CHAPTER II

SOME STUDIES ON ALKYL COUMARINS

CHAPTER II

Some studies on alkyl-coumarins.

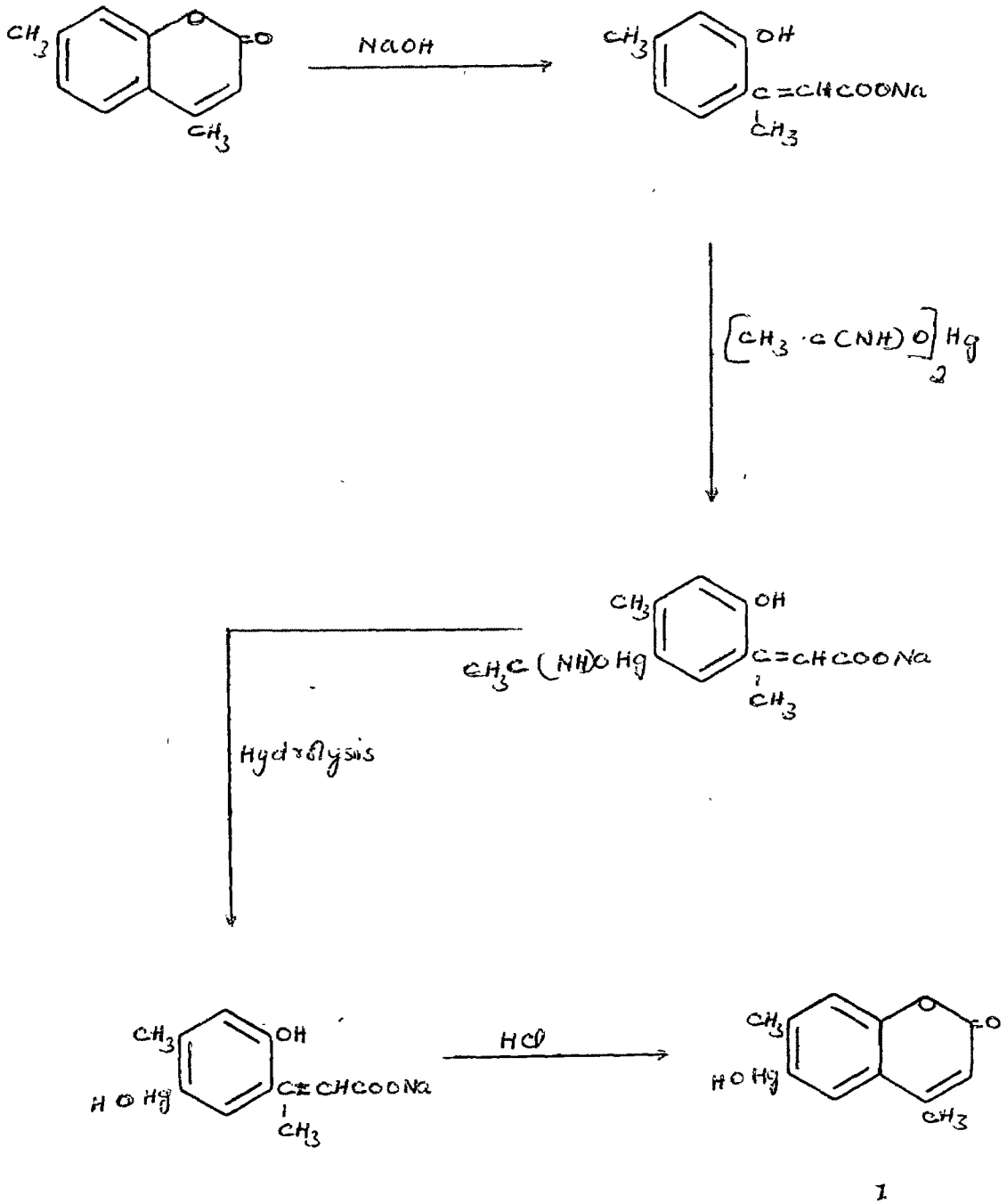
Theoretical

Extensive studies have been made on substitution in hydroxycoumarins and in building up additional heterocyclic rings on the hydroxycoumarins. The studies on substitution in alkylcoumarins have been comparatively fewer. As the present work deals with studies on 4,6-dimethyl-, 4,7-dimethyl-, 7-methyl- and 6-methylcoumarin, previous studies on substitution in these coumarins have been briefly reviewed here to illustrate the pattern of substitution and the types of studies made.

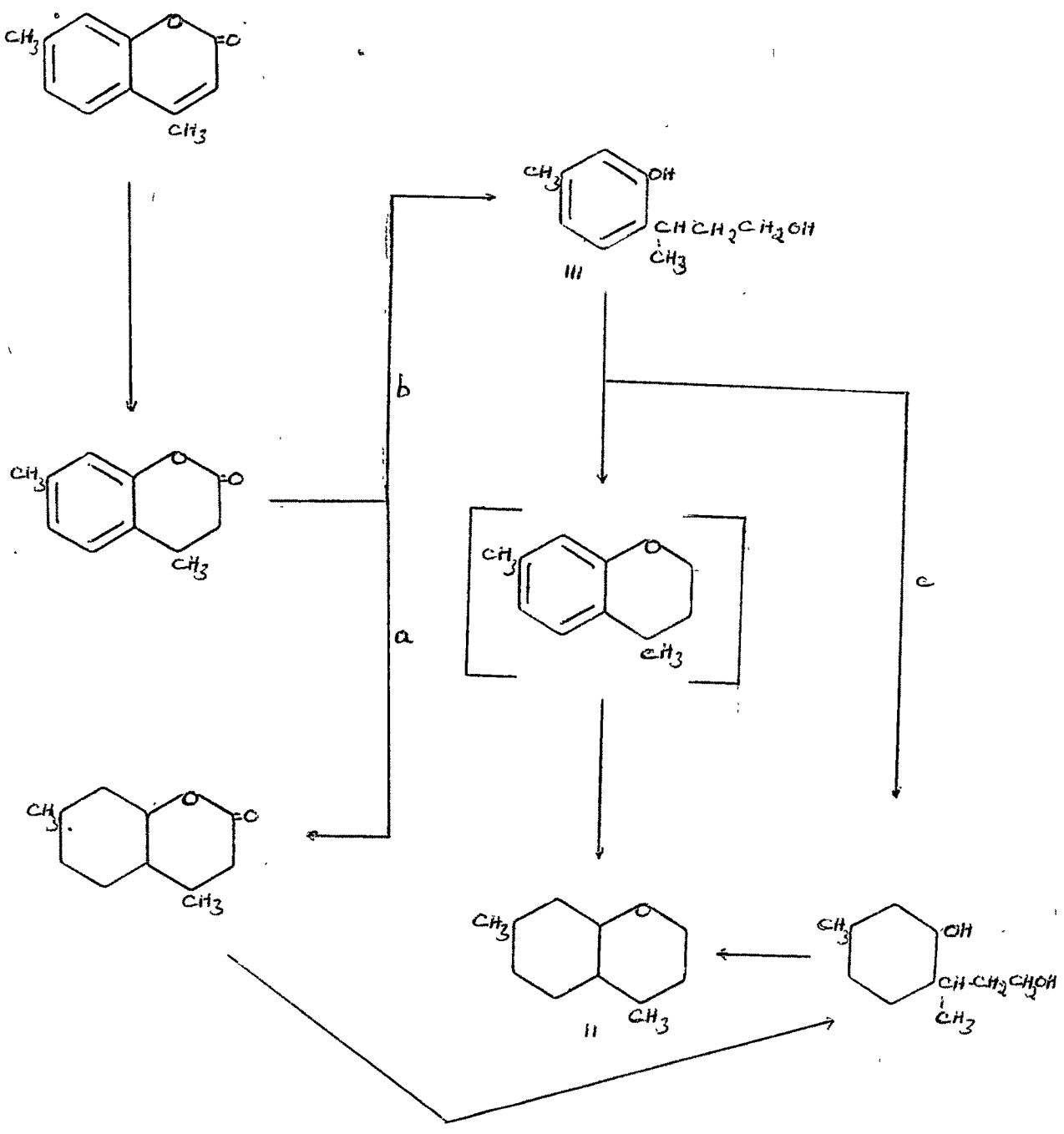
4,6-Dimethyl- and 4,7-dimethylcoumarin on sulphonation with sulphuric acid containing 20 % sulphur trioxide gave 4,6-dimethylcoumarin-8-sulphonic acid and 4,7-dimethylcoumarin-6-sulphonic acid respectively[1]. Their sulphonyl chlorides on reduction with zinc and hydrochloric acid yielded 4,6-dimethylcoumarin-8-thiol and 4,7-dimethylcoumarin-6-thiol.

