CHAPTER III

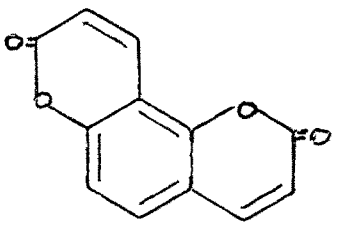
SYNTHESIS OF SOME (A) COUMARINO-α-PYRONES AND (B) FUROCOUMARINS

CHAPTER III

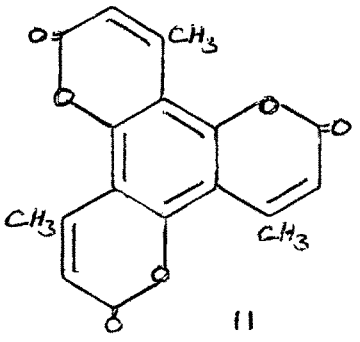
Synthesis of some (A) coumarino-α-pyrones and (B) furo-coumarins.

(A) **Coumarino-α-pyrones** :

Hantzsch and Zürcher[1] synthesised coumarino-α-pyrones(I) and (II) by the Pechmann condensation of resorcinol and phloroglucinol with ethyl acetoacetate.

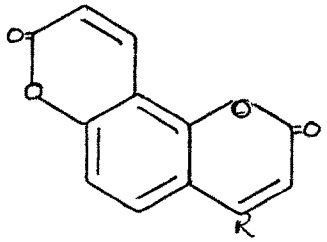


I

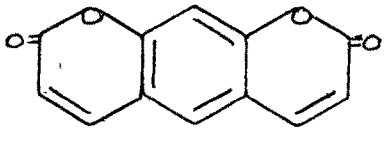


II

Sen and Chakravarti[2] condensed 7-hydroxy- and 7-hydroxy-4-methylcoumarin with malic acid in the presence of sulphuric acid and obtained coumarino-(7,8 ; 6',5')-α-pyrone (IIIa) and 4-methylcoumarino(7,8; 6',5')α-pyrone(IIIb) respectively.



III (a) R=H
(b) R=CH3



IV

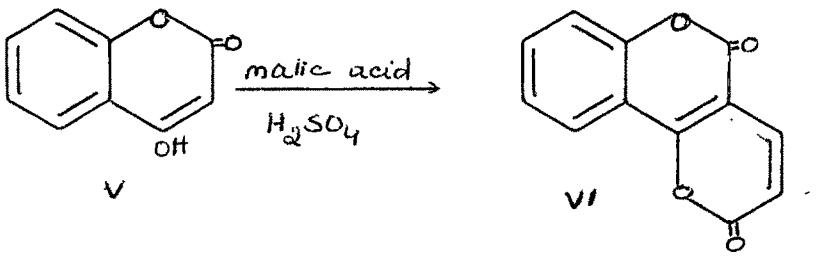
Similar condensationswere carried out by the above authors with 7,8-dihydroxy-4-methyl-,7,8-dihydroxy-, 5-hydroxy-7-methyl- and 5-hydroxy-4,7-dimethylcoumarin and they obtained coumarino-α-pyrone derivatives, the structures of which were not established. Rangaswami and Seshadri[3] reported the formation of both the angular (IIIa) and the linear(IV) coumarino-α-pyrone derivatives in the condensation of 7-hydroxycoumarin with malic acid, the latter being obtained in poor yield. Under the same experimental conditions 7-hydroxy-4-methylcoumarin gives only the angular coumarino-α-pyrone (IIIb). The structure of(IIIa)was established by its synthesis from 7-hydroxy-8-formylcoumarin by Perkin reaction. In a similar way, the constitution of (IIIb) was also established.

Biswas[4] synthesised 3-chloro-4-methylcoumarino-(7,8: 6',5')α-pyrone, 7-methyl-3-chloro-4-methylcoumarino-(5,6:6',5')α-pyrone and 8-hydroxy-3-chloro-4-methylcoumarino-(7,6 :6',5')α-pyrone by the condensation of 3-chloro-4-methyl-7-hydroxy-, 3-chloro-5-hydroxy-4,7-dimethyl- and 3-chloro-4-methyl-7,8-dihydroxycoumarin respectively, with malic acid in the presence of sulphuric acid.

Trivedi and Sethna[5] prepared 3,4-dimethyl-coumarino-(7,8:6',5')α-pyrone and 3,4,7-trimethylcoumarino-(5,6:6',5')α-pyrone by the condensation of 7-hydroxy-3,4-dimethylcoumarin and 5-hydroxy-3,4,7-trimethylcoumarin with malic acid. Similarly 8-hydroxy-3,4-dimethylcoumarino-(7,6:6',5')α-pyrone, 3-bromo-4-methylcoumarino(7,8:6',5')α-pyrone and 3-bromo-4-methyl-8-hydroxycoumarino(7,6:6',5')α-

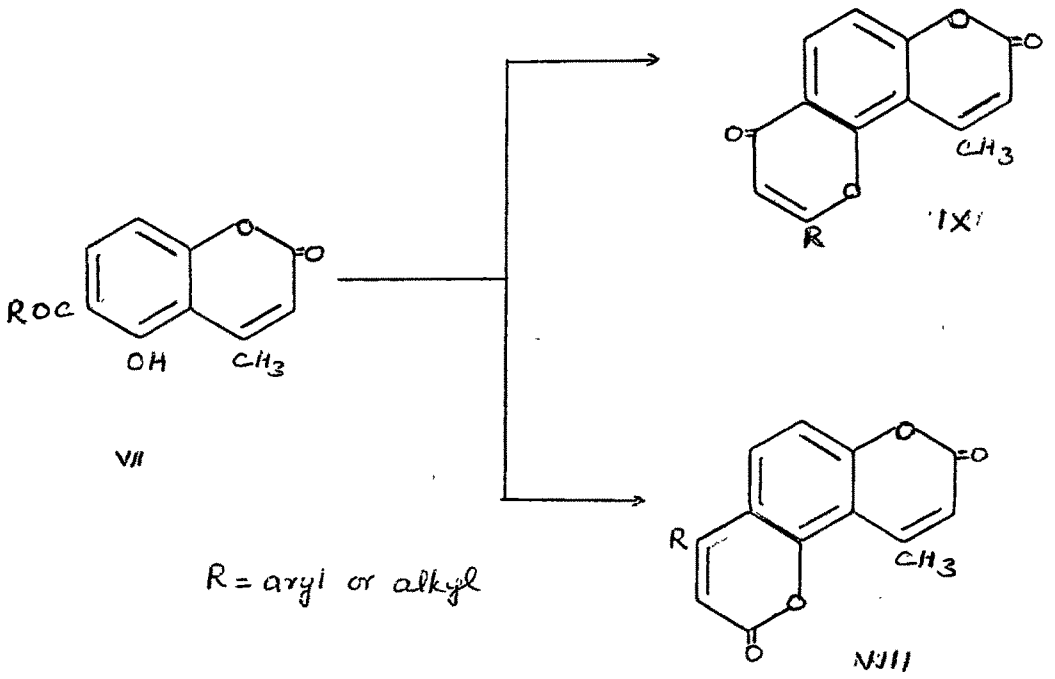
pyrone were also synthesised from 7,8-dihydroxy-3,4-dimethylcoumarin, 7-hydroxy-3-bromo-4-methylcoumarin and 7,8-dihydroxy-3-bromo-4-methylcoumarin respectively. They established the structures by Perkin acetylation of the corresponding formylated coumarin derivatives.

Dholakia and Trivedi[6] recently synthesised coumarino-α-pyrone (VI) from 4-hydroxycoumarin(V) by the Pechmann condensation with malic acid.



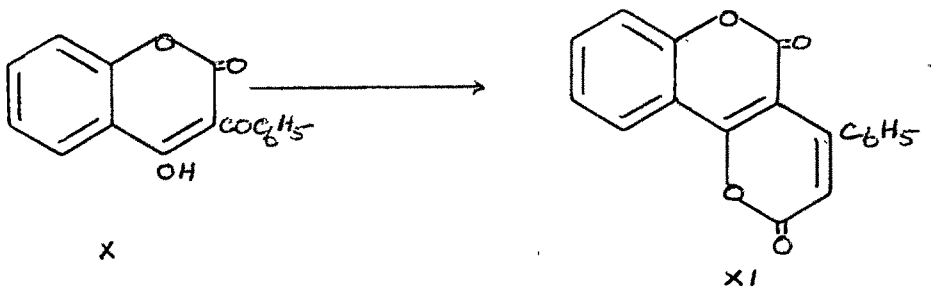
Similarly, 7-methoxy-8-methyl-4-methylcoumarino(4,3:6',5')α-pyrone and 6-methylcoumarino(4,3:6',5')α-pyrone were also synthesised from 7-methoxy-8-methyl-4-hydroxy- and 6-methyl-4-hydroxycoumarin, respectively.

Shah and co-workers[7] carried out Kostanecki-Robinson acylation of 5-hydroxy-6-acylcoumarins(VII) and obtained coumarino-α-pyrones(VIII) and coumarino-γ-pyrones (IX).



Limaye and Ghate[8] obtained 4,4'-dimethyl-8-ethylcoumarino-(7,6:6',5')α-pyrone and 2',4-dimethyl-8-ethyl-3'-acetylcoumarino-4-pyrone from 7-hydroxy-8-ethyl-6-acetyl-4-methylcoumarin by Kostanecki-Robinson acetylation.

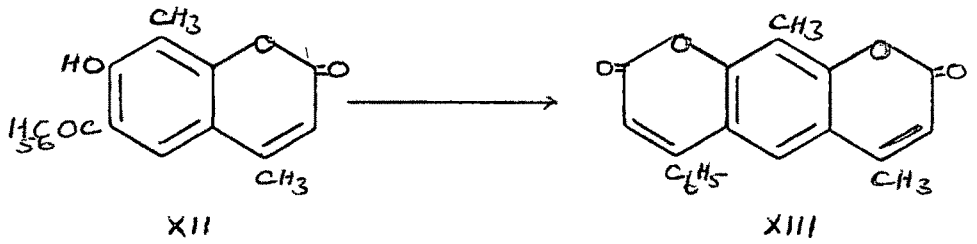
Mustafa and co-workers[9] carried out Kostanecki-Robinson acetylation on 4-hydroxy-3-benzoylcoumarin(X) and obtained 4'-phenylcoumarino-(4,3:6',5')α-pyrone(XI).



X XI

4-Hydroxycoumarin on Pechmann condensation with ethyl acetoacetate yielded 4'-methylcoumarino(4,3:6,5')α-pyrone.

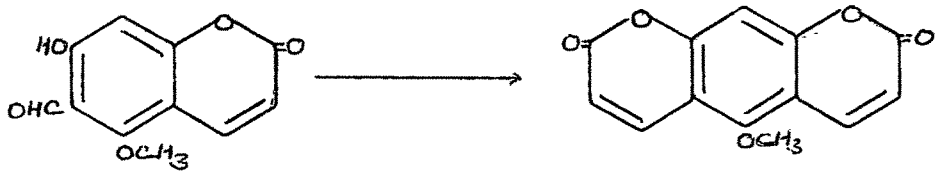
Trivedi and co-workers[10] synthesised 4-methyl-4'-phenylcoumarino (7,6:6,5')α-pyrone (XIII) by carrying out Kostanecki-Robinson acetylation of 7-hydroxy-6-benzoyl-4,8-dimethylcoumarin (XII). The structure of this coumarino-α-pyrone was established by infra red spectra.



