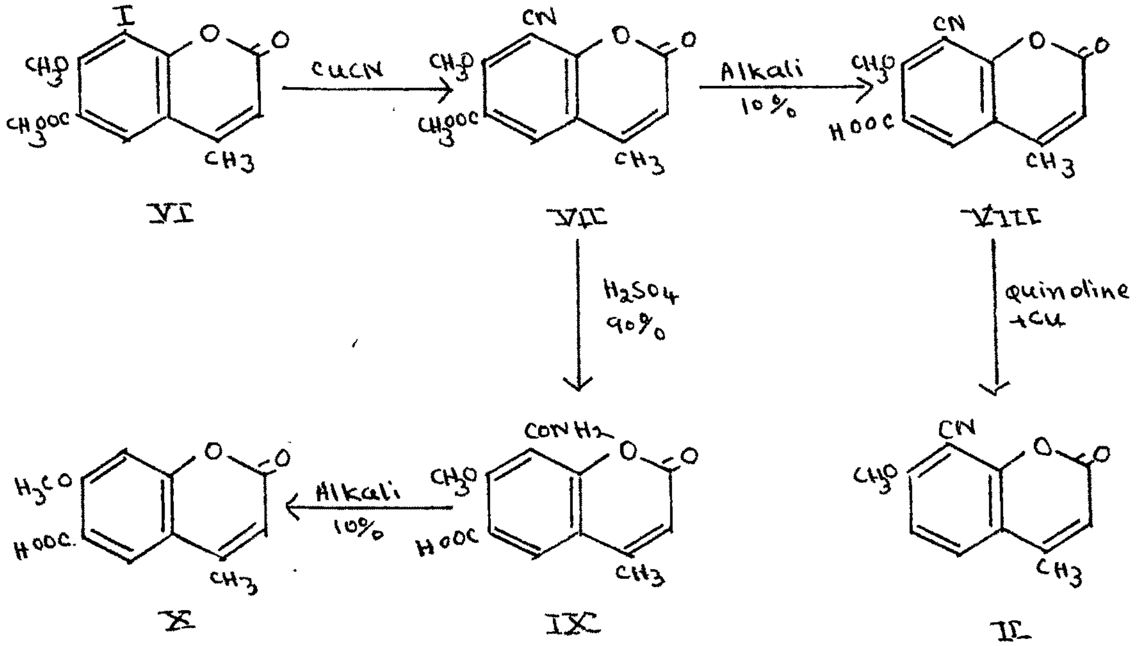
Rosenmund-von Braun reaction on 7-methoxy-8-iodo-4-methylcoumarin : 7-Methoxy-8-cyano-4-methylcoumarin.

7-Methoxy-8-iodo-4-methylcoumarin (I) when heated with anhydrous cuprous cyanide above its melting point gave the corresponding 8-cyano derivative (II) in excellent yield. With pure cuprous cyanide yields were extremely poor but cuprous cyanide of some standing gave better results. For small lots upto 3 g. no diluent was used. When working with larger quantities sand was used as diluent. On heating with alcoholic as well as aqueous potassium hydroxide solution (10 % and 20 %) ~~it~~ (II) remained unchanged. On heating with sulphuric acid (90 %), (II) was only partially hydrolysed and yielded the corresponding 8-amido derivative (III), which on further hydrolysis with sulphuric acid (50 %) or with alkali (10 %) yielded the known 7-methoxy-4-methylcoumarin-8-carboxylic acid (IV) (Limaye and Kulkarni, Rasayanam, 1943, 1, 251 ; C. A., 1944, 38, 4264). Attempts to prepare the 8-formyl derivative from 7-methoxy-8-cyano-4-methylcoumarin by treatment with anhydrous stannous chloride dissolved in ether and saturated with hydrogen chloride (Stephen Reaction) failed, the original cyanocoumarin was recovered unchanged. On demethylation with hydriodic acid, (II) yielded 7-hydroxy-8-cyano-4-methylcoumarin (V).



Methyl-7-methoxy-8-iodo-4-methylcoumarin-6-carboxylate (VI) when heated with anhydrous cuprous cyanide above its melting point gave the corresponding 8-cyano derivative (VII). On heating with alcoholic as well as aqueous potassium hydroxide solution (10 %) the ester was only hydrolysed to the corresponding acid (VIII) the cyano group remaining intact. On decarboxylation the acid (VIII) gave 7-methoxy-8-cyano-4-methylcoumarin (II) described earlier. On heating with sulphuric acid (90 %) the cyano ester (VII) gave 7-methoxy-8-amido-4-methylcoumarin-6-carboxylic acid (IX) which on further hydrolysis with alkali (10 %) gave a product identical with the known 7-methoxy-4-methylcoumarin-6-carboxylic acid (X) (Dalvi and Sethna,