4,6-Dimethyl- and 4,7-dimethylcoumarin on mercuration with mercury acetamide in alkaline solution yielded 4,6-dimethyl-8-hydroxy mercury- and 4,7-dimethyl-6-hydroxy mercurycoumarin[2] (I).

Sastri and Seshadri[3] carried out mercuration of 4,7-dimethylcoumarin with mercury acetate in methanol and obtained 3,6-diacetoxy mercury-4,7-dimethyl-4-methoxy



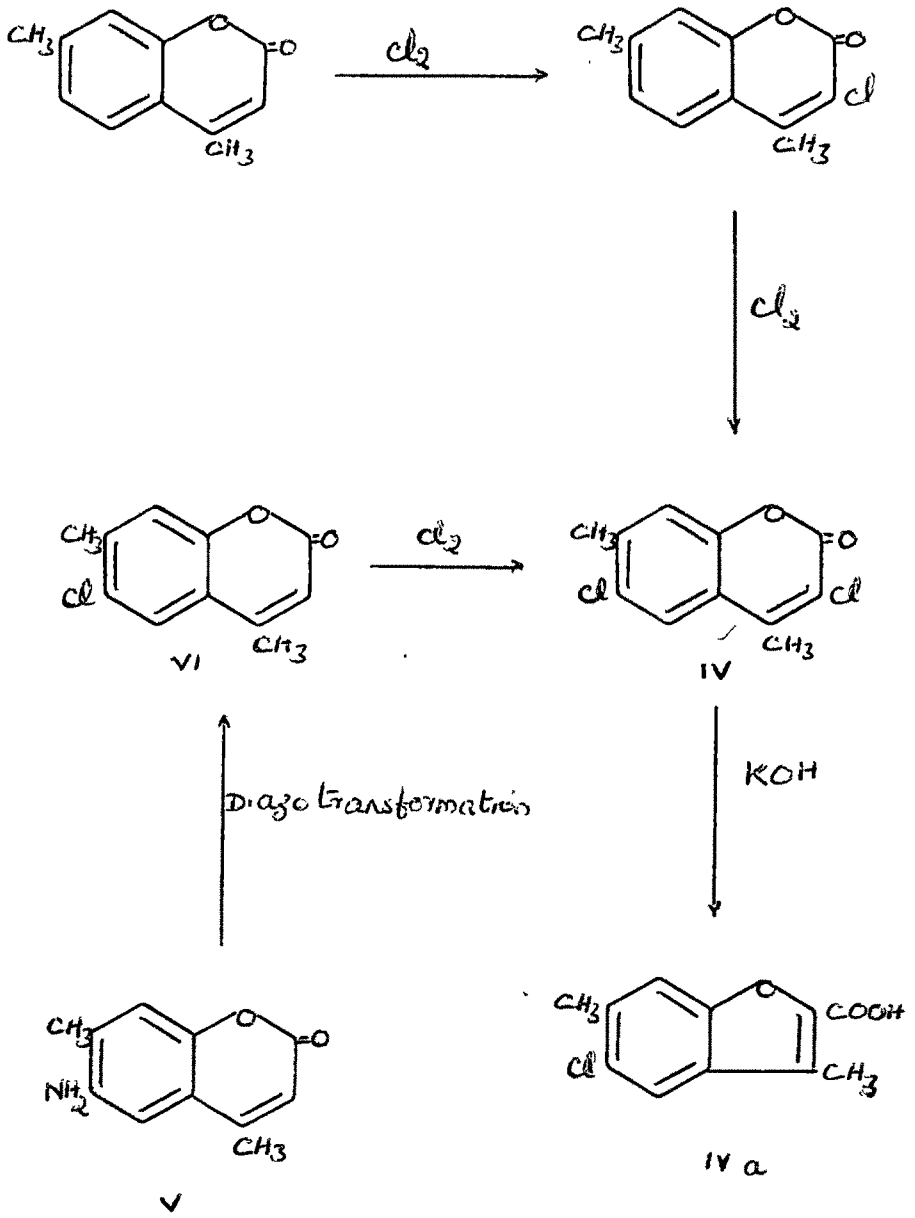
1


III
II
a
b
c

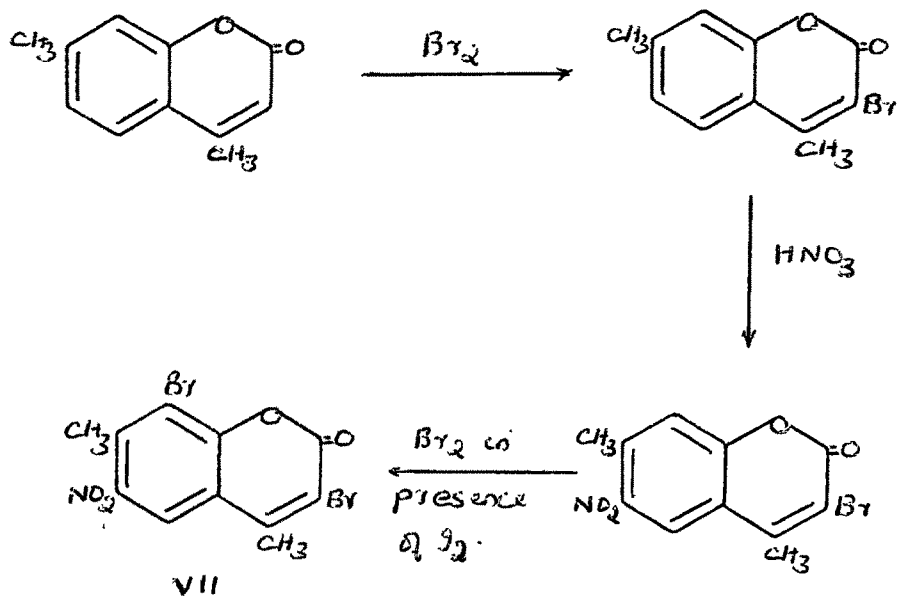
The isolation of the phenolic alcohol (III) seems to indicate that the formation of the cyclic ether from coumarin occurs by hydrogenation of the ester group in the normal manner giving the dihydroxy compound, followed by the dehydration of the latter. Similarly, 7-methylcoumarin gave 2-(γ-hydroxypropyl)-5-methylphenol on hydrogenation with Raney nickel and 6-methylcoumarin gave the 4-methyl isomer.

Halogenation of alkyl coumarins has been studied by Dey and Dalal[8]. They observed that the introduction of a halogen atom directly into the benzenoid part of the coumarin molecule is not possible because the substitution occurs in the lactone ring which is more susceptible to attack. The diazotransformation of aminocoumarins which are readily obtained by the nitration and reduction of coumarins is employed in the preparation of substituted coumarins with the halogen in the benzenoid part. They found that when 4,7-dimethylcoumarin was chlorinated or brominated, the first halogen atom enters the pyrone ring in accordance with the usual rule. This was proved by the behaviour of the compound with alcoholic potash, which removed the halogen atom and gave 2,5-dimethylcoumarilic acid. On further chlorination, a dichloro derivative (IV) was produced which lost a molecule of hydrogen chloride and yielded a monochloro dimethylcoumarilic acid (IVa) when heated with boiling alcoholic potash. In this way, they proved that the second atom of chlorine is evidently attached to the benzene ring. Its position was determined

by the preparation of the same compound from 6-amino-4,7-dimethylcoumarin (V) by the diazotransformation and further chlorination of the product (VI).



Dey and Row[9] in their study of bromonitrocoumarins, carried out the nitration and bromination of 4,7-dimethylcoumarin and obtained the 3,8-dibromo-6-nitro derivative (VII) through the following sequence of reactions.

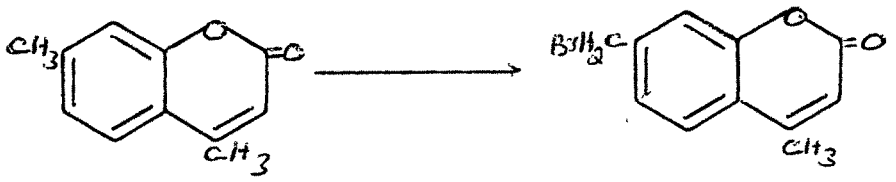


VII

6-Methylcoumarin gave a dibromo derivative the structure of which was not established, on bromination with bromine in carbon disulphide[6].