XII XIII

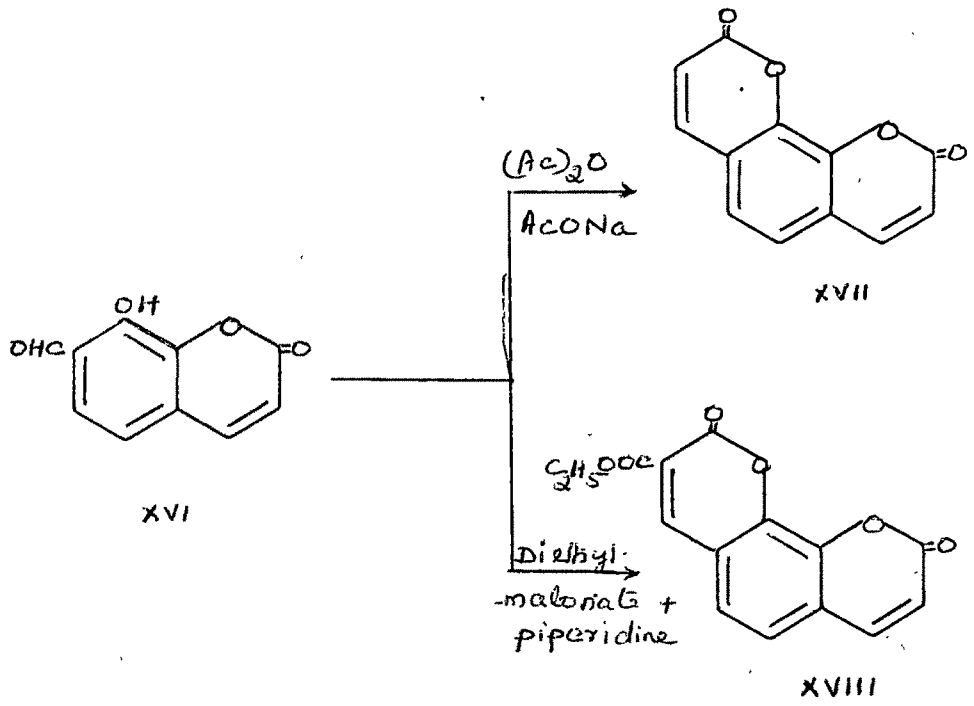
Similarly they prepared 4,8-dimethyl-4'-phenyl-coumarino (7,6:6,5')α-pyrone from 7-hydroxy-6-benzoyl-4,8-dimethylcoumarin. Mustafa, Starkovsky and Zaki[11] prepared 5-methoxycoumarino (7,6:6,5')α-pyrone (XV) by Perkin

acetylation of 5-methoxy-7-hydroxy-6-formylcoumarin (XIV).



XIV XV

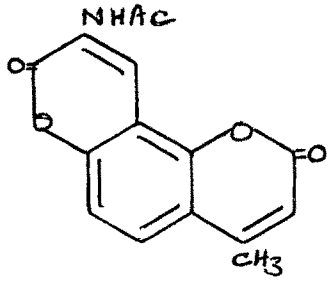
Mehta[12] carried out Perkin acetylation and Knoevenagel reaction on 8-hydroxy-7-formylcoumarin (XVI) and obtained coumarino(8,7:6',5')α-pyrone (XVII) and 3'-carbethoxycoumarino(8,7:6',5')α-pyrone (XVIII).



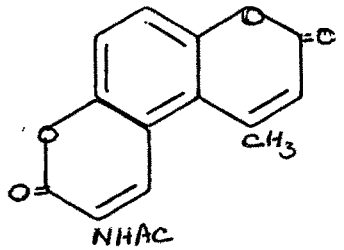
XVI XVII XVIII

Chakravarti and co-workers[13] condensed 7-hydroxy-8-formyl-4-methyl-and 6-hydroxy-5-formyl-4-methylcoumarin with glycine and obtained 3'-acetamido-4-methylcoumarino-

(7,8:6',5')α-pyrone (XIX) and 4-methyl-3'-acetamidocoumarino (6,5:6',5')α-pyrone (XX).



XIX



XX

Shaikh and Trivedi[14] synthesised 3'-acetamidocoumarino(7,8:6',5')α-pyrone, 4-methyl-3'-acetamidocoumarino (7,8:6',5')α-pyrone and 4-methyl-8-hydroxy-3'-acetamidocoumarino(7,6:6',5')α-pyrone through a similar procedure.

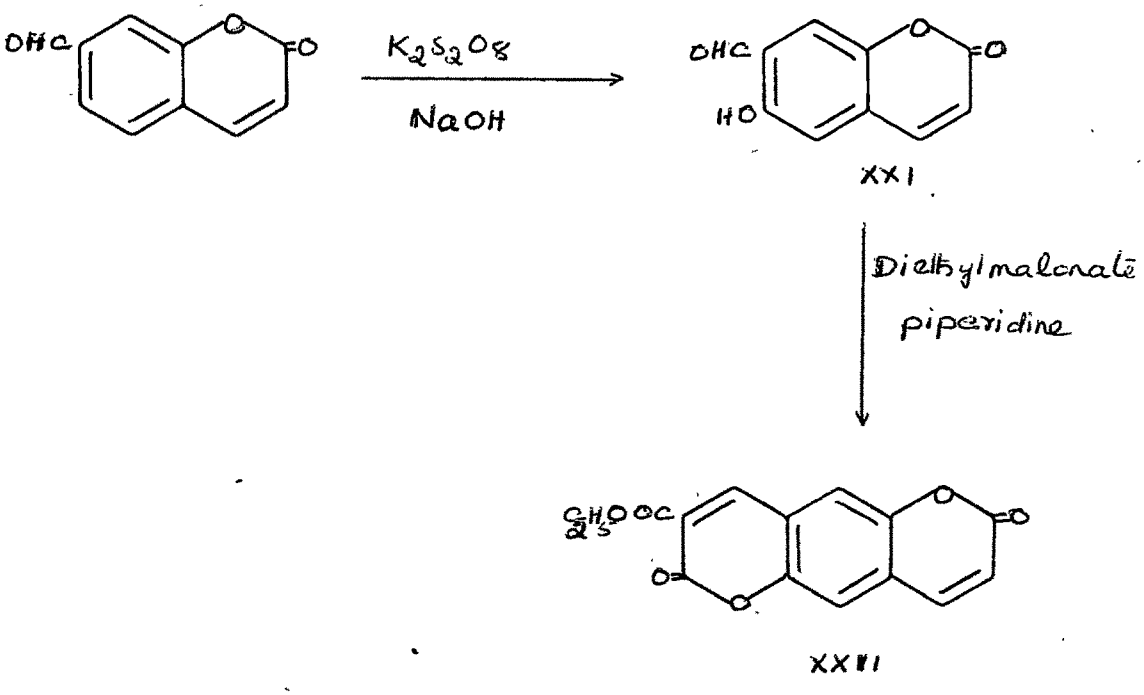
The present work deals with the attempted synthesis of coumarino(6,7:6',5')α-pyrone and 4-methylcoumarino(6,7:6',5')α-pyrone.

Attempted synthesis of coumarino(6,7:6',5')α-pyrone :

7-Formylcoumarin was synthesised from 7-bromomethylcoumarin as described in chapter II. This was subjected to Elbs persulphate oxidation by treating an alkaline solution of 7-formylcoumarin with a solution of potassium persulphate. The unreacted coumarin was removed by acidifying the solution to congo-red and removing the precipitated material. The filtrate on heating with excess of hydrochloric acid gave a product which was soluble in sodium hydroxide solution. It gave reddish brown

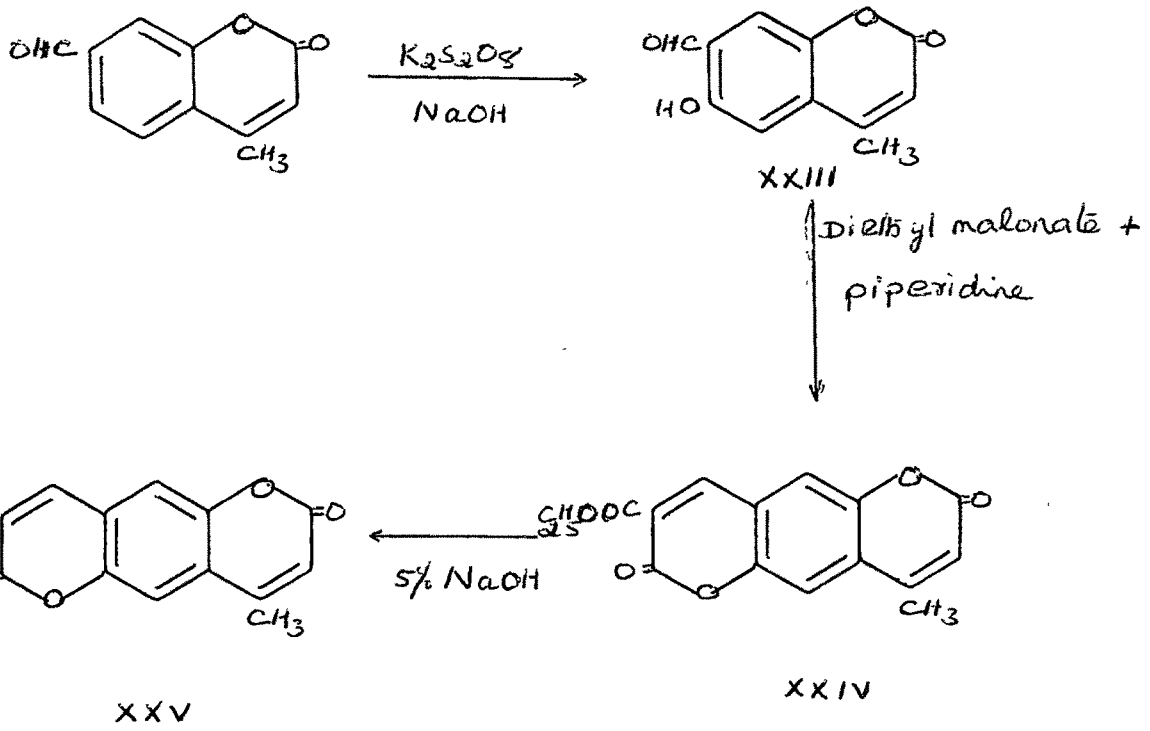
colouration with alcoholic ferric chloride solution.

The application of this reaction to coumarin derivatives has been studied by a number of workers and it has been shown that the oxidation takes place in the 6-position of the coumarin ring system[15]. 6-Hydroxy-7-formyl-coumarin structure (XXI) has therefore been assigned to the above oxidation product. This hydroxy coumarin was then condensed with diethylmalonate in the presence of a few drops of piperidine. The alkali insoluble product obtained was assigned 3'-carbethoxycoumarino-(6,7:6',5')α-pyrone structure (XXII). As the hydroxyformylcoumarin (XXI) was obtained in a very low yield, the hydrolysis and decarboxylation of the ester (XXII) could not be attempted. Attempts to carry out Perkin acetylation on (XXI) gave a polymeric product which was insoluble in various solvents and which did not melt.