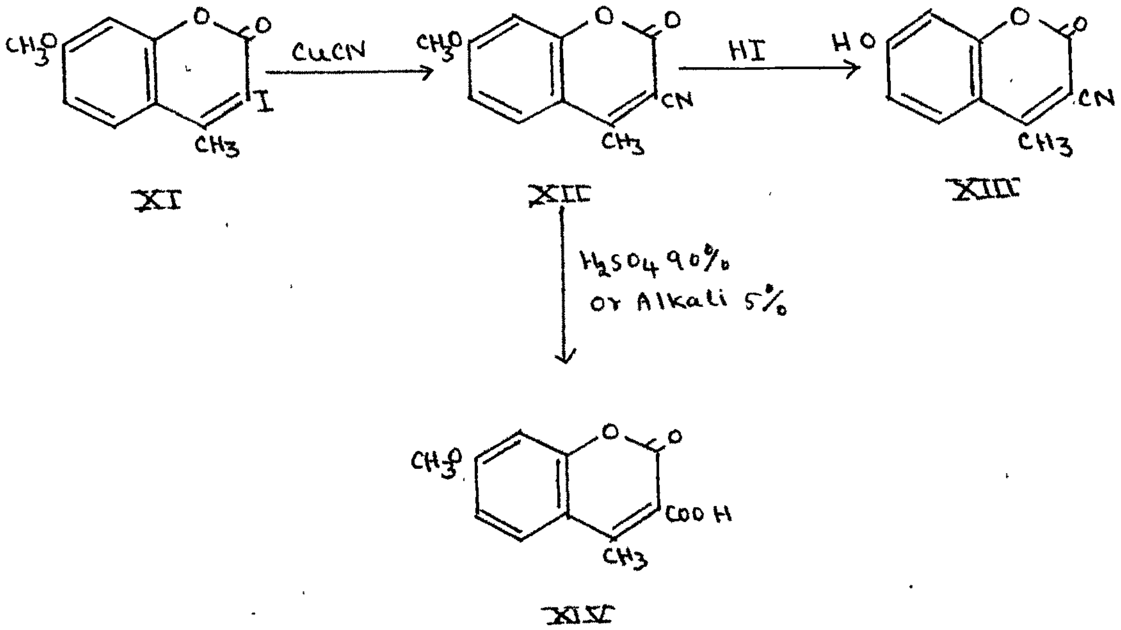
J. Indian Chem. Soc., 1949, 26, 405). Stephen aldehyde reaction on (VII) did not succeed, the original cyanocoumarin was recovered unchanged.



<u>7-Methoxy-3-cyano-4-methylcoumarin.</u>

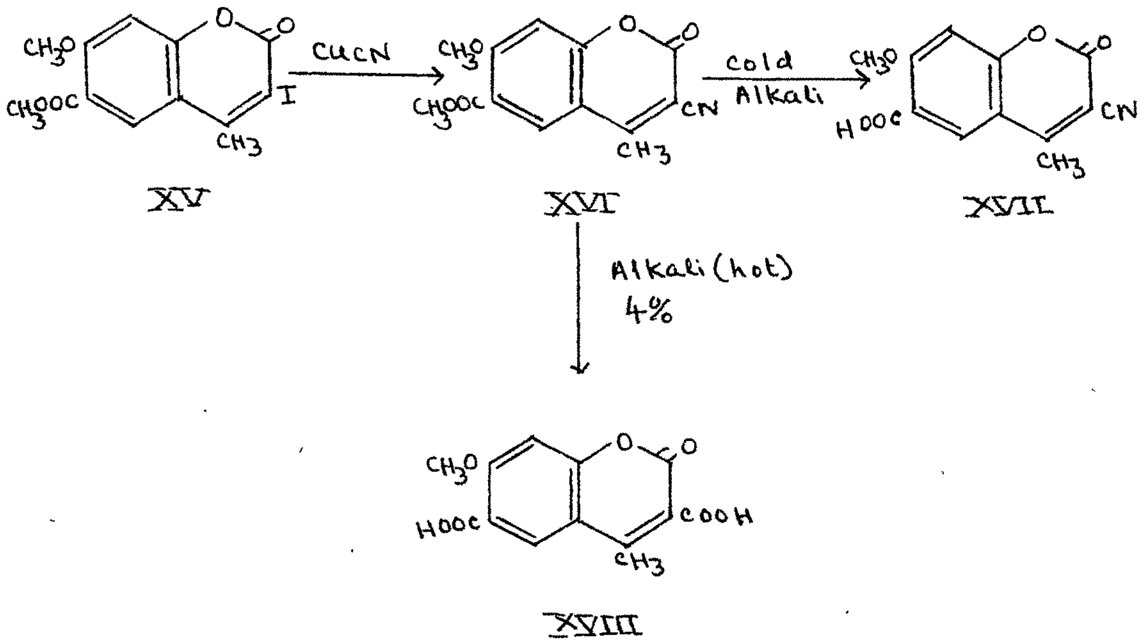
7-Methoxy-3-iodo-4-methylcoumarin (XI) when heated with anhydrous cuprous cyanide above its melting point gave the corresponding 3-cyano derivative (XII) in good yield. On demethylation it gave 7-hydroxy-3-cyano-4-methylcoumarin (XIII) m.p.298°. This was previously prepared by Kendall and Axford (Brit. Patent, 1952, 672741) by the condensation of resacetophenone with ethyl cyanacetate in presence of triethyl amine. They reported the same melting point. On heating with alcoholic or aquoeous potassium hydroxide solution (5 %) or with sulphuric acid (90 %) it gave 7-methoxy-4-methylcoumarin-3-carboxylic acid (XIV), m.p. 182°, previously prepared by Baker, Collis and Banks

(J. Chem. Soc., 1949, S 12) by condensing 2-acetoxy-4-methoxyacetophenone with bromomalonic ester in presence of zinc turnings and hydrolysis of the ester formed. They reported m.p. 184-85°.