Sastri and Seshadri[3] brominated 4,7-dimethylcoumarin to 3,6-dibromo-4,7-dimethylcoumarin which was then converted by refluxing with alcoholic potassium hydroxide into 2,5-dimethyl-4-bromocoumarilic acid. The action of N-bromosuccinimide on methylated coumarin has been extensively studied by Lecocq and Buu-Hoi[10,11]. They observed that N-bromosuccinimide reacts only with the methyl group in the benzene ring but not with the methyl group in

the heterocyclic ring. Thus they prepared 4-methyl-7-bromomethyl(VIII) , 4-methyl-6-bromomethyl-, and 6-bromomethylcoumarin.



During these reactions Lacocq and Buu-Hoi never observed nuclear bromination on the ortho or the para position to the hetero oxygen atom.

Taunk et al.[12] synthesised the 3-aryl derivative of 4,6-dimethylcoumarin by the application of Meerwein reaction on 4,6-dimethylcoumarin.

Chloromethylation of coumarins :

In the course of the present work the chloromethylation of some alkyl coumarins has been studied with a view to see the pattern of substitution as both the steric and polar effects of the methyl group would play their role in directing the incoming group in addition to the other factors. Further, chloromethylation is an excellent tool in the synthetic work as the chloromethyl group undergoes substitution reactions with various reagents, for example, the chlorine of the chloromethyl group can be replaced by hydroxy,cyano,methoxy,acetoxy or other groups by treating it with appropriate reagents.

Further, on Sommelet reaction, the chloromethyl group can be replaced by the formyl group. On oxidation, the chloromethyl derivative is readily converted into the corresponding acid and on reduction it gives rise to the methyl derivative.

Mannich bases which are compounds of potential therapeutic value are obtained from the chloromethyl derivatives on condensation with various secondary amines such as dimethylamine, diethylamine, morpholine etc.

A survey of chloromethylation upto 1941 has been made by Fuson and McKeever[13] and some of the more recent work has been reviewed by Olah and Tolgyesi[14]. These authors have reviewed in detail the various aspects of chloromethylation such as the application of this reaction to various classes of compounds, the mechanism of this reaction advanced by different workers, and the role of the solvents, catalysts and temperature in this reaction.

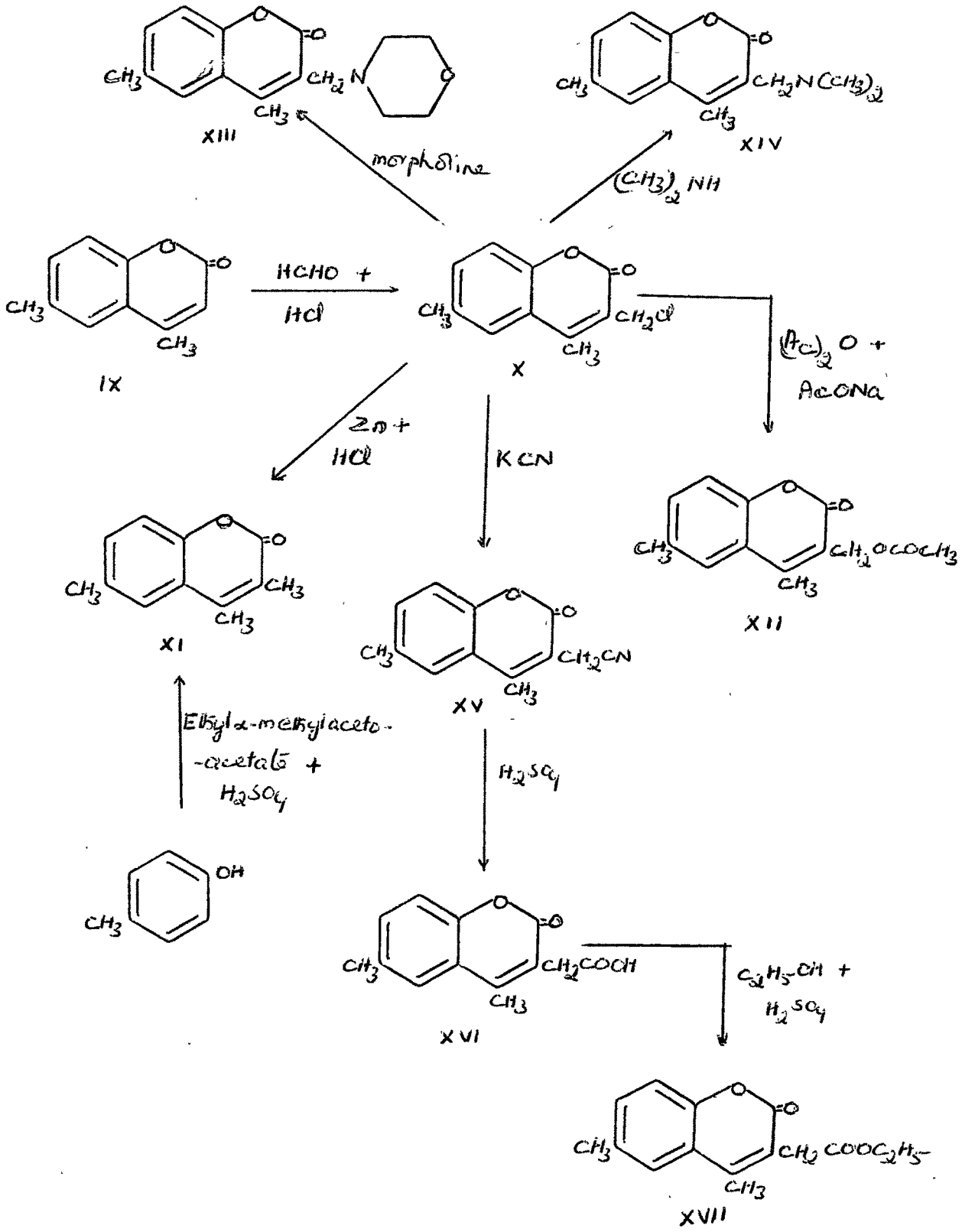
Chloromethylation of a number of coumarin derivatives has been studied by Sethna and co-workers[15,16]. Coumarin, 4-methylcoumarin and 7,8-dimethoxy-4-methylcoumarin gave 3-chloromethyl derivatives. 5-Methoxy-4-methylcoumarin gave the 3,8-dichloromethyl derivative. 7-Methoxy-4-methylcoumarin gave under different conditions, 6-chloromethyl,3,8-dichloromethyl- and 3,6,8-trichloromethyl derivatives. 6-Hydroxy-4-methylcoumarin gave the 5-chloromethyl derivative. Its methyl ether gave the 3,7-dichloromethyl derivative. The chloromethylation of some other substituted coumarinssuch as methyl-7-hydroxy-

4-methyl- and methyl-5-hydroxy-4-methylcoumarin-6-carboxylate and 4'-methyl-1,2-naphtha-α-pyrone have also been studied. The chloromethyl derivatives were reduced to the corresponding methyl derivatives and compared with the methyl coumarins of known orientation. Chloromethylation of alkyl substituted coumarins has not been reported so far. Dey and Radhabai[17] observed that chlorination of 7-methylcoumarin-4-acetic acid and 6-methylcoumarin-4-acetic acid in hot acetic acid with a stream of chlorine led to simultaneous chlorination and decarboxylation with the formation of 7-methyl-4-chloromethyl- and 6-methyl-4-chloromethylcoumarins respectively.

The present work deals with the chloromethylation of 4,6-dimethyl-and 4,7-dimethylcoumarin.

Chloromethylation of 4,6-dimethylcoumarin :

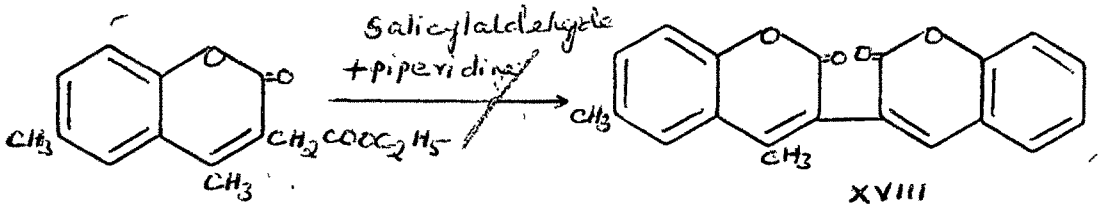
4,6-Dimethylcoumarin (IX) on chloromethylation with 1 mole of paraformaldehyde in acetic acid at room temperature did not give a pure product. But at 70°, in the presence of fused zinc chloride, it gave a monochloromethyl derivative which on reduction with zinc and hydrochloric acid gave 3,4,6-trimethylcoumarin (XI), identical with the known 3,4,6-trimethylcoumarin prepared by the Pechmann reaction of p-cresol with ethyl-α-methyl acetoacetate. 4,6-Dimethyl-3-chloromethylcoumarin structure (X) has been therefore assigned to the chloromethyl product.