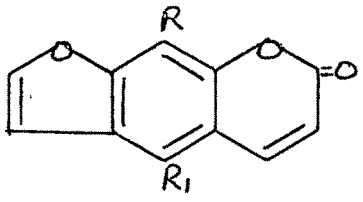
Attempted synthesis of 4-methylcoumarino(6,7:6',5')α-pyrone :

7-Formyl-4-methylcoumarin, synthesised from 7-bromomethyl-4-methylcoumarin as described in chapter II, on oxidation with potassium persulphate gave 6-hydroxy-7-formyl-4-methylcoumarin (XXIII). This was then condensed with diethylmalonate in the presence of a few drops of piperidine and 3'-carbethoxy-4-methylcoumarino(6,7:6',5') α-pyrone (XXIV) was obtained. This ester on hydrolysis with 5% sodium hydroxide solution gave 4-methyl-3'-carboxy-coumarino(6,7:6',5')α-pyrone (XXV). As this acid was obtained in very low yield, the decarboxylation could not be studied.

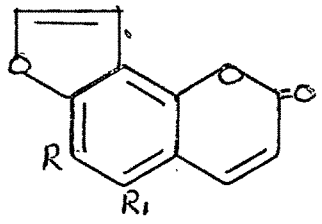


(B) Furocoumarins :

A number of furocoumarins have been isolated from plants. Psoralene, angelicin, bergapten, xanthotoxin, pimpinellin, isopimpinellin and oreoselone (XXVI, XXVII and XXVIII) are a few members of this group.



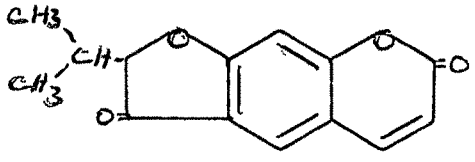
XXVI



XXVII

	R	R_1
Psoralene	H	H
Xanthotoxin	OMe	H
Bergapten	H	OMe
Isopimpinellin	OMe	OMe
Imperatorin	$OCH_2CH=C(Me)_2$	H

	R	R_1
Angelicin	H	H
Pimpinellin	OMe	OMe



XXVIII

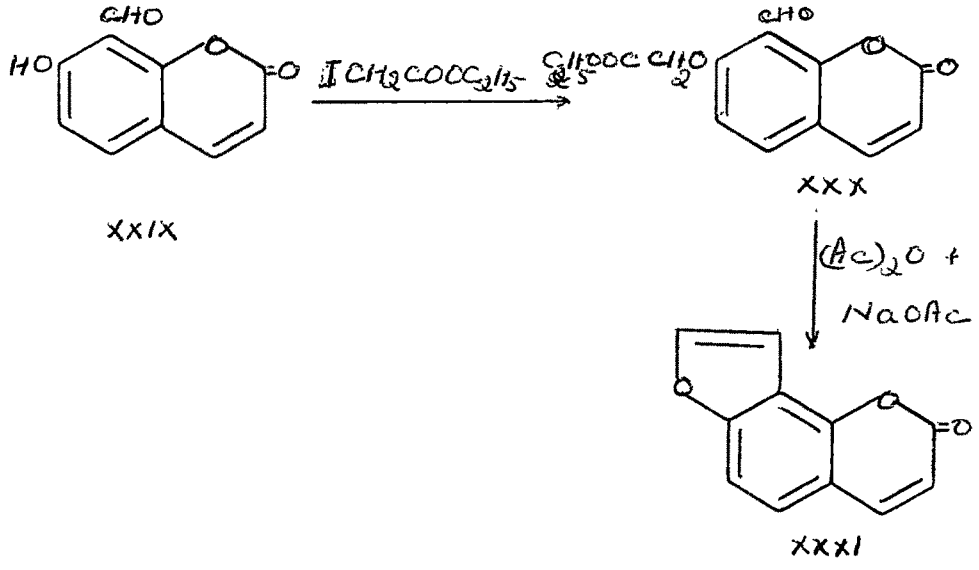
Oreoselone

Some furocoumarins such as bergapten, pimpinellin and isopimpinellin are toxic to fish and others such as psoralene, xanthotoxin, imperatorin and bergapten are found to be photosenzitizing agents. Furocoumarins such as

psoralene and imperatorin have also been found to have antifungal activity[16].

A furocoumarin can be synthesised (A) by building up a furan ring on a suitably substituted coumarin derivative or (B) by building an α-pyrone ring on an appropriate benzofuran derivative.

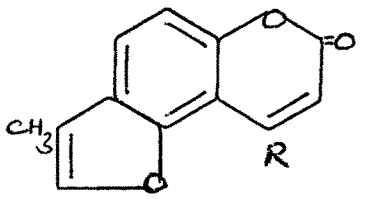
(A) 1. A very convenient method for the synthesis of a furocoumarin from a coumarin derivative is illustrated by the synthesis of angelicin by Späth and Pailer[17]. 7-Hydroxy-8-formylcoumarin (XXIX) was condensed with iodoacetic ester and the product obtained (XXX) was hydrolysed to the acid and cyclised in the presence of acetic anhydride to angelicin (XXXI).



Ethyl bromoacetate is generally used instead of ethyl iodoacetate. This method has been extensively used by later workers for the synthesis of a number of furocoumarins. A few examples are given below:

Shah and Shah[18] synthesised 3-methyl-furo-

(5',4':5,6)coumarin (XXXIIa) from 5-hydroxy-6-acetyl-3-carbethoxycoumarin. Chudgar and Shah[19] prepared 3',4'-dimethyl-furo(5',4':5,6)coumarin (XXXIIb) from 5-hydroxy-6-acetyl-4-methylcoumarin.

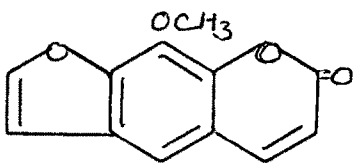


XXXII

(a) R = H

(b) R = CH_3

Rodighiero and Antonello[20] applied this method to the synthesis of xanthotoxin (XXXIII) from 7-hydroxy-8-methoxy-6-formylcoumarin.

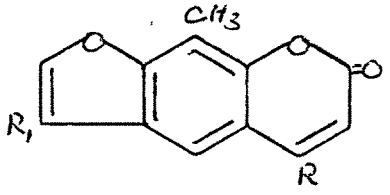


XXXIII

Limaye and Gangal[21] synthesised 4,3'-dimethyl-furo (5',4':7,6)coumarin from 7-hydroxy-6-acetyl-4-methyl-coumarin using the same procedure.

Trivedi and co-workers[22] have recently synthesised different alkyl psoralenes having alkyl or aryl substituents

in 4-position. 7-Hydroxy-6-acyl-4-alkyl or aryl-8-methyl-coumarin on condensation with ethyl bromoacetate followed by hydrolysis and subsequent cyclisation yielded different substituted psoralenes (XXXIV).

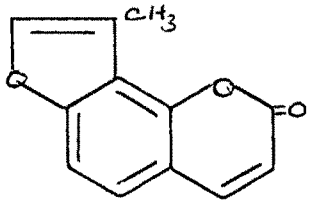


XXXIV

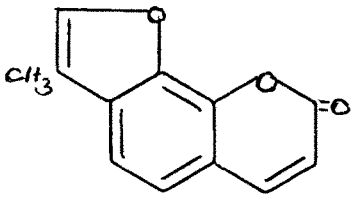
R = alkyl or aryl

R_1 = CH_3, C_2H_5 etc.

Using the above method, Shah and Shah[23] synthesised 3'-methyl-furo(5',4':7,8)coumarin (XXXV) from 7-hydroxy-8-acetylcoumarin.



XXXV



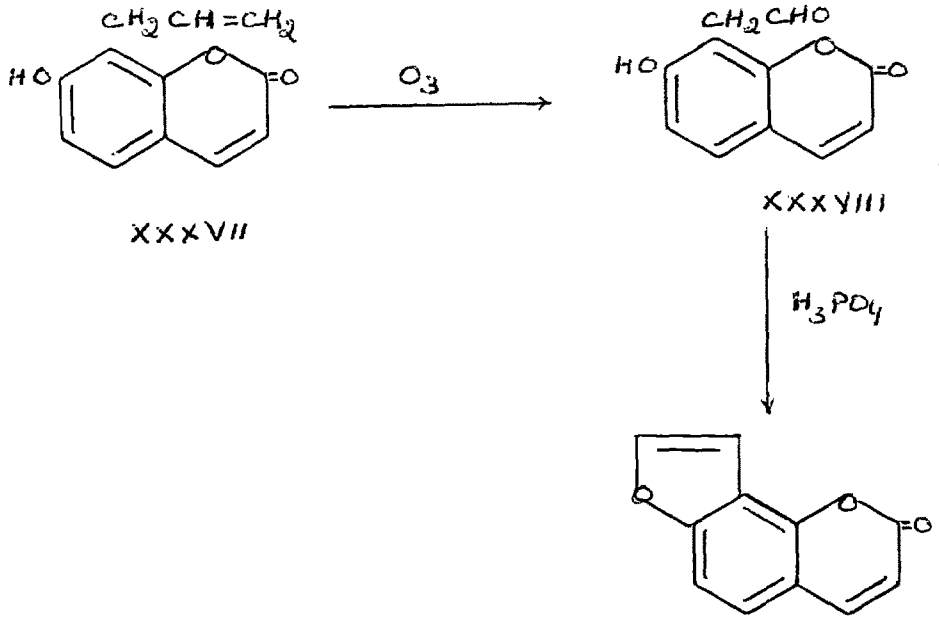
XXXVI

Mehta and Sethna[24] synthesised 3'-methyl-furo (5',4':8,7)coumarin (XXXVI) by condensing 8-hydroxy-7-acetylcoumarin with ethyl bromoacetate followed by hydrolysis and cyclisation.

Mehta[25] has also prepared 3',8-dimethyl-furo

(5',4':7,6)coumarin from 7-hydroxy-6-acetyl-8-methylcoumarin and 3',5-dimethyl-furo(5',4':7,8)coumarin from 7-hydroxy-8-acetyl-5-methylcoumarin.

(2). Seshadri and co-workers[26] have developed an interesting method for the synthesis of furocoumarins. They synthesised angelicin by subjecting 7-hydroxy-8-allylcoumarin (XXXVII) to ozonolysis and cyclised the 7-hydroxycoumarin-8-acetaldehyde (XXXVIII) formed with ortho phosphoric acid.