Methyl-7-methoxy-3-cyano-4-methylcoumarin-6-carboxylate.

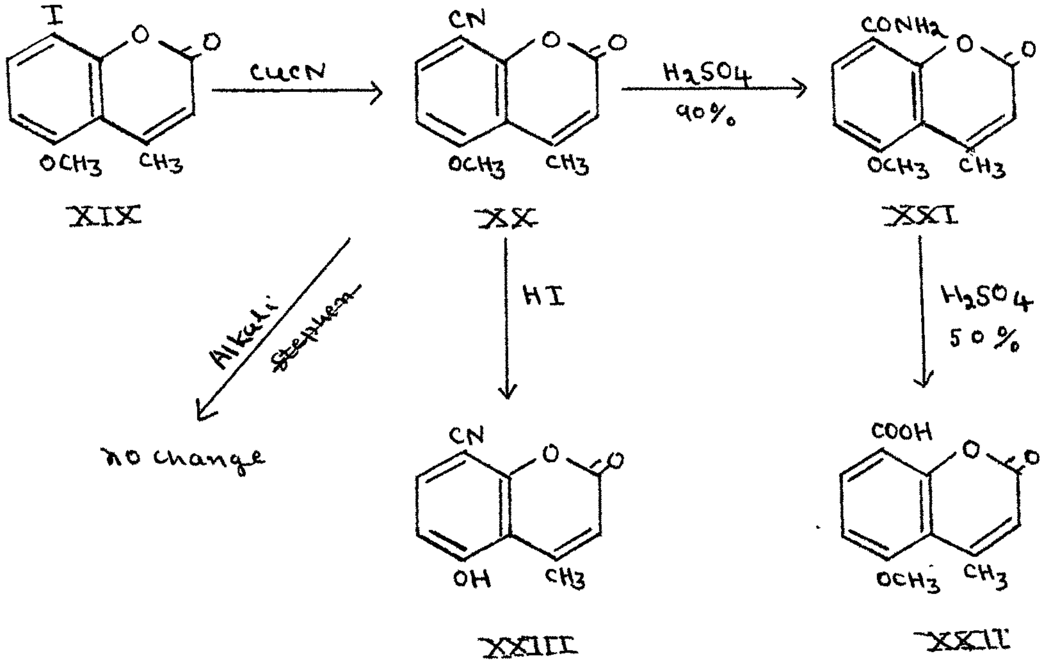
Methyl-7-methoxy-3-iodo-4-methylcoumarin-6-carboxylate (XV) when heated with anhydrous cuprous cyanide above its melting point gave the corresponding 3-cyano derivative (XVI) in good yield. When kept with alkali (10 %) at room temperature for 72 hours it gave 7-methoxy-3-cyano-4-methylcoumarin-6-carboxylic acid (XVII). On decarboxylation it did not give a pure product. On heating with alcoholic potassium hydroxide solution (4 %) or with sulphuric acid (90 %) the cyano ester gave 7-methoxy-3,6-dicarboxy-4-methylcoumarin (XVIII).



<u>5-Methoxy-8-cyano-4-methylcoumarin</u>.

5-Methoxy-8-iodo-4-methylcoumarin (XIX) when heated with anhydrous cuprous cyanide above its melting point gave the corresponding 8-cyano derivative (XX) in good yield. Heating with cuprous cyanide had to be continued for a longer time than in the case of 7-methoxy-8-iodo-4-methylcoumarin. Diluent was not used for this reaction. On heating with alcoholic as well as aqueous potassium hydroxide solution (10 %) the cyano derivative remained unchanged. On heating with sulphuric acid (90 %) it gave 5-methoxy-8-amido-4-methylcoumarin (XXI) which on further hydrolysis with sulphuric acid (50 %) yielded the hitherto unknown 5-methoxy-4-methylcoumarin-8-carboxylic acid (XXII). Stephen aldehyde reaction on (XX) did not succeed, the original product was recovered unchanged. 5-Methoxy-8-cyano-4-