XIII
morpholine
XIV
$(CH_3)_2NH$
IX
HCHO +
HCl
X
$(Ac)_2O$ +
AcONa
Zn +
HCl
KCN
XI
XII
XV
Ethyl α-methylaceto-
-acetate +
H_2SO_4
H_2SO_4
XVI
C_2H_5OH +
H_2SO_4
XVII

On heating with acetic anhydride in the presence of fused sodium acetate, the chloromethyl derivative gave 4,6-dimethyl-3-acetoxymethylcoumarin (XII). When heated with hexamine in chloroform or in acetic acid, the product obtained was not the 3-formyl derivative. It did not give a 2,4-dinitro phenylhydrazone nor did the analysis correspond to that for 4,6-dimethyl-3-formylcoumarin. The structure of this product has not been established. 4,6-dimethyl-3-chloromethylcoumarin on reaction with morpholine and dimethylamine in dry benzene gave the corresponding Mannich bases (XIII,XIV).

As mentioned in the general introduction the Mannich bases from coumarins have been found to act as central nervous system stimulants[18]. A number of Mannich bases have therefore been prepared in the course of this work and their physiological properties are being investigated.

On heating with alcoholic potassium cyanide, the chloromethylcoumarin afforded 4,6-dimethyl-3-cyanomethyl coumarin (XV) which was then hydrolysed with 70 % sulphuric acid to 4,6-dimethylcoumarin-3-acetic acid (XVI). This acid was converted into ethyl 4,6-dimethylcoumarin-3-acetate (XVII) by heating with ethyl alcohol in the presence of concentrated sulphuric acid. Attempt was then made to synthesise 4,6-dimethyl-3,3'-bicoumarinyl (XVIII) from this ester by condensing it with salicylaldehyde in the presence of piperidine.

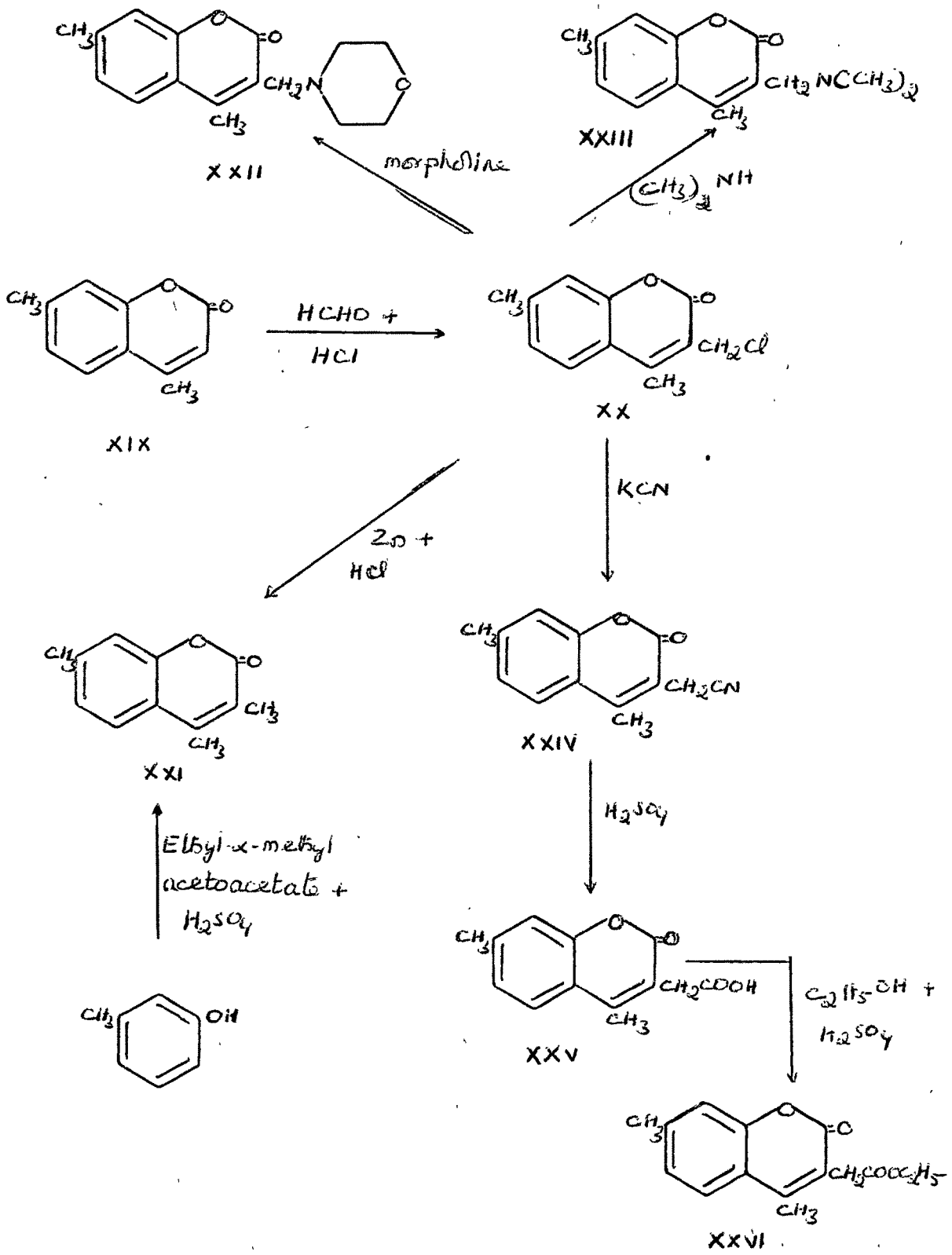


But the condensation did not take place even on long heating and the original ester was obtained back.

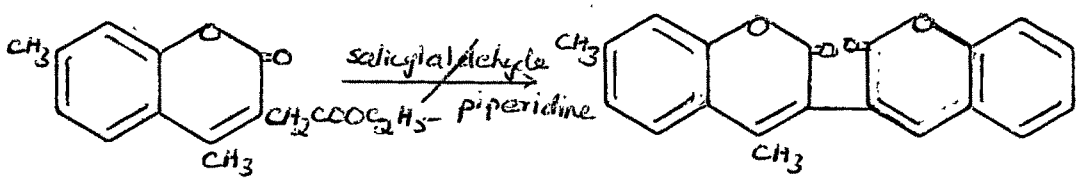
Chloromethylation of 4,7-dimethylcoumarin :

4,7-Dimethylcoumarin (XIX) on chloromethylation in acetic acid at 70° in the presence of fused zinc chloride gave a monochloromethyl derivative (XX) which on reduction with zinc and hydrochloric acid afforded 3,4,7-trimethylcoumarin (XXI) identical with 3,4,7-trimethylcoumarin prepared by the Pechmann reaction between m-cresol and ethyl-α-methyl-acetoacetate. The product (m.p. 193°) obtained on heating the chloromethyl derivative with hexamine in acetic acid or chloroform was not the 3-formyl derivative. It did not give a 2,4-dinitrophenyl hydrazone nor did the analysis correspond to that for 4,7-dimethyl-3-formylcoumarin. The structure of this product has not been ascertained.

4,7-Dimethyl-3-chloromethylcoumarin, on reaction with morpholine and dimethylamine in dry benzene gave the corresponding Mannich bases (XXII,XXIII) . 4,7-Dimethyl-3-cyanomethylcoumarin (XXIV) was prepared by heating 4,7-dimethyl-3-chloromethylcoumarin with alcoholic potassium


XXII
morpholine
XXIII
$(CH_3)_2NH$
XIX
HCHO + HCl
XX
KCN
Zn + HCl
XXIV
XXI
H_2SO_4
Ethyl-α-methyl acetoacetate + H_2SO_4
XXV
C_2H_5OH + H_2SO_4
XXVI

cyanide. This cyanomethylcoumarin was hydrolysed with 70 % sulphuric acid to 4,7-dimethylcoumarin-3-acetic acid (XXV). This acid was esterified with ethyl alcohol in the presence of concentrated sulphuric acid and the condensation of the ester (XXVI) thus obtained, with salicylaldehyde in the presence of piperidine to get the bicoumarinyl derivative (XXVII) was attempted. But no condensation took place even on prolonged heating.



XXVI XXVII

Chloromethylation of 7-methyl-and 6-methylcoumarin was attempted under different conditions using zinc chloride as catalyst but no pure chloromethyl derivative could be isolated from the reaction mixture.

Studies on some bromomethylcoumarins :

Bromomethylcoumarins are as important as the chloromethyl derivatives as the bromomethyl group undergoes similar reactions with various reagents as the chloromethyl group. The previous work on the synthesis and utilization of bromomethylcoumarinsfor further synthetic work may be briefly described here.