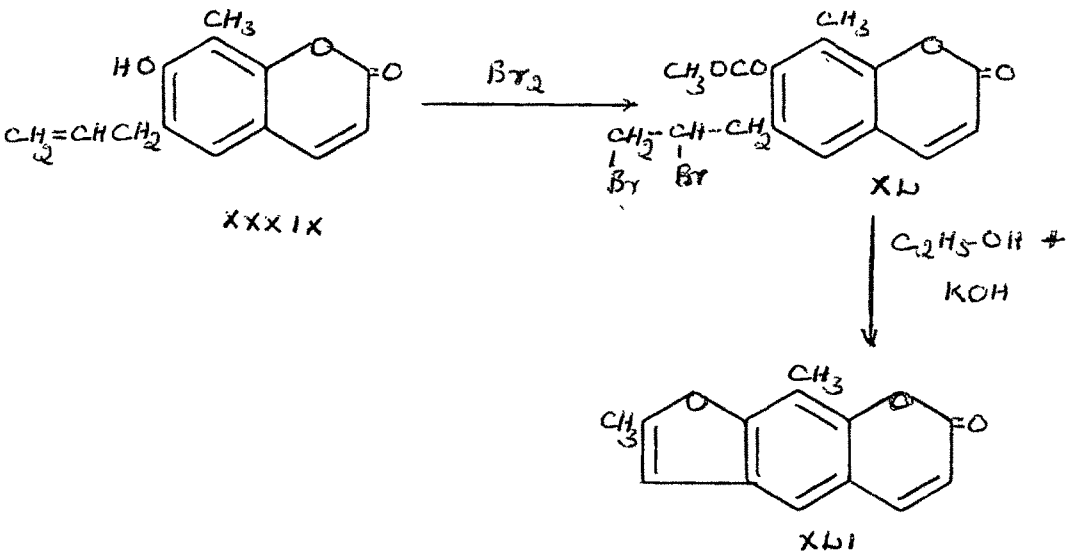


Pardanani and Trivedi[27] used this method for the synthesis of 8-methyl-4-phenyl-furo(5',4':7,6)coumarin from 7-hydroxy-4-phenyl-8-methylcoumarin-6-acetaldehyde.

Following the same procedure, Seshadri and co-workers[26] also synthesised psoralene and xanthotoxin.

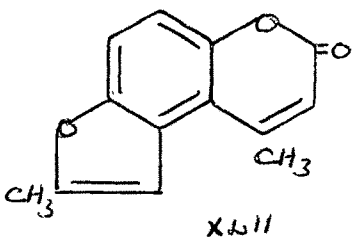
(3) Kaufman[28] has developed a versatile method which has proved useful in the synthesis of several furocoumarins. The synthesis of a dimethylpsoralene by this method is given below.

7-Allyloxy-8-methylcoumarin on Claisen rearrangement gave 7-hydroxy-6-allyl-8-methylcoumarin (XXXIX). This was then acetylated and brominated. The dibromo derivative (XL) was cyclised to get the psoralene derivative (XLI).

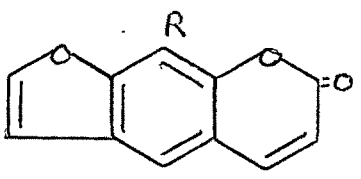


XXXIX XL XLI

This method was then extended to the synthesis of furo-2',4-dimethyl-(5',4':6,5)coumarin (XLII) from 6-hydroxy-5-allyl-4-methylcoumarin[29].



XLII

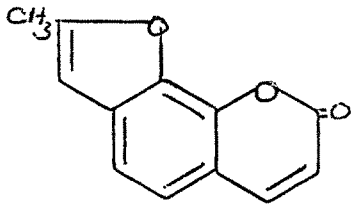


XLIII

R = Cl, Br, CN, NCCH3)2

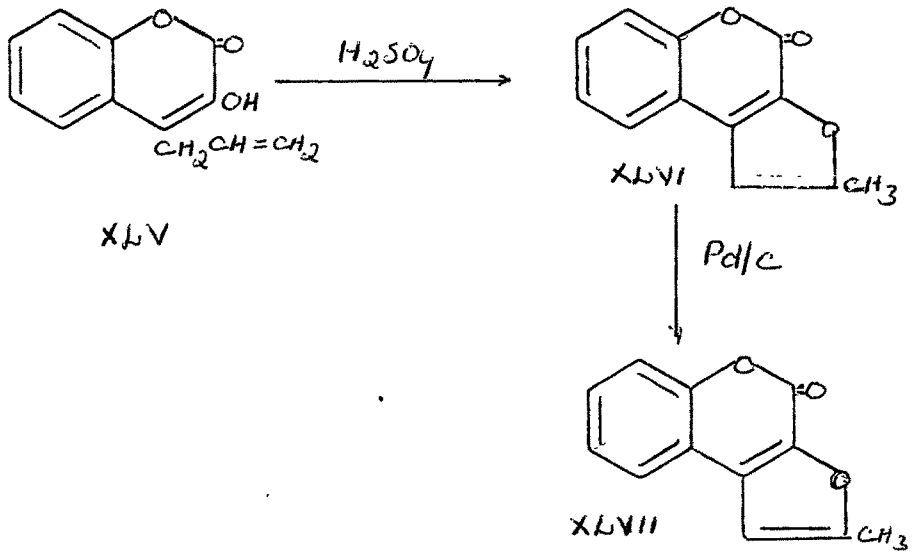
Kaufman and co-workers[30] synthesised psoralene derivative (XLIII) having different groups such as Cl, Br, CN and $N(CH_3)_2$ in the 8-position using 8-aminopsoralene as an intermediate product.

Kaufman and Russey[31] also synthesised 2'-methyl-furo(5',4':8,7)coumarin (XLIV) from 7-allyl-8-hydroxycoumarin by this method.

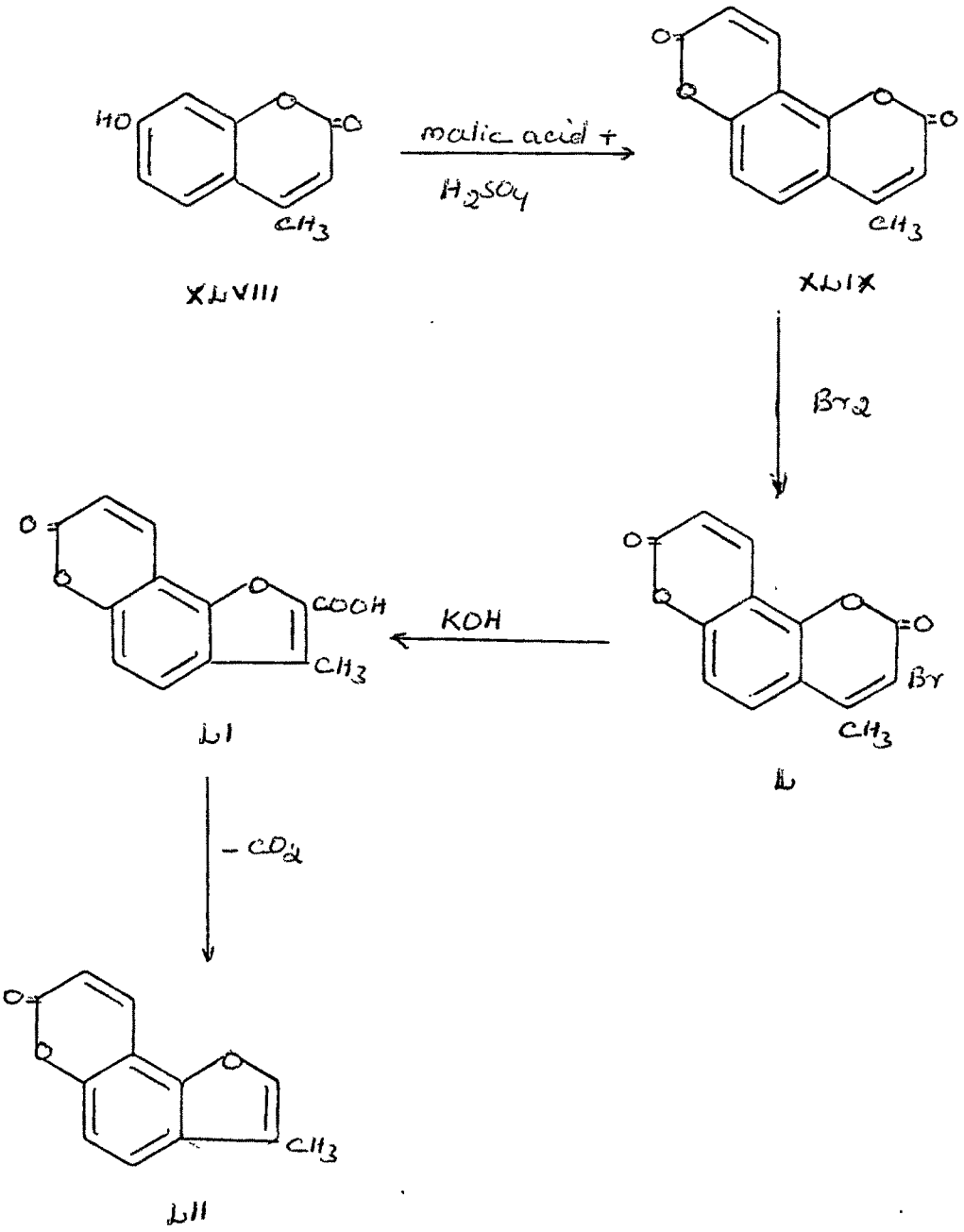


XLIV

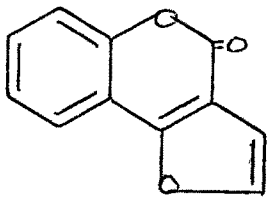
Shaikh and Trivedi[32] recently synthesised 2'-methyl-furo(5',4':3,4)coumarin (XLVII) from 3-hydroxy-coumarin. 3-Hydroxycoumarin was allylated and the allyloxy coumarin on Claisen rearrangement afforded 3-hydroxy-4-allylcoumarin (XLV) which was cyclised by treatment with concentrated sulphuric acid. The dihydrofurocoumarin (XLVI) was then dehydrogenated with palladised charcoal to 2'-methyl-furo(5',4':3,4)coumarin (XLVII).



4. Trivedi and Sethna[33] synthesised 3'-methyl-furo (5',4':5,6)coumarin (LII) using a different approach. The coumarino-α-pyrone (XLIX) obtained from 7-hydroxy-4-methyl-coumarin (XLVIII) was brominated and the 3-bromo derivative (L) obtained was treated with alcoholic potassium hydroxide and the acid (LI) decarboxylated.

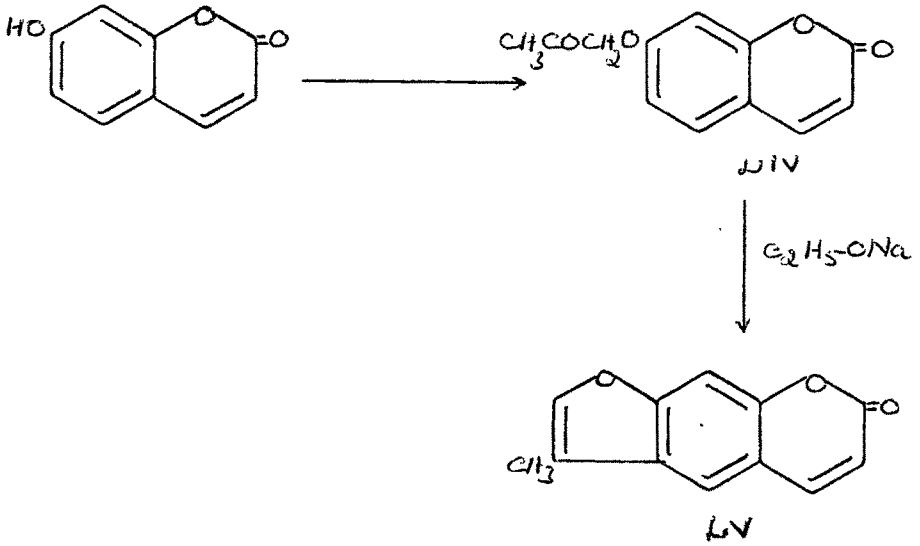


Dholakia and Trivedi[34] applied this method to the synthesis of furo-(5',4':4,3)coumarin (LIII) starting from 4-hydroxycoumarin.