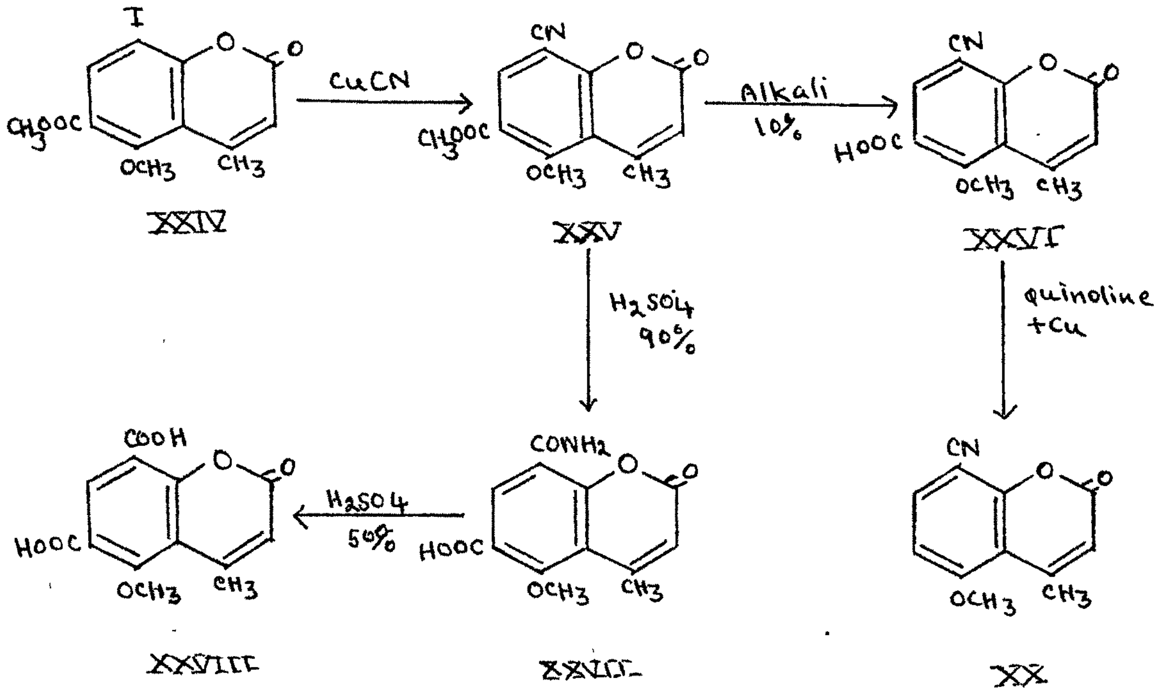
methylcoumarin was demethylated to the corresponding hydroxy derivative (XXIII).



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

Methyl-5-methoxy-8-iodo-4-methylcoumarin-6-carboxylate (XXIV) when heated with anhydrous cuprous cyanide above its melting point gave the corresponding 8-cyano derivative (XXV) in good yield. On heating with aqueous or alcoholic potassium hydroxide solution (10 %) the cyano compound gave the corresponding acid viz. 5-methoxy-8-cyano-4-methylcoumarin-6-carboxylic acid (XXVI), the cyano group remaining unaffected. On decarboxylation, this acid yielded 5-methoxy-8-cyano-4-methylcoumarin (XX). On heating with sulphuric acid (90 %) the cyano ester (XXV) gave 5-methoxy-8-amido-4-methylcoumarin-6-carboxylic acid (XXVII) which on further hydrolysis with sulphuric acid

(50 %) yielded 5-methoxy-6,8-dicarboxy-4-methylcoumarin (XXVIII).



~~As~~ It will be seen from the foregoing discussion that Stephen reaction has been tried on 7-methoxy-8-cyano -4-methylcoumarin, methyl-7-methoxy-8-cyano-4-methylcoumarin-6-carboxylate and 5-methoxy-8-cyano-4-methylcoumarin. In all these cases the reaction failed and the original cyanocoumarins were recovered unchanged. Stephen (J. Chem. Soc., 1925, 127, 1874) found that o-substituted nitriles give poor yields of the corresponding aldehydes due to steric hindrance. The sparing solubility of the cyanocoumarins in ether and chloroform may also be the cause of the failure to undergo this reaction.

EXPERIMENTAL

Rosenmund-von Braun reaction on 7-methoxy-8-iodo-4-methylcoumarin : 7-Methoxy-8-cyano-4-methylcoumarin.

An intimate mixture of 7-methoxy-8-iodo-4-methylcoumarin (3.16 g. ; 0.01 mole) and anhydrous cuprous cyanide (1.78 g. ; 0.02 mole) was heated in an oil bath at 220-30° for 15 minutes. The reaction mixture melts first and resolidifies again. The solid mass was powdered and extracted several times with hot acetic acid. The product obtained on cooling the acetic acid extracts was crystallised from fresh glacial acetic acid in yellow needles, m.p. 289-91°. Yield 1.2 g. It was sparingly soluble in common organic solvents. Its alcoholic solution shows blue fluorescence. It remained unchanged on boiling with aqueous as well as alcoholic potassium hydroxide solution (10 %) for 2 hours.

Analysis :

9.80 mg. of the substance gave 24.06 mg. of carbon dioxide and 3.74 mg. of water.

6.48 mg. of the same substance gave 0.377 ml. of nitrogen at t = 32°C and p = 761 mm.

Found : C = 67.00 % ; H = 4.27 % ; N = 6.52 %.

$C_{12}H_9O_3N$ requires : C = 66.97 % ; H = 4.22 % ; N = 6.51 %.

7-Hydroxy-8-cyano-4-methylcoumarin.

7-Methoxy-8-cyano-4-methylcoumarin (0.5 g.) was heated with acetic anhydride (8 ml.) and hydriodic acid

(8 ml. ; d. 1.7) in an oil bath at 130-40° for 2 hours. The reaction mixture was then cooled and poured in cold sodium bisulphite solution. The product obtained was purified through sodium hydroxide solution. It crystallised from acetic acid in yellow needles, m.p.272°. It did not give any ferric chloride colouration.