Dey and Radhabai[17] reported the formation of two products in bromination of 7-methylcoumarin-4-acetic acid with 50 % bromine in acetic acid viz. 7-methylcoumarin-4-bromoacetic acid and 7-methyl-4-bromomethylcoumarin. Similarly 6-methylcoumarin-4-acetic acid also gave 6-methylcoumarin-4-bromo acetic acid and 6-methyl-4-bromomethylcoumarin. Several attempts were made by them to confirm the 4-bromomethylcoumarin structure. Their attempts to replace the halogen by OH, NH_2 and C_6H_5NH groups by treatment with appropriate reagents were unsuccessful. Even by heating the bromomethylcoumarin with moist silver oxide at 100° for 5 hours, the halogen was not removed. Aqueous alkali, however, eliminated the halogen completely in the course of a few minutes. This difference was explained by the fact that the alkali does not initially attack the bromine, but that it is the pyrone ring which is first opened up, the subsequent rearrangement to the stable benzo-dihydrofuran ring involves the interaction of the bromine and the phenolic hydrogen. The preparation of the compounds of the Grignard type with magnesium in dry ether was also attempted by the same workers without success.

7-Methyl-4-bromomethylcoumarin was reduced to 4,7-dimethylcoumarin with zinc-copper couple in acetone. Oxidation of 7-methyl-4-bromomethylcoumarin with potassium permanganate in acetone solution gave m-cresotinic acid. 6-Methyl-4-bromomethylcoumarin on oxidation yielded p-cresotinic acid.

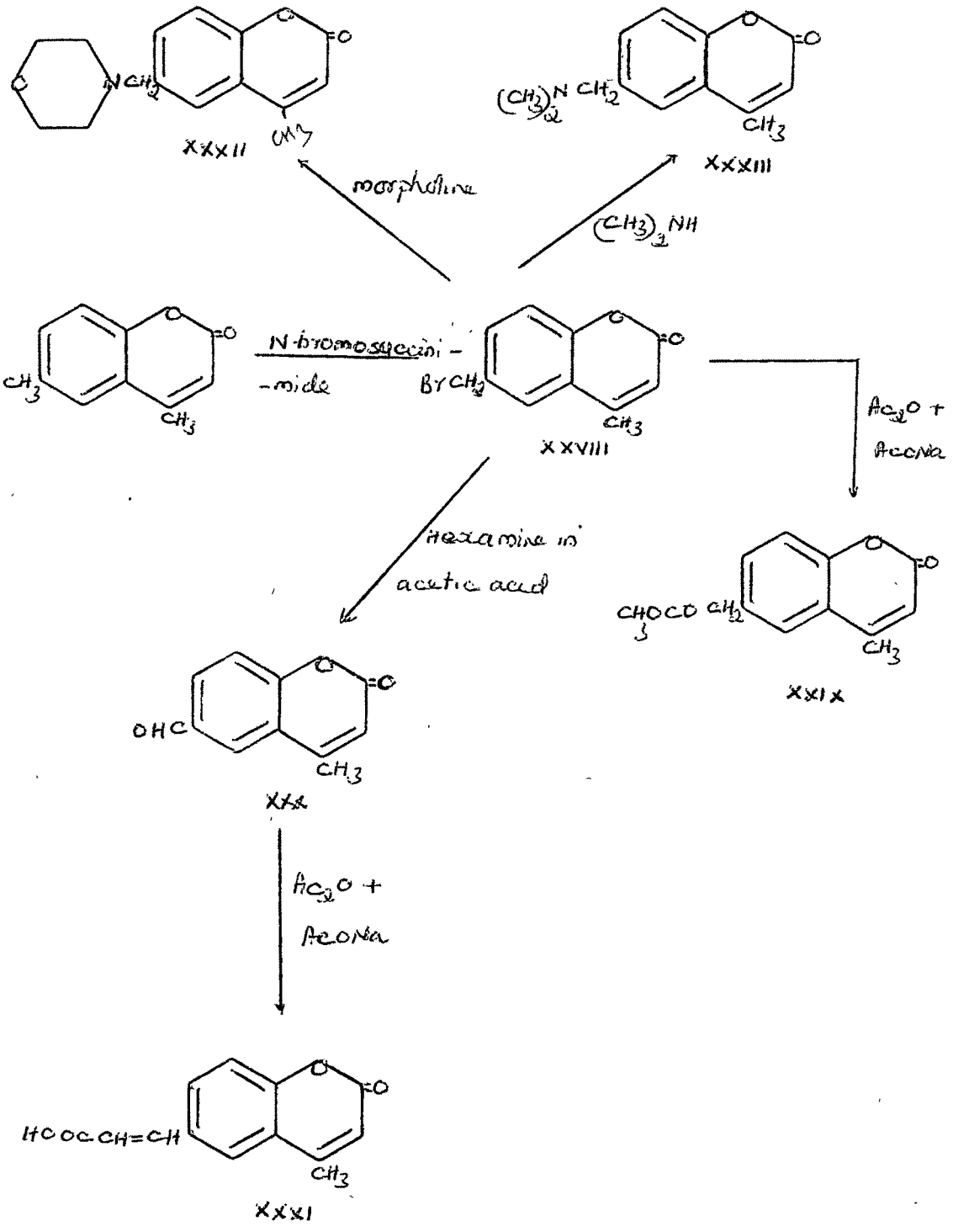
Dey and Sankaranarayanan[19] established the structure of 7-methyl-4-bromomethylcoumarin by its synthesis from m-cresol and γ-bromo acetoacetic ester by Pechmann reaction.

The present work deals with several synthesis starting with four bromomethylcoumarins ; (i) 4-methyl-6-bromomethylcoumarin (ii) 4-methyl-7-bromomethylcoumarin (iii) 7-bromomethyl- and (iv) 6-bromomethylcoumarin.

Studies on 4-methyl-6-bromomethylcoumarin :

4-Methyl-6-bromomethylcoumarin (XXVIII), prepared according to Lecocq and Bun-Hoi[10], gave an acetoxy derivative (XXIX) on refluxing with acetic anhydride and fused sodium acetate. When heated with hexamine in acetic acid, 4-methyl-6-bromomethylcoumarin gave 4-methyl-6-formylcoumarin (XXX) which was characterised by the formation of the 2,4-dinitrophenyl hydrazone derivative. This formylcoumarin (XXX) cannot be prepared by the Pechmann condensation of p-hydroxy benzaldehyde with ethyl acetoacetate as the condensation of phenolic aldehydes with ethyl acetoacetate in the presence of usual condensing agents used in the Pechmann reaction gives unworkable products.

When heated with acetic anhydride and fused sodium acetate in an oil bath at 170-80° for 12 hours the formyl coumarin gave β-(4-methyl-6-coumarinyl)acrylic acid (XXXI) . This acid decolourised neutral potassium permanganate solution and bromine water showing the


XXXII
morpholine
$(CH_3)_2NH$
XXXIII
N-bromosuccini-
-mide
XXVIII
Ac_2O +
AcONa
XXIX
Hexamine in
acetic acid
XXX
Ac_2O +
AcONa
XXXI

presence of unsaturation.

4-Methyl-6-bromomethylcoumarin on condensation with morpholine and dimethylamine in dry benzene gave the corresponding Mannich bases (XXXII, XXXIII)