LIII

Ray, Silooja and Vaid[35] prepared 3-methylpsoralene (LV) by the cyclisation of 7-acetonyloxycoumarin (LIV) with sodium ethoxide.



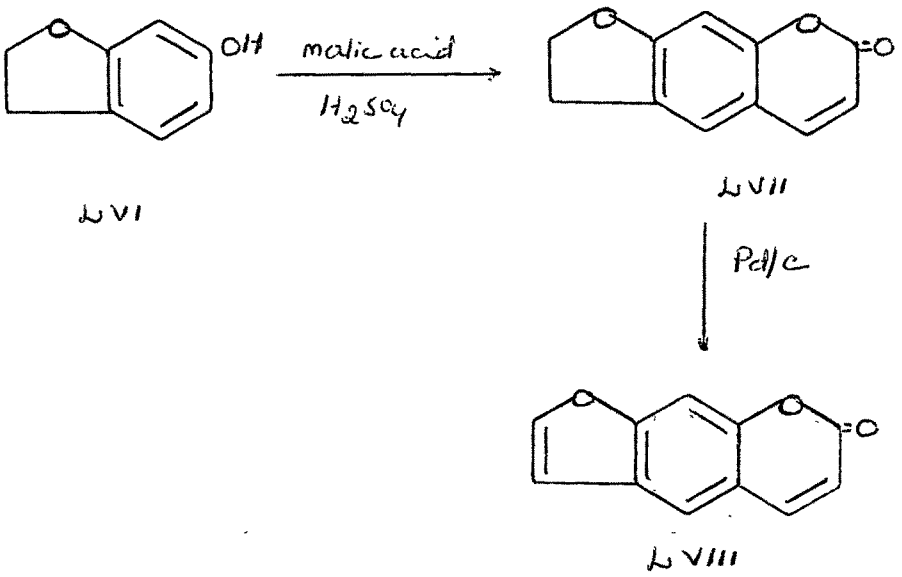
LIV

LV

(B) A few examples of the other approach viz. building up α-pyrone ring on a substituted benzo furan derivative may now be cited.

Späth et al.[36] carried out the condensation of 6-hydroxy-2,3-dihydro-benzofuran (LVI) with malic acid in

the presence of sulphuric acid and obtained 2,3-dihydropsoralene (LVII) which was dehydrogenated to psoralene (LVIII).

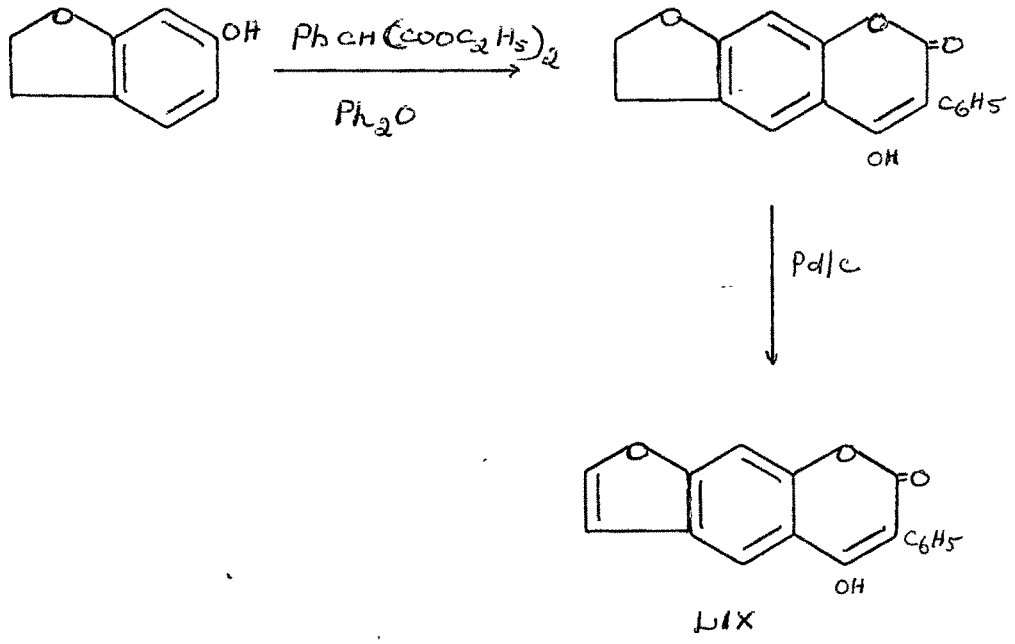


LVI LVII LVIII

Later, Horning and Reisner[37] prepared different 2,3-dihydropsoralenes by condensing 6-acetoxy-2,3-dihydrobenzofuran with a variety of β-ketonic esters in the presence of sulphuric acid. Esse and Christensen[38] have extended this reaction to obtain 6-alkyl-2,3-dihydro-5-methylpsoralene by condensing appropriate α-alkyl-β-ketonic ester with 6-acetoxy-2,3-dihydrobenzofuran.

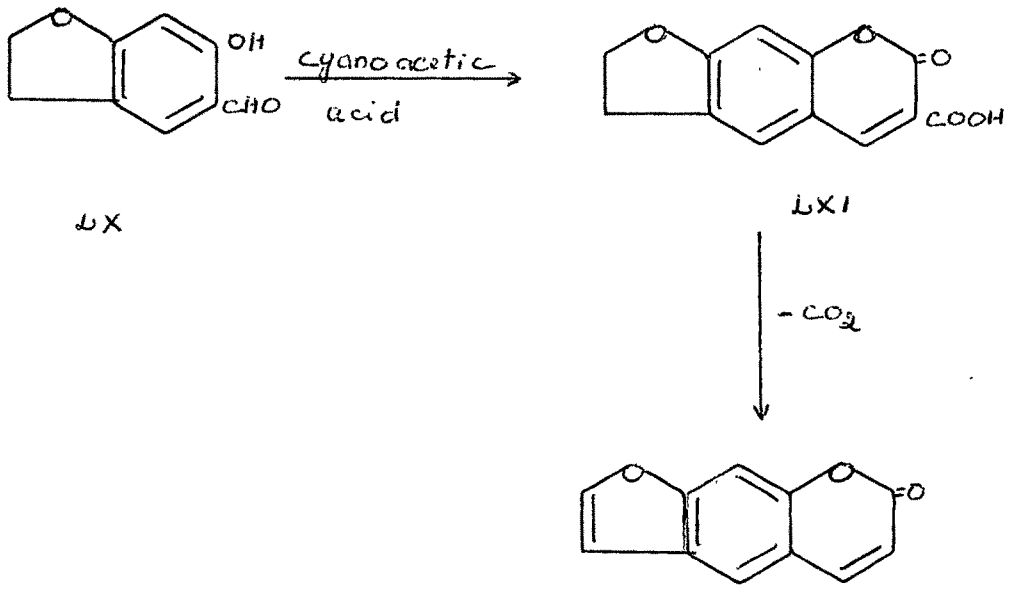
Goudau and Blanchecotte[39] synthesised 4-hydroxy-3-phenylpsoralene (LIX) from 6-hydroxy-2,3-dihydrobenzofuran.

Foster et al.[40] synthesised psoralene by first subjecting 6-hydroxy-2,3-dihydrobenzofuran to Gattermann formylation and then condensing the 5-formyl derivative (LX) with cyanoacetic acid under the conditions of



LIX

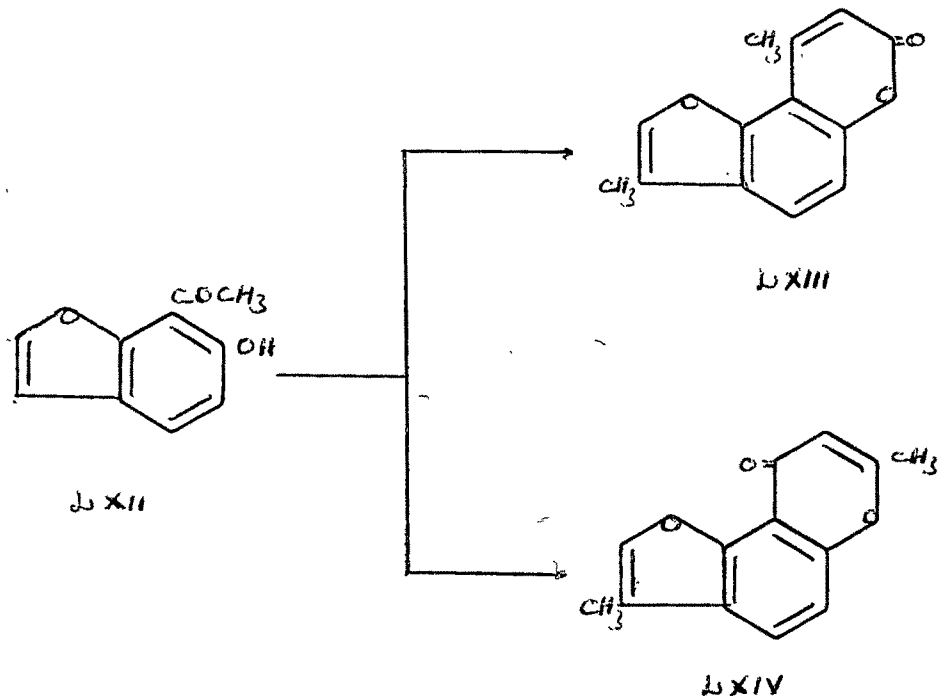
Knoevenagel reaction. The acid obtained (LXI) was decarboxylated and dehydrogenated to psoralene.



LX

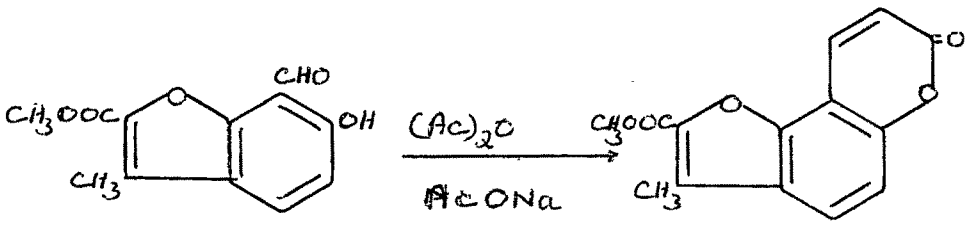
LXI

Limaye and Sathe[41] subjected 6-hydroxy-7-acetyl-3-methylbenzofuran (LXII) to Kostanecki-Robinson acetylation and obtained furo-3,4-dimethyl(5',4':5,6) coumarin (LXIII) in poor yield along with furo-2,3-dimethyl-(5',4':5,6) chromone (LXIV).



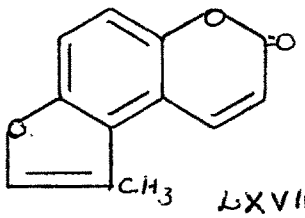
LXII LXIII LXIV

Salvi and Sethna[42] synthesised 2'-carbmethoxy-3'-methylfuro (5',4':5,6)coumarin (LXVI) from methyl-6-hydroxy-7-formyl-3-methylcoumarilate (LXV) by Perkin acetylation.