Analysis :

9.70 mg. of the substance gave 23.20 mg. of carbon dioxide and 3.48 mg. of water.

5.008 mg. of the same substance gave 0.327 ml. of nitrogen at $t = 32°C$ and $p = 757$ mm.

Found : C = 65.27 % ; H = 4.01 % ; N = 7.28 %.

$C_{11}H_7O_3N$ requires : C = 65.67 % ; H = 3.51 % ; N = 6.96 %

7-Methoxy-8-amido-4-methylcoumarin.

7-Methoxy-8-cyano-4-methylcoumarin (0.5 g.) was heated with sulphuric acid (9 ml.) and water (1 ml.) on a steam bath for 2 hours. The reaction mixture was then cooled and poured in ice water. The separated product crystallised from acetic acid in colourless shining plates, m.p. 278°.

Analysis :

8.62 mg. of the substance gave 19.48 mg. of carbon dioxide and 3.50 mg. of water.

5.32 mg. of the same substance gave 0.288 ml. of nitrogen at $t = 31°C$ and $p = 756$ mm.

Found : C = 61.66 % ; H = 4.54 % ; N = 6.05 %.

$C_{12}H_{11}O_4N$ requires : C = 61.80 % ; H = 4.75 % ; N = 6.01 %.

7-Methoxy-4-methylcoumarin-8-carboxylic acid

The above amido derivative (0.5 g.) was heated with a mixture of sulphuric acid (6 ml.), acetic acid (8 ml.) and water (4 ml.) in an oil bath at 120-30° for 3 hours. The product obtained after pouring the reaction mixture in ice water was purified through sodium bicarbonate solution. It crystallised from acetic acid in needles, m.p. 246° (effer.). Mixed melting point with the authentic specimen prepared according to Limaye and Kulkarni (loc.cit.) was not depressed.

The same acid was also obtained by refluxing the above amido derivative with alcoholic potassium hydroxide solution (10 %) for 2 hours.

Attempted Stephen reaction on 7-methoxy-8-cyano-4-methylcoumarin.

Anhydrous hydrochloric acid gas was passed through a suspension of anhydrous stannous chloride (2.3 g.) in dry ether (100 ml.) for 2 hours when two layers appeared. 7-Methoxy-8-cyano-4-methylcoumarin (0.4 g.) was then added with good stirring. A little chloroform was added to keep the nitrile in solution and the mixture was stirred for 3 hours. Ether was then removed by decantation and the residue was boiled with water. 7-Methoxy-8-cyano-4-methylcoumarin was recovered unchanged.

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

An intimate mixture of methyl-7-methoxy-8-iodo-4-methylcoumarin-6-carboxylate (3.74 g. ; 0.01 mole) and anhydrous cuprous cyanide (1.78 g. ; 0.02 mole) was heated in an oil bath at 240-45° for 15 minutes. The solid reaction mixture was well extracted with acetone. The product obtained after removal of acetone crystallised from acetic acid in yellow needles, m.p.276°. Yield 1.9 g. It is moderately soluble in acetic acid and alcohol and insoluble in benzene and ether. Its alcoholic solution shows blue fluorescence.

Analysis :

8.82 mg. of the substance gave 19.80 mg. of carbon dioxide and 3.46 mg. of water.

7.12 mg. of the same substance gave 0.337 ml.of nitrogen at t = 30°C and p = 761 mm.

Found : C = 61.26 % ; H = 4.39 % ; N = 5.34 %.

$C_{14}H_{11}O_5N$ requires : C = 61.54 % ; H = 4.06 % ; N = 5.13 %.

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

The above 8-cyanoester (0.5 g.) was refluxed with alcoholic potassium hydroxide solution (10 % ; 20 ml.) on a steam bath for 2 hours. The product obtained after acidification was purified through sodium bicarbonate solution. It crystallised from glacial acetic acid in small needles, m.p. 283° (effer.). Its alcoholic solution shows blue fluorescence.

Analysis :

7.04 mg. of the substance gave 15.54 mg. of carbon dioxide and 2.28 mg. of water.

5.90 mg. of the same substance gave 0.307 ml. of nitrogen at t = 30°C and p = 760 mm.

Found : C = 60.24 % ; H = 3.62 % ; N = 5.86 %.

$C_{13}H_9O_5N$ requires : C = 60.23 % ; H = 3.50 % ; N = 5.40 %.

The above acid (0.3 g.) in quinoline (8 ml.) was heated in an oil bath at 240° with a speck of copper powder for half an hour. The mixture was then filtered and poured in dilute hydrochloric acid solution. The separated product crystallised from acetic acid, m.p.289°. Mixed m.p. with 7-methoxy-8-cyano-4-methylcoumarin, described earlier was not depressed.

7-Methoxy-8-amido-4-methylcoumarin-6-carboxylic acid

Methyl-7-methoxy-8-cyano-4-methylcoumarin-6-carboxylate (0.5 g.) was heated with sulphuric acid (9 ml.) and water (1 ml.) on a steam bath for 3 hours. The product obtained on pouring the reaction mixture in ice water was purified through sodium bicarbonate solution. It crystallised from acetic acid in shining plates,m.p.272° (effer.).