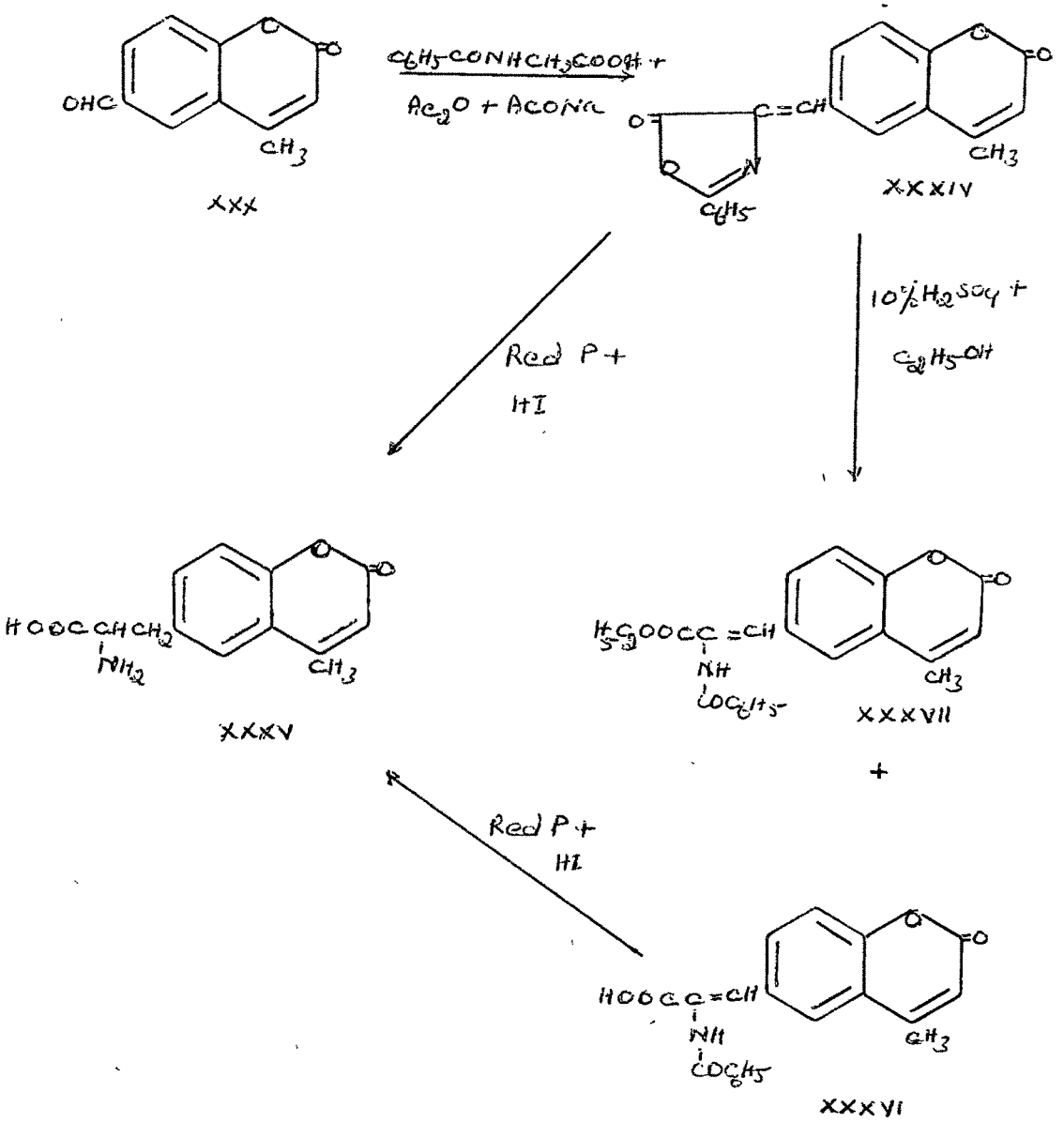
Synthesis of β-(4-methyl-6-coumarinyl)alanine (XXXV) :

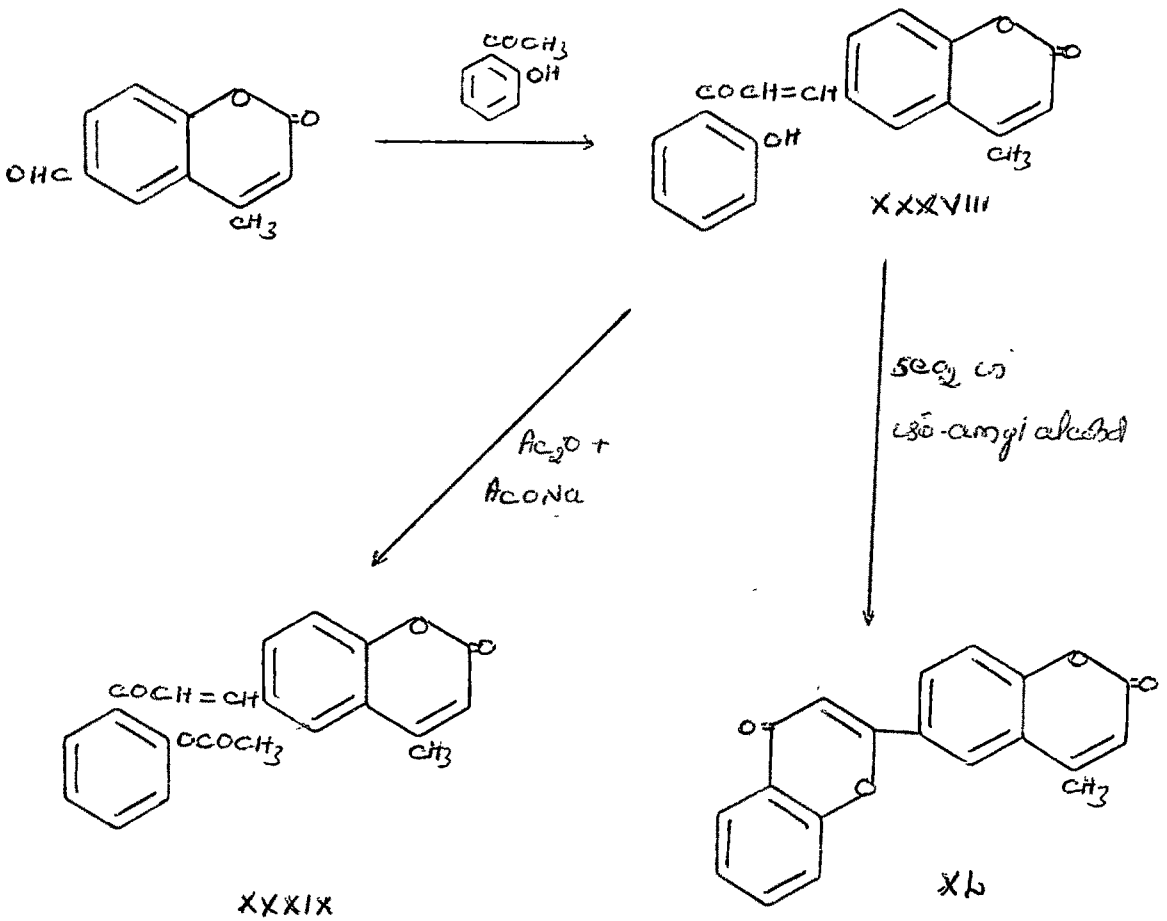
The α-aminoacids are substances of interest as many of them are found to occur in nature either in the free state or as building units of proteins. α-Aminoacids with oxygen heterocyclic units such as benzo-α-pyrone units, do not appear to be known. It was therefore thought of interest to synthesise such acids.

4-Methyl-6-formylcoumarin was therefore condensed with hippuric acid in the presence of fused sodium acetate and acetic anhydride when the azlactone (XXXIV) was obtained. This azlactone on heating with red phosphorous and hydriodic acid in acetic anhydride solution, gave β-(4-methyl-6-coumarinyl)alanine (XXXV). The above azlactone on hydrolysis with 10 % alcoholic sulphuric acid gave a mixture of two products , which was separated with sodium bicarbonate solution. The sodium bicarbonate extract on acidification gave the acid (XXXVI) and the part insoluble in sodium bicarbonate solution was the ester (XXXVII). The acid (XXXVI) also gave the amino acid(XXXV) on reduction with red phosphorus and hydriodic acid.

Synthesis of 4-methyl-6-(2'-chromonyl)coumarin (XL) :

With a view to further exploit the synthetic possibilities of the reactive intermediate (XXX) and to synthesise 4-methyl-6-(2'-chromonyl)coumarin,


OHC
CH3
XXX
C6H5CONHCH2COOH +
Ac2O + AcONa
C6H5
XXXIV
Red P +
HI
10% H2SO4 +
C2H5OH
HOOCCH CH2
NH2
XXXV
H5C2OOCC =CH
NH
COC6H5
XXXVII
+
Red P +
HI
HOOCC=CH
NH
COC6H5
XXXVI


COCH3
OH
OHC
CH3
COCH=CH
OH
CH3
XXXVIII
Ac2O +
AcONa
SeO2 ca
iso-amyl alcohol
COCH=CH
OCOCH3
CH3
XXXIX
CH3
XL

4-methyl-6-formylcoumarin was condensed with o-hydroxy-acetophenone in the presence of alcoholic potassium hydroxide. After keeping the reaction mixture overnight, it was acidified. The yellow solid which separated has been assigned the β-(4-methyl-6-coumarinyl)vinyl-o-hydroxyphenyl ketone structure (XXXVIII) as it gave a red colouration with concentrated sulphuric acid and a positive Wilson test[20]. Moreover, it gave an acetoxy derivative (XXXIX) when heated with acetic anhydride and fused sodium acetate showing the presence of a free hydroxyl group.