LXV LXVI

They also prepared 3'-methylfuro(5',4':5,6)coumarin (LXVII) from methyl-4-formyl-5-hydroxy-3-methylcoumarilate by Knoevenagel reaction with diethyl malonate.

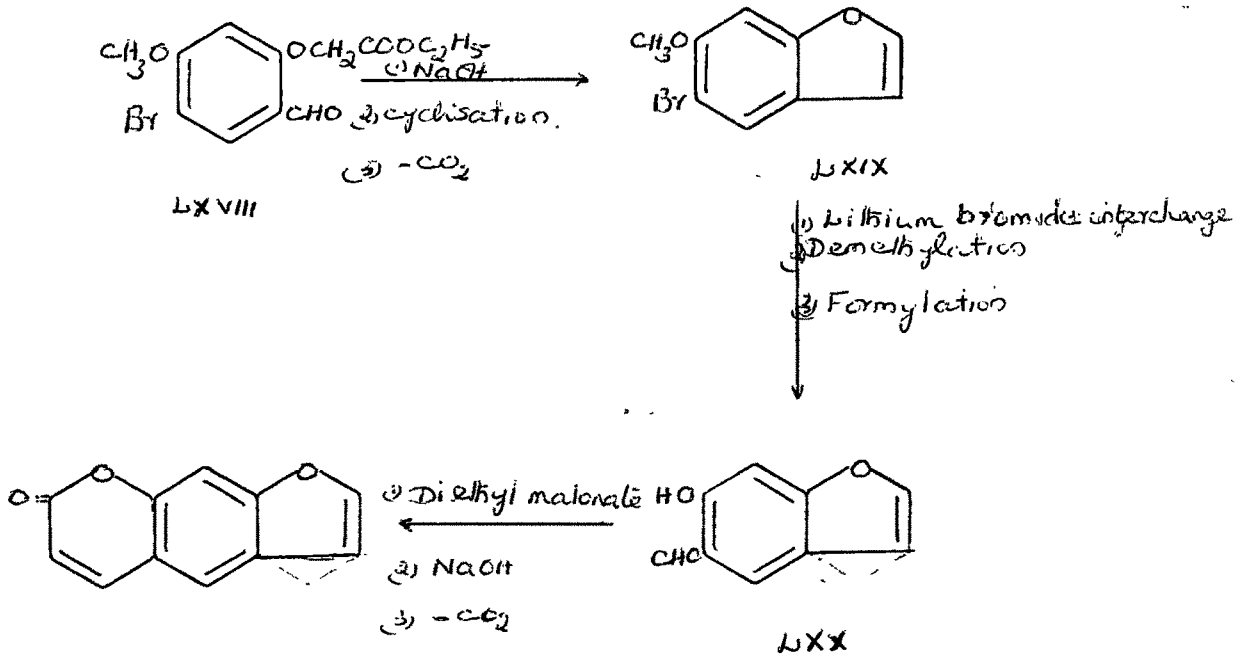


LXVII

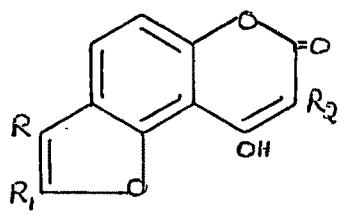
Limaye[43] synthesised angelicin by preparing 4-hydroxy-5-formylbenzofuran from 4-hydroxybenzofuran and then subjecting it to Perkin reaction.

Recently Kaufman and co-workers[44] have developed a new synthetic route to synthesise psoralens as follows. Bromination of ethyl(2-formyl-5-methoxyphenoxy)acetate gave the 4-bromo derivative (LXVIII) which was saponified and simultaneously cyclised and decarboxylated to 5-bromo-6-methoxybenzofuran (LXIX). Lithium bromide interchange and then formylation and demethylation gave 5-formyl-6-hydroxybenzofuran (LXX) which was condensed with

diethylmalonate to furnish psoralene after hydrolysis and decarboxylation of the condensation product.



Shaikh and Trivedi[45] have synthesised 4-hydroxy-furo(5',4';5,6)coumarin(LXXIa) by the action of sodium and ethyl carbonate on 6-hydroxy-7-acetylbenzofuran. Through a similar procedure the furocoumarins (LXXI b and c) were synthesised from 6-hydroxy-7-acetyl-3-methylbenzofuran and 6-hydroxy-7-propionyl-3-methylbenzofuran.



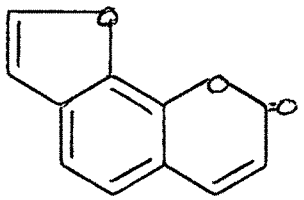
LXXI

(a) $R = R_1 = R_2 = H$

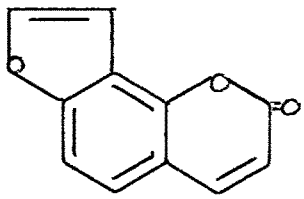
(b) $R = CH_3$, $R_1 = R_2 = H$

(c) $R = R_2 = CH_3$; $R_1 = H$

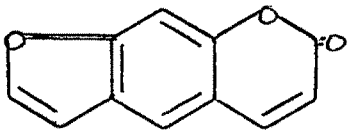
The following types of furocoumarins are theoretically possible.



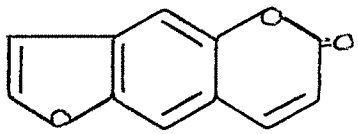
LXXII



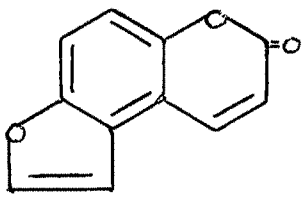
LXXIII



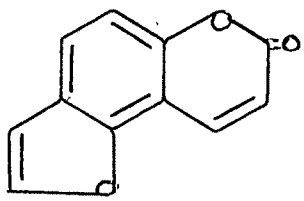
LXXIV



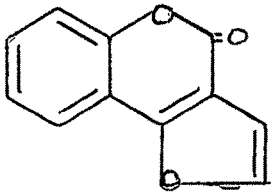
LXXV



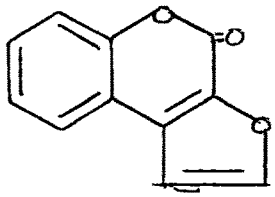
LXXVI



LXXVII



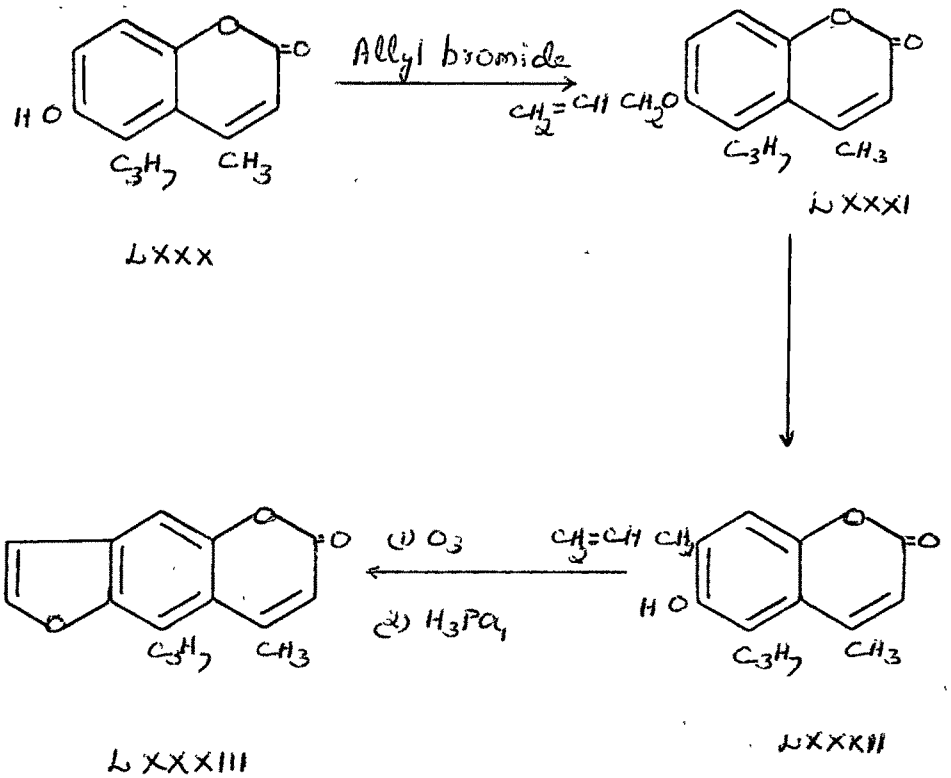
LXXVIII



LXXIX

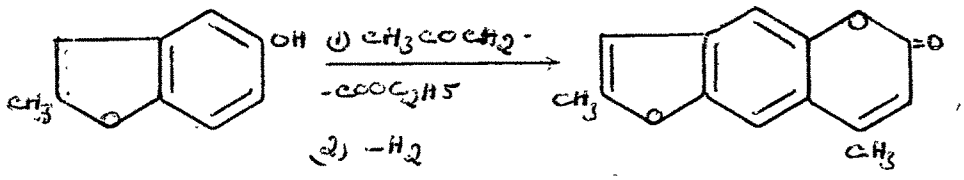
As will be seen from the previous discussion that many of these have been synthesised. However, as far as the type (LXXV) is concerned, the parent compound has not been synthesised. Only two derivatives, viz. 4-methyl-5-n-propyl-furo(5',4':6,7)coumarin (LXXXIII) and 2',4-dimethylfuro(5',4':6,7)coumarin (LXXXIV)have been synthesised by Kaufman et al.[30] as follows :

6-Hydroxy-5,n-propyl-4-methylcoumarin (LXXX) was allylated and the allyl ether (LXXXI) on Claisen rearrangement gave 7-allyl-6-hydroxy-5-n-propyl-4-methyl-coumarin (LXXXII). This on ozonolysis, [illegible] and heating with o-phosphoric acid gave 4-methyl-5-n-propyl-furo(5',4':6,7)coumarin (LXXXIII).



LXXX LXXXI LXXXII LXXXIII

2,4-Dimethyl-furo(5,4:6,7)coumarin (LXXXIV) was synthesised by the above authors from 5-hydroxy-2-methyl-2,3-dihydrobenzofuran by Pechmann reaction with ethyl acetoacetate and subsequent dehydrogenation.