Analysis :

10.92 mg. of the substance gave 22.40 mg. of carbon dioxide and 3.58 mg. of water.

6.082 mg. of the same substance gave 0.268 ml. of nitrogen at t = 32°C and p = 759 mm.

Found : C = 55.98 % ; H = 3.66 % ; N = 4.91 %.

$C_{13}H_{11}O_6N$ requires : C = 56.32 % ; H = 4.00 % ; N = 5.05 %.

7-Methoxy-4-methylcoumarin-6-carboxylic acid

The above amido derivative (0.5 g.) was heated with a mixture of sulphuric acid (6 ml.), acetic acid (8 ml.) and water (4 ml.) in an oil bath at 140° for 3 hours. The product obtained after pouring the reaction mixture in ice water was purified through sodium bicarbonate solution. It crystallised from acetic acid in needles, m.p. 268°. Mixed melting point with the authentic specimen of 7-methoxy-4-methylcoumarin-6-carboxylic acid prepared according to Dalvi and Sethna (loc.cit.) was not depressed.

Attempted Stephen reaction on methyl-7-methoxy-8-cyano-4-methylcoumarin-6-carboxylate.

Anhydrous hydrogen chloride was passed through a suspension of anhydrous stannous chloride (2.3 g.) in dry ether (100 ml.) till two layers appeared. The above nitrile was then added with good stirring. The product obtained on working up the reaction mixture as before was found to be the original nitrile.

7-Methoxy-3-cyano-4-methylcoumarin.

An intimate mixture of 7-methoxy-3-iodo-4-methylcoumarin (3.16 g. ; 0.01 mole) and anhydrous cuprous cyanide (1.78 g. ; 0.02 mole) was heated in an oil bath at 180-85° for 15 minutes. The solid was powdered and well extracted with acetone. The product obtained after removal of acetone crystallised from acetic acid in yellow needles, m.p.223°. Yield 1.62 g. It is soluble in alcohol, acetone, acetic acid and sparingly soluble in benzene and ether. Its alcoholic solution shows blue fluorescence.

Analysis :

9.02 mg. of the substance gave 22.12 mg. of carbon dioxide and 3.36 mg. of water.

6.04 mg. of the same substance gave 0.332 ml. of nitrogen at t = 32°C and p = 761 mm.

Found : C = 66.93 % ; H = 4.16 % ; N = 6.16 %.

$C_{12}H_9O_3N$ requires : C = 66.97 % ; H = 4.22 % ; N = 6.51 %.

7-Hydroxy-3-cyano-4-methylcoumarin.

The above 3-cyano derivative (0.5 g.) was heated with acetic anhydride (8 ml.) and hydriodic acid (8 ml. ; d. 1.7) in an oil bath at 130-40° for 2 hours. The product obtained on pouring the reaction mixture in cold sodium bisulphite solution, was purified through dilute sodium hydroxide solution. It crystallised from acetic acid, m.p. 298°. Kendell and Axford (loc.cit) reported the same melting point.

Analysis :

7.56 mg. of the substance gave 18.12 mg. of carbon dioxide and 2.58 mg. of water.

6.754 mg. of the same substance gave 0.417 ml. of nitrogen at t = 33°C and p = 756 mm.

Found : C = 65.41 % ; H = 3.82 % ; N = 6.85 %.

$C_{11}H_7O_3N$ requires : C = 65.67 % ; H = 3.51 % ; N = 6.96 %.

7-Methoxy-4-methylcoumarin-3-carboxylic acid

7-Methoxy-3-cyano-4-methylcoumarin (0.5 g.) was refluxed with alcoholic potassium hydroxide solution (10 % ; 10 ml.) on a steam bath for 2 hours. The product obtained after acidification was purified through sodium bicarbonate solution. It crystallised from glacial acetic acid,m.p.182°. Baker, Collis and Banks (loc.cit.) who prepared the same acid reported m.p. 184-85°.

Analysis :

7.86 mg. of the substance gave 17.64 mg. of carbon dioxide and 3.04 mg. of water.

Found : C = 61.24 % ; H = 4.33 %.

$C_{12}H_{10}O_5$ requires : C = 61.54 % ; H = 4.30 %.

Methyl-7-methoxy-3-cyano-4-methylcoumarin-6-carboxylate.

An intimate mixture of methyl-7-methoxy-3-iodo-4-methylcoumarin-6-carboxylate (3.74 g. ; 0.01 mole) and anhydrous cuprous cyanide (1.78 g. ; 0.02 mole) was heated in an oil bath at 250-55° for 15 minutes. The solid mass was powdered and extracted several times with acetone. The product obtained after removal of acetone crystallised from acetic acid in brown needles, m.p. 249°. Yield 1.9 g. It is soluble in alcohol, acetone, acetic acid and sparingly soluble in benzene and ether. Its alcoholic solution shows blue fluorescence.

Analysis :

9.56 mg. of the substance gave 21.66 mg. of carbon dioxide and 3.78 mg. of water.

7.2 mg. of the same substance gave 0.307 ml. of nitrogen at t = 30°C and p = 761 mm.