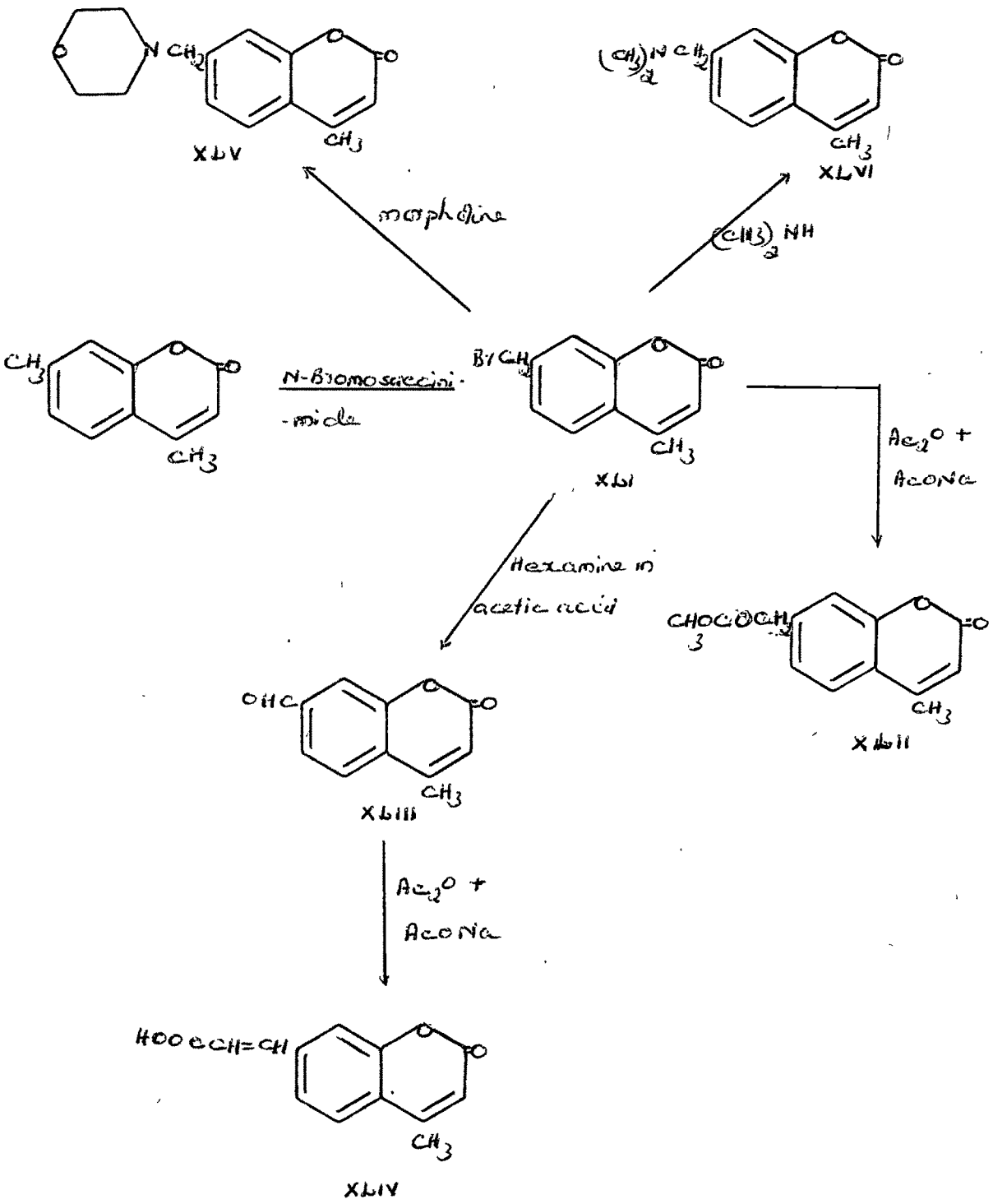
The above ketone (XXXVIII) when refluxed with selenium dioxide in iso amyl alcohol at 140-50° for 24 hours, underwent cyclisation to 4-methyl-6-(2'-chromonyl) coumarin (XL).

Studies on 4-methyl-7-bromomethylcoumarin :

Having successfully accomplished the above syntheses, it was thought of interest to study similar reactionswith 4-methyl-7-formylcoumarin which could be synthesised from the known 4-methyl-7-bromomethylcoumarin.

4-Methyl-7-bromomethylcoumarin (XLI) prepared according to Lecocq and Buu-Hoi[10] on heating with acetic anhydride and fused sodium acetate gave 4-methyl-7-acetoxy-methylcoumarin (XLII). 4-Methyl-7-bromomethylcoumarin was converted into 4-methyl-7-formylcoumarin (XLIII) by heating with hexamine in acetic acid. It was characterised by the formation of a 2,4-dinitrophenylhydrazone derivative.

4-Methyl-7-formylcoumarin when heated with acetic anhydride and fused sodium acetate at 170-80° for 12 hours,


morpholine
(CH3)2NH
N-Bromosuccinimide
Ac2O + AcONa
Hexamine in acetic acid
Ac2O + AcONa
XLV
XLVI
XLI
XLII
XLIII
XLIV

yielded β-(4-methyl-7-coumarinyl)acrylic acid (XLIV).

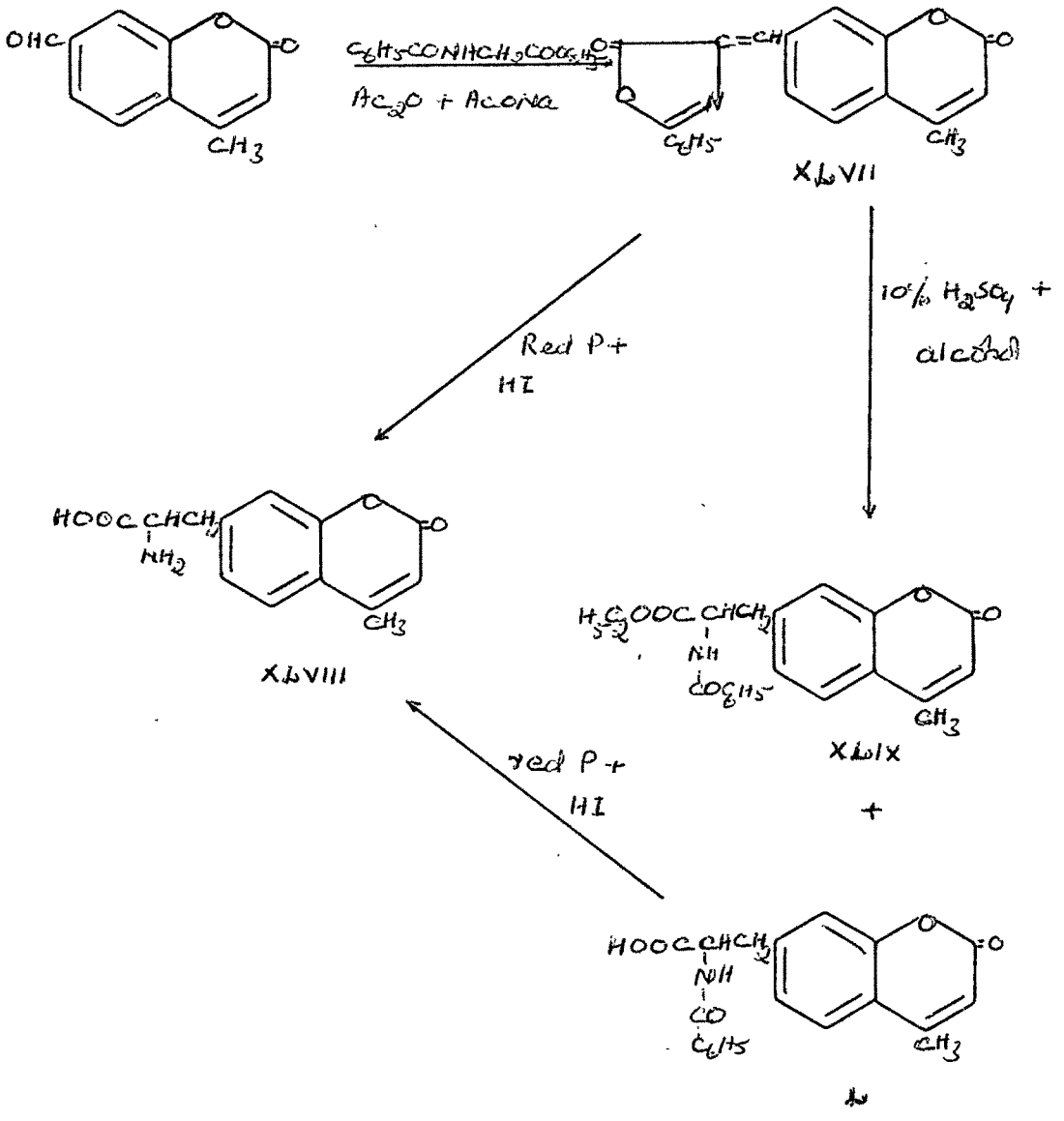
4-Methyl-7-bromomethylcoumarin on condensation with morpholine and dimethylamine in dry benzene gave the corresponding Mannich bases (XLV, XLVI) respectively.