LXXXIV

Attempted synthesis of furo(5,4:6,7)coumarin: (LXXV):

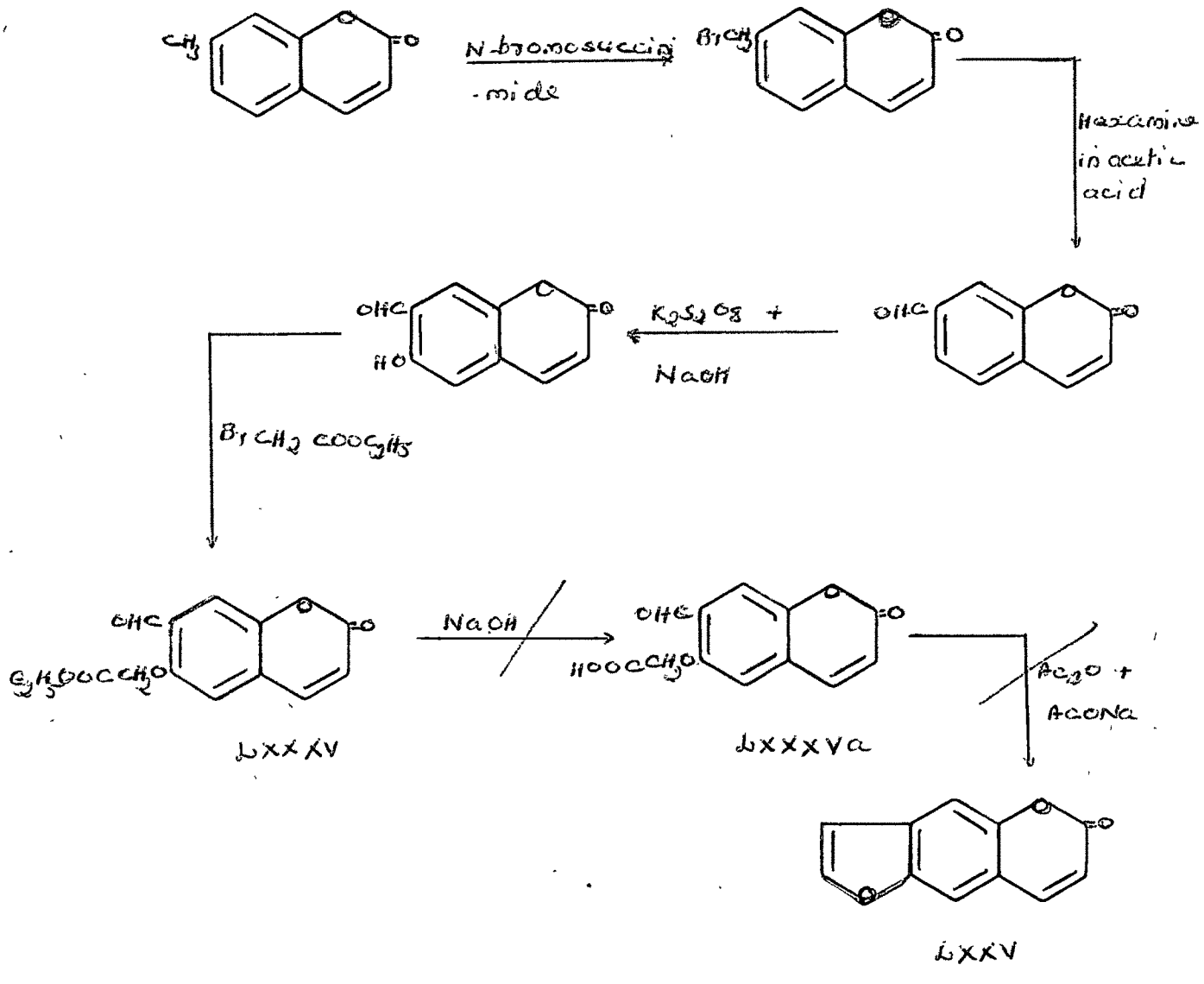
The parent furocoumarin (LXXV) cannot be synthesised directly from 6-hydroxycoumarin as it formylates in 5-position and the allyl group from 6-allylether migrates to the 5-position. The present work deals with a new approach to the synthesis of this furocoumarin from 7-methylcoumarin through the sequence of reactions given on the next page.

However, the hydrolysis of the ester (LXXXV) with 5 % sodium hydroxide gave an acid which does not correspond to the desired acid (LXXXVa). The structure of this acid has not been established.

Because of this difficulty in getting this acid Tanaka's[46] method of condensing an o-hydroxy aldehyde with ethyl bromomalonate in ethyl methyl ketone in the presence of anhydrous potassium carbonate, was tried.

6-Hydroxy-7-formylcoumarin, prepared as

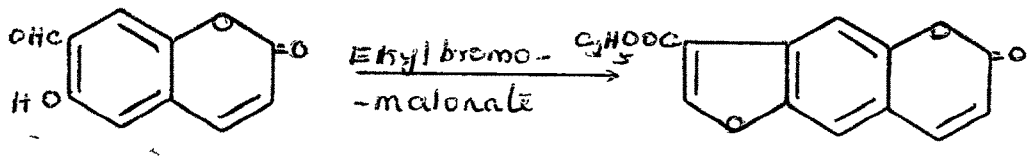
described before was condensed with ethyl bromomalonate in ethyl methyl ketone in the presence of anhydrous potassium carbonate. The solvent was then removed and the residue when treated with water gave a product which was insoluble in sodium hydroxide solution. 3-Carbethoxy-furo(5',4':6,7) coumarin structure (LXXXVI) has been assigned to this product. However, the hydrolysis and decarboxylation met with failure. Hydrolysis with sodium hydroxide gave a polymeric product and with concentrated sulphuric acid in the cold no hydrolysis took place.



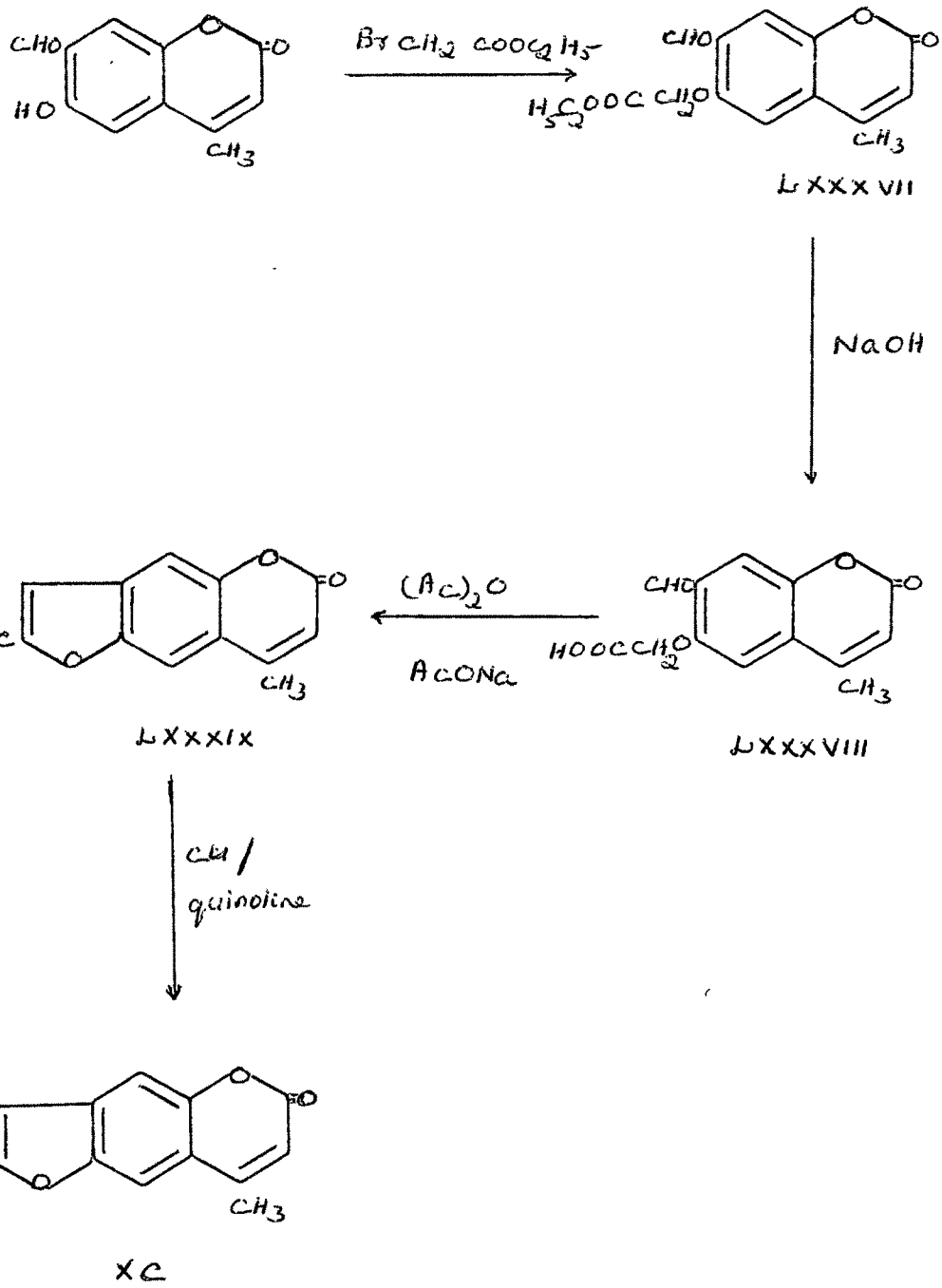
Synthesis of 4-methyl-furo(5',4':6,7)coumarin (XC) :

Although the removal of the carbethoxy group from the above compound was unsuccessful, it was thought of interest to see if 4-methylfuro(5',4':6,7)coumarin could be synthesised starting with 4-methyl-7-formyl-coumarin. It has been possible to achieve this synthesis through the following sequence of reactions.

6-Hydroxy-4-methyl-7-formylcoumarin, prepared as described before (p.103) was condensed with ethyl bromo-acetate in acetone in the presence of anhydrous potassium carbonate. On Removal of acetone and dilution of the residue with water afforded a product, which was insoluble in sodium hydroxide solution. 4-Methyl-6-carbethoxymethoxy-7-formylcoumarin (LXXXVII) thus obtained was hydrolysed by keeping it with 5 % sodium hydroxide solution for 24 hours to 6-carboxymethoxy-4-methyl-7-formylcoumarin (LXXXVIII). This acid on heating with sodium acetate and acetic anhydride underwent cyclisation to 3'-carboxy-4-methylfuro-(5',4':6,7)coumarin (LXXXIX). This was then decarboxylated to 4-methyl-furo(5',4':6,7)coumarin (XC) by refluxing in quinoline with copper bronze.



LXXXVI


CHO
HO
CH3
BrCH2COOC2H5
H5C2OOCCH2O
LXXXVII
NaOH
(Ac)2O
AcONa
HOOCCH2O
LXXXVIII
HOOC
LXXXIX
CH3
quinoline
XC

EXPERIMENTAL

6-Hydroxy-7-formylcoumarin :

A saturated aqueous solution of potassium persulphate (0.6 g.) was added during 4 hours to a well stirred solution of 7-formylcoumarin (1 g.) in sodium hydroxide. On the next day this solution was just acidified and filtered. The filtrate on heating on a steam bath for 30 minutes with excess of hydrochloric acid gave a product which crystallised from nitrobenzene in pale yellow prisms (0.25 g.), m.p. 268°. It gave reddish brown colour with alcoholic ferric chloride.

Analysis : Found : C, 62.94 ; H, 2.75 %.

$C_{10}H_6O_4$ requires : C, 63.16 ; H, 3.15 %.

3'-Carbethoxycoumarino(6',5':6,7)g-pyrone :

A mixture of 6-hydroxy-7-formylcoumarin (1 g.), diethyl malonate (0.67 g.) and piperidine (4 drops) was kept overnight. The reaction mixture was decomposed with ice cold hydrochloric acid (50 ml. ; 1:1). The product which separated was washed with dilute sodium hydroxide solution and crystallised from dilute acetic acid in pale yellow needles (0.55 g.), m.p. 295-97°.