Found : C = 61.83 % ; H = 4.42 % ; N = 4.81 %.

$C_{14}H_{11}O_5N$ requires : C = 61.54 % ; H = 4.06 % ; N = 5.13 %.

7-Methoxy-3-cyano-4-methylcoumarin-6-carboxylic acid

The above 3-cyano ester (0.5 g.) was kept at room temperature with potassium hydroxide solution (10 % ; 20 ml.) for 72 hours. The product obtained on acidification was purified through sodium bicarbonate solution. It crystallised from acetic acid in small needles, m.p.248°. Its alcoholic solution shows blue fluorescence.

Analysis :

9.16 mg. of the substance gave 20.20 mg. of carbon dioxide and 2.82 mg. of water.

6.18 mg. of the same substance gave 0.307 ml. of nitrogen at t = 31°C and p = 759 mm.

Found : C = 60.19 % ; H = 3.45 % ; N = 5.57 %.

$C_{13}H_9O_5N$ requires : C = 60.23 % ; H = 3.50 % ; N = 5.40 %.

7-Methoxy-3,6-dicarboxy-4-methylcoumarin

Methyl-7-methoxy-3-cyano-4-methylcoumarin-6-carboxylate (0.5 g.) was refluxed with alcoholic potassium hydroxide solution (4 % ; 20 ml.) on a steam bath for 2 hours. The product obtained on acidification was purified through sodium bicarbonate solution. It crystallised from glacial acetic acid in needles, m.p. 208-10° (effer.).

Analysis :

10.04 mg. of the substance gave 20.82 mg. of carbon dioxide and 3.22 mg. of water.

Found : C = 56.60 % ; H = 3.59 %.

$C_{13}H_{10}O_7$ requires : C = 56.12 % ; H = 3.62 %.

The same product was obtained when the cyanoester was heated at 120° in an oil bath for 2 hours with a mixture of sulphuric acid (6 ml.), acetic acid (8 ml.) and water (4 ml.).

5-Methoxy-8-cyano-4-methylcoumarin

An intimate mixture of 5-methoxy-8-iodo-4-methylcoumarin (3.16 g. ; 0.01 mole) and anhydrous cuprous cyanide (1.78 g. ; 0.02 mole) was heated in an oil bath at 260-70° for half an hour. The solid mass was powdered and extracted several times with acetone. The product obtained after removal of acetone crystallised from acetic acid in brown shining needles, m.p. 227-30°. Yield 1 g. It is sparingly soluble in alcohol, acetone, acetic acid and insoluble in benzene and ether. Its alcoholic solution shows blue fluorescence. It remained unchanged on boiling with aqueous or alcoholic potassium hydroxide solution (10 %). Stephen reaction also did not succeed.

Analysis :

8.24 mg. of the substance gave 20.32 mg. of carbon dioxide and 3.10 mg. of water.

5.606 mg. of the same substance gave 0.342 ml. of nitrogen at t = 32°C and p = 756 mm.

Found : C = 67.30 % ; H = 4.21 % ; N = 6.79 %.

$C_{12}H_9O_3N$ requires : C = 6$\overset{6}{\cancel{7}}$.97 % ; H = 4.22 % ; N = 6.51 %.

5-Hydroxy-8-cyano-4-methylcoumarin

The above 8-cyanocoumarin (0.5 g.) was heated with acetic anhydride (10 ml.) and hydriodic acid (10 ml. ; d. 1.7) in an oil bath at 130-40° for 2 hours. The product obtained on pouring the reaction mixture in cold sodium bisulphite solution was purified through dilute sodium hydroxide solution. It crystallised from glacial acetic acid in shining yellow needles, m.p. 276°. It did not give any ferric chloride colouration.

Analysis :

10.14 mg. of the substance gave 24.48 mg. of carbon dioxide and 3.24 mg. of water.

6.320 mg. of the same substance gave 0.407 ml. of nitrogen at t = 31°C and p = 756 mm.

Found : C = 65.90 % ; H = 3.57 % ; N = 7.19 %.

$C_{11}H_7O_3N$ requires : C = 65.67 % ; H = 3.51 % ; N = 6.96 %.

5-Methoxy-8-amido-4-methylcoumarin

5-Methoxy-8-cyano-4-methylcoumarin (0.5 g.) was heated with sulphuric acid (9 ml.) and water (1 ml.) on a steam bath for 2 hours. The product obtained on pouring the reaction mixture in water was crystallised from glacial acetic acid in brown shining plates, m.p. 286°.

Analysis :

8.46 mg. of the substance gave 19.06 mg. of carbon dioxide and 3.52 mg. of water.

6.70 mg. of the same substance gave 0.352 ml. of nitrogen at t = 28°C and p = 760 mm.

Found : C = 61.47 % ; H = 4.65 % ; N = 5.96 %.

$C_{12}H_{11}O_4N$ requires : C = 61.80 % ; H = 4.75 % ; N = 6.01 %.