Analysis : Found : C, 62.69 ; H, 3.25 %.

$C_{15}H_{10}O_6$ requires : C, 62.94 ; H, 3.49 %.

6-Hydroxy-4-methyl-7-formylcoumarin :

4-Methyl-7-formylcoumarin (1 g.) prepared as on (p.91) was dissolved in sodium hydroxide solution (15 ml. ; 10 %) by heating. A saturated aqueous solution

of potassium persulphate (1.6 g.) was added during 4 hours with continuous stirring and external cooling. After keeping this solution overnight, it was acidified to congo red. The precipitated unreacted substance was removed by filtration. The filtrate was treated with excess of hydrochloric acid and heated on a steam bath for 30 minutes. The product obtained crystallised from acetic acid in yellow needles (0.3 g.), m.p. 287°. It gave a reddish brown colour with neutral ferric chloride solution.

Analysis : Found : C, 64.54 ; H, 3.60 %.
$C_{11}H_8O_4$ requires : C, 64.71 ; H, 3.92 %.

3'-Carbethoxy-4-methylcoumarino(6',5':6,7)α-pyrone :

6-Hydroxy-4-methyl-7-formylcoumarin (1 g.) was mixed with diethylmalonate (0.62 g.) and three drops of piperidine. After keeping the reaction mixture for 24 hours it was decomposed with hydrochloric acid (1:1). The product which separated was washed with dilute sodium hydroxide solution and it crystallised from dilute acetic acid in pale yellow needles (0.6 g.), m.p.252°.

Analysis : Found : C, 63.93 ; H, 3.92 %.
$C_{16}H_{12}O_6$ requires : C, 64.00 ; H, 4.00 %.

3'-Carboxy-4-methylcoumarino(6',5':6,7)α-pyrone :

The above ester (0.5 g.) was mixed with sodium hydroxide solution (5 ml. ; 5 %) and kept overnight. The clear solution was then diluted and acidified. The separated acid was purified by taking it in sodium hydroxide solution.

The product obtained on acidification was crystallised from dilute acetic acid. M.P. 300°. Yield 0.3 g.

Analysis : Found : C,61.65 ; H,3.02 %.

$C_{14}H_8O_6$ requires : C,61.76 ; H,2.94 %.

6-Carbethoxymethoxy-7-formylcoumarin :

A solution of 6-hydroxy-7-formylcoumarin (1 g.) in dry acetone was refluxed with anhydrous potassium carbonate (3 g.) and ethyl bromoacetate (3 ml.) on a steam bath until the solution became colourless. The solid obtained on removal of acetone was treated with water. The separated product crystallised from benzene-petroleum ether in white needles (0.4 g.), m.p.128°.

Analysis : Found : C,60.91 ; H,4.66 %.

$C_{14}H_{12}O_6$ requires : C,60.87 ; H,4.34 %.

6-Carboxymethoxy-7-formylcoumarin :

The above ester (0.3 g.) was mixed with sodium hydroxide solution (5 ml. ; 5 %) and kept overnight. This was then diluted and acidified. The solid separated was extracted with sodium bicarbonate solution and the bicarbonate extract on acidification afforded a product. It crystallised from dilute acetic acid in white needles (0.1 g.), m.p. 178°.

Analysis : Found : C,57.38 ; H,3.68 %.

6-Carboxymethoxy-7-formylcoumarin

requires : C,58.06 ; H,3.22 %.

3'-Carbethoxyfuro(5',4':6,7) coumarin :

6-Hydroxy-7-formylcoumarin (1 g.) was dissolved in ethyl methyl ketone (50 ml.) by warming and ethyl bromo malonate (0.56 g.) and anhydrous potassium carbonate (3 g.) were added. This mixture was heated on a steam bath for 5 hours. The solvent was then removed and the residue was treated with water. The solid obtained crystallised from acetic acid in pale yellow needles (0.55 g.), m.p. 238°.

Analysis : Found : C,65.39 ; H, 3.89 %.
$C_{14}H_{10}O_5$ requires : C,65.12 ; H, 3.87 %.

6-Carbethoxymethoxy-4-methyl-7-formylcoumarin :

A solution of 6-hydroxy-4-methyl-7-formyl-coumarin (1.5 g.) in dry acetone was mixed with ethyl bromoacetate in the presence of anhydrous potassium carbonate and heated on a steam bath until the solution became colourless. Acetone was then removed and the residue was treated with excess of water. The solid obtained crystallised from benzene in white needles (0.75 g.), m.p. 173°.

Analysis : Found : C,62.19 ; H,4.97 %.
$C_{15}H_{14}O_6$ requires : C,62.07 ; H,4.82 %.

6-Carboxymethoxy-4-methyl-7-formylcoumarin :

The above ester (0.5 g.) was kept with sodium hydroxide solution (10 ml. ; 5 %) for 24 hours when a clear solution was obtained. This solution was then diluted and acidified. The precipitated acid crystallised from acetic acid in white tiny needles (0.39 g.), m.p.237°.

Analysis : Found : C, 59.14 ; H, 4.06 %.

$C_{13}H_{10}O_6$ requires : C, 59.54 ; H, 3.81 %.

3'-Carboxy-4-methylfuro(5',4':6,7)coumarin :

The above acid (0.5 g.) was heated with fused sodium acetate (2.5 g.) and acetic anhydride (5 ml.) for 2 1/2 hours directly on a wire gauze. The solid separating on adding the reaction mixture to water crystallised from dilute acetic acid, M.P. 320-25°. Yield 0.3 g. The product was soluble in sodium bicarbonate solution.

Analysis : Found : C, 63.98 ; H, 3.23 %.

$C_{13}H_8O_5$ requires : C, 63.93 ; H, 3.28 %.

4-Methylfuro(5',4':6,7)coumarin :

The above acid (0.45 g.) was refluxed with quinoline (5 ml.) and copper bronze (1 g.) for 1 hour. The solution was filtered hot and the filtrate on decomposition with ice cold hydrochloric acid gave a product which crystallised from dilute alcohol in yellow wooly needles (0.2 g.)m.p.186°.

Analysis : Found : C, 72.33 ; H, 4.08 %.

$C_{12}H_8O_3$ requires : C, 72.00 ; H, 4.00 %.

REFERENCES

1. H.A.Harbzsch and H.Zurcher., Ber., 20, 1328 (1887).
2. R.N.Sen and D.Chakravarti., J.Indian Chem.Soc., 6, 793 (1929).
3. S.Rangaswami and T.R.Seshadri., Proc.Indian Acad.Sci., 6A, 112 (1936).
4. H.G.Biswas., Science and Culture., 2, 225 (1936).
5. K.N.Trivedi and S.Sethna., J.Indian Chem.Soc., 40, 562 (1963).
6. V.N.Dholakia and K.N.Trivedi., Chem. and Ind., 4, 160 (1966).
7. N.M.Shah and R.C.Shah., J.Chem.Soc., 228, 1424 (1938).
8. D.B.Limaye and I.Ghate., Rasayanam., 1, 169 (1939).
9. A.Mustafa, O.H.Hsihmat, S.M.A.D. Zayed and A.A.Nawar., Tetrahedron., 19, 1831 (1963).
10. N.H.Pardanani, M.G.Parekh and K.N.Trivedi., J.Indian Chem.Soc., 47, 36 (1970).
11. A.Mustafa, N.A.Starkovsky and E.Zaki., J.Org.Chem., 26, 523 (1961).
12. R.H.Mehta., Indian J.Chem., 3(4), 186 (1965).
13. D.Chakravarti, R.Das and S.Bhattacharya., Sci.Cult., 36(10), 571 (1970).
14. Y.A.Shaikh and K.N.Trivedi., J.Indian Chem.Soc., 48(3), 237 (1971).
15. S.Sethna., Chem.Revs., 49, 91-101 (1951).
16. D.P.Chakraborty, A.D.Gupta and P.K.Bose., Ann.Biochem. Exp. Med., 17, 59 (1957) ; C.A. 52, 1352 (1958).

17. E.Spath and M.Pailer., Ber., 68B, 940 (1935).

18. H.A.Shah and R.C.Shah., J.Indian Chem.Soc., 17, 41(1940).

19. M.C.Chudgar and N.M.Shah., J.Univ.of Bombay., 13, pt. III, p. 15 (1944).

20. G.Rodighiero and C.Antonello., Ann.Chem.Rome., 46, 960 (1956).

21. D.B.Limaye and D.D.Gangal., Rasayanam., 1, 15 (1936).

22. N.H.Pardanani, M.G.Parekh and K.N.Trivedi., J.Indian Chem.Soc., 46, 1014 (1969).

23. D.N.Shah and N.M.Shah., J.Org.Chem., 19, 1938 (1954).

24. R.H.Mehta and S.Sethna., J.Indian Chem.Soc., 40, 384 (1963).

25. R.H.Mehta ., Indian J.Chem., 3(12), 574 (1965).

26. R.Aneja, S.K.Mukerjee and T.R.Seshadri., Tetrahedron., 4, 256 (1958).

27. N.H.Pardanani and K.N.Trivedi., J.Indian Chem.Soc., 48, 339 (1971).

28. K.D.Kaufman., J.Org.Chem., 26, 117 (1961).

29. K.D.Kaufman, J.F.W.Keana, R.C.Kelly, D.W.McBride and G.Slomp., J.Org.Chem., 27, 2567 (1962).

30. K.D.Kaufman, W.E.Russey and L.R.Worden., J.Org.Chem., 27, 875 (1962).

31. K.D.Kaufman and W.E.Russey., J.Org.Chem., 27, 670(1962).

32. Y.A.Shaikh and K.N.Trivedi., Current Science., 38, No. 17,409 (1969).

33. K.N.Trivedi and S.Sethna., J.Indian Chem.Soc., 40, 562 (1963).

34. V.N.Dholakia and K.N.Trivedi., J.Indian Chem.Soc., 43(12), 804 (1966).

35. J.N.Ray , S.C.Silooja and V.R.Vaid., J.Chem.Soc., 813 (1935).

36. E.Spath, B.L.Manjunath, M.Pailer and H.S.Jois., Ber., 69, 1087 (1936).

37. E.C.Horning and D.D.Reisner., J.Amer.Chem.Soc., 70, 3619 (1948).

38. R.E.Esse and B.E.Christensen., J.Org.Chem., 25, 1565 (1960).

39. A.V.Goudou and N.Blanchecotte., Compt.rend., ser.C., 263(3), 255 (1966).

40. R.T.Foster, A.Robertson and A.Bushra., J.Chem.Soc., 2254 (1948).

41. D.B.Limaye and N.R.Sathe., Rasayanam., 1, 87 (1937).

42. V.S.Salvi and S.Sethna., J.Indian Chem.Soc., 45, 439 (1968).

43. D.B.Limaye., Rasayanam., 1, 1-14 (1936).

44. L.R.Worden, K.D.Kaufman, J.A.Weiz and T.K.Schaaz., J.Org.Chem., 34, 2311 (1969).

45. Y.A.Shaikh and K.N.Trivedi., J.Indian Chem.Soc., 48, 1041 (1971).

46. S.Tanaka., J.Amer.Chem.Soc., 73, 872 (1951).