5-Methoxy-4-methylcoumarin-8-carboxylic acid

The above amido derivative (0.5 g.) was heated with a mixture of sulphuric acid (6 ml.), acetic acid (8 ml.) and water (4 ml.) in an oil bath at 120-30° for 3 hours. The product obtained after pouring the reaction mixture in water was purified through sodium bicarbonate solution. It crystallised from glacial acetic acid in colourless needles, m.p. 286° (effer.).

Analysis :

9.22 mg. of the substance gave 20.68 mg. of carbon dioxide and 3.76 mg. of water.

Found : C = 61.21 % ; H = 4.56 %.

$C_{12}H_{10}O_5$ requires : C = 61.54 % ; H = 4.30 %.

The same acid was also obtained by hydrolysis of the above amido derivative by refluxing with alcoholic potassium hydroxide solution (10 %) for 2 hours.

Methyl-5-methoxy-4-methylcoumarin-8-carboxylate

5-Methoxy-8-amido-4-methylcoumarin (0.4 g.) was heated with a mixture of sulphuric acid (6 ml.), methyl alcohol (8 ml.) and water (4 ml.) in an oil bath at 120-30° for 3 hours. The product obtained on pouring the reaction mixture in water crystallised from dilute acetic acid in needles, m.p. 180-82°.

Analysis :

8.76 mg. of the substance gave 20.16 mg. of carbon dioxide and 3.78 mg. of water.

Found : C = 62.80 % ; H = 4.83 %.

$C_{13}H_{12}O_5$ requires : C = 62.90 % ; H = 4.83 %.

Methyl-5-methoxy-8-cyano-4-methylcoumarin-6-carboxylate

An intimate mixture of methyl-5-methoxy-8-iodo-4-methylcoumarin-6-carboxylate (3.74 g. ; 0.01 mole) and anhydrous cuprous cyanide (1.78 g. ; 0.02 mole) was heated in an oil bath at 230° for half an hour. The reaction mixture turned black. The solid mass was powdered and extracted several times with acetone. The product obtained after removal of acetone crystallised from glacial acetic acid in shining brown needles, m.p. 236°. Yield 1.2 g. It is moderately soluble in acetone and acetic acid and insoluble in benzene and ether. Its alcoholic solution shows blue fluorescence.

Analysis :

8.08 mg. of the substance gave 18.34 mg. of carbon dioxide and 3.04 mg. of water.

5.590 mg. of the same substance gave 0.247 ml. of nitrogen at t = 34°C and p = 756 mm.

Found : C = 61.94 % ; H = 4.21 % ; N = 4.88 %.

$C_{14}H_{11}O_5N$ requires : C = 61.54 % ; H = 4.06 % ; N = 5.13 %.

5-Methoxy-8-cyano-4-methylcoumarin-6-carboxylic acid

The above 8-cyanoester (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 was purified through sodium bicarbonate solution. It crystallised from glacial acetic acid in needles, m.p. 248° (effer.). Its alcoholic solution shows blue fluorescence.

Analysis :

9.26 mg. of the substance gave 20.40 mg. of carbon dioxide and 3.20 mg. of water.

6.30 mg. of the same substance gave 0.307 ml. of nitrogen at t = 31°C and p = 761 mm.

Found : C = 60.12 % ; H = 3.87 % ; N = 5.48 %.

$C_{13}H_9O_5N$ requires : C = 60.23 % ; H = 3.50 % ; N = 5.40 %.

The above acid (0.3 g.) in quinoline (10 ml.) was heated in an oil bath at 240° with a speck of copper powder for half an hour. The mixture was then filtered and poured in dilute hydrochloric acid solution. The separated product crystallised from acetic acid, m.p.228°. Mixed m.p. with 5-methoxy-8-cyano-4-methylcoumarin, described earlier, was not depressed.

5-Methoxy-8-amido-4-methylcoumarin-6-carboxylic acid

Methyl-5-methoxy-8-cyano-4-methylcoumarin-6-carboxylate (0.5 g.) was heated with sulphuric acid (9 ml.) and water (1 ml.) on a steam bath for 3 hours. The product obtained on pouring the reaction mixture in water was purified through sodium bicarbonate solution. It crystallised from acetic acid in shining plates m.p. 272° (effer.).

Analysis :

8.08 mg. of the substance gave 16.64 mg. of carbon dioxide and 2.88 mg. of water.

6.182 mg. of the same substance gave 0.267 ml. of nitrogen at t = 34°C and p = 756 mm.

Found : C = 56.20 % ; H = 3.99 % ; N = 4.78 %.

$C_{13}H_{11}O_6N$ requires : C = 56.32 % ; H = 4.00 % ; N = 5.05 %.

5-Methoxy-6,8-dicarboxy-4-methylcoumarin

The above 8-amido acid (0.5 g.) was refluxed with a mixture of sulphuric acid (6 ml.), acetic acid (8 ml.) and water (4 ml.) in an oil bath at 120-30° for 3 hours. The product dissolved and crystalline precipitate separated at the end of the reaction. It was filtered and recrystallised from glacial acetic acid in needles, m.p. 284° (effer.).

Analysis :

6.82 mg. of the substance gave 14.04 mg. of carbon dioxide and 2.18 mg. of water.

Found : C = 56.16 % ; H = 3.58 %.

$C_{13}H_{10}O_7$ requires : C = 56.12 % ; H = 3.62 %.