Synthesis of β-(4-methyl-7-coumarinyl)alanine (XLVIII) :

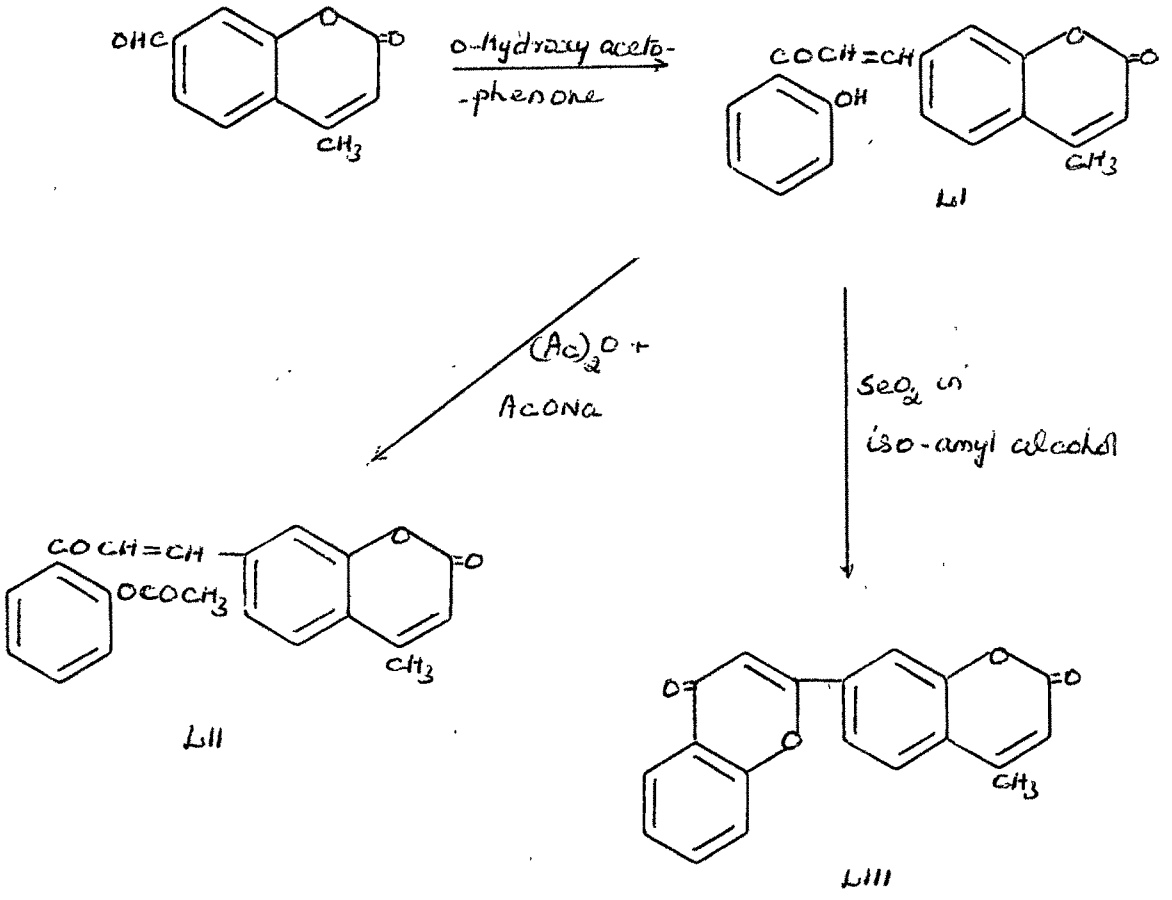
4-Methyl-7-formylcoumarin on condensation with hippuric acid in the presence of fused sodium acetate and acetic anhydride gave the corresponding azlactone (XLVII). This azlactone, on heating with red phosphorus and hydriodic acid in acetic anhydride solution afforded β-(4-methyl-7-coumarinyl)alanine (XLVIII). The azlactone on hydrolysis with 10 % alcoholic sulphuric acid gave a mixture of the ester (XLIX) and the acid (L) which was separated by treatment with sodium bicarbonate solution. This acid (L) also gave the same amino acid (XLVIII) on treatment with red phosphorus and hydriodic acid.

Synthesis of 4-methyl-7-(2'-chromonyl)coumarin (LIII):

4-Methyl-7-formylcoumarin was condensed with o-hydroxyacetophenone in the presence of alcoholic potassium hydroxide. The yellow product separating on acidification of the reaction mixture gave red colouration with concentrated sulphuric acid and a positive Wilson test. It gave an acetoxy derivative (LII) on heating with acetic anhydride and fused sodium acetate indicating the presence of a free hydroxy group. β-(4-Methyl-7-coumarinyl)vinyl-o-hydroxyphenyl ketone structure (LI) was therefore assigned to this product. This ketone


OHC
CH3
C6H5CONHCH2COOC2H5
Ac2O + AcONa
C6H5
CH3
XLVII
10% H2SO4 +
alcohol
Red P +
HI
HOOC CHCH2
NH2
CH3
XLVIII
H5C2OOC CHCH2
NH
COC6H5
CH3
XLIX
+
red P +
HI
HOOC CHCH2
NH
CO
C6H5
CH3
L

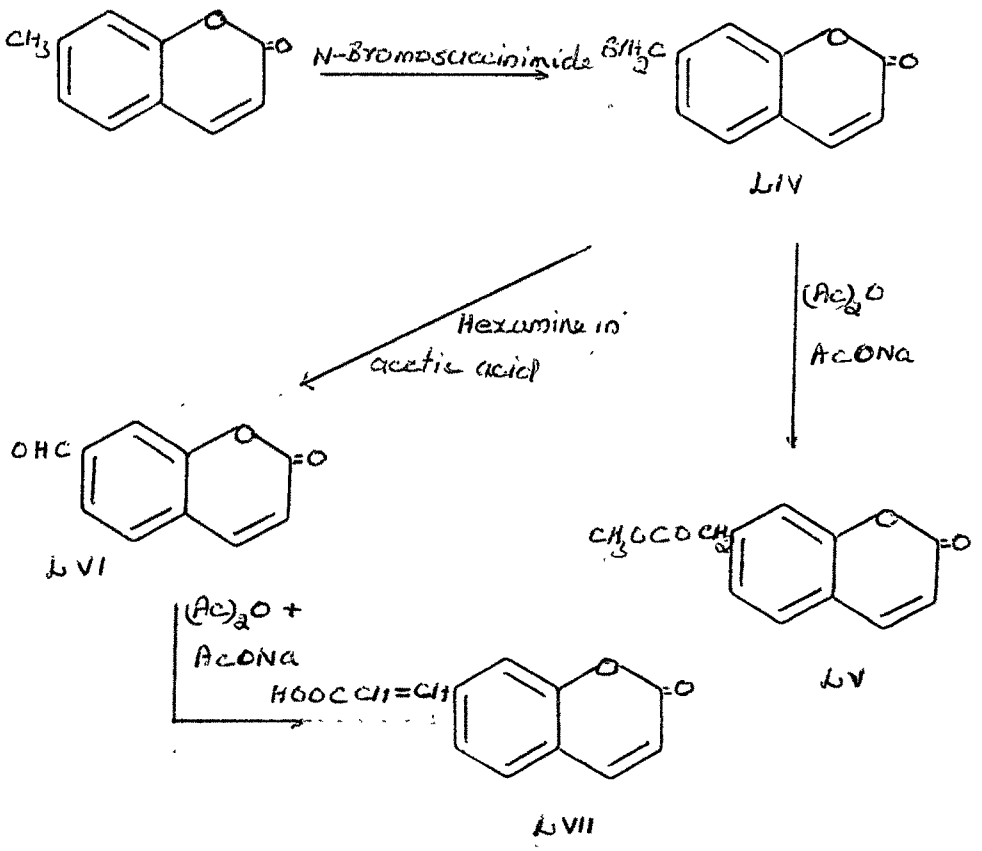
on refluxing with selenium dioxide in iso-amyl alcohol underwent cyclization to 4-methyl-7-(2'-chromonyl)-coumarin (LIII).



Studies on 7-bromomethylcoumarin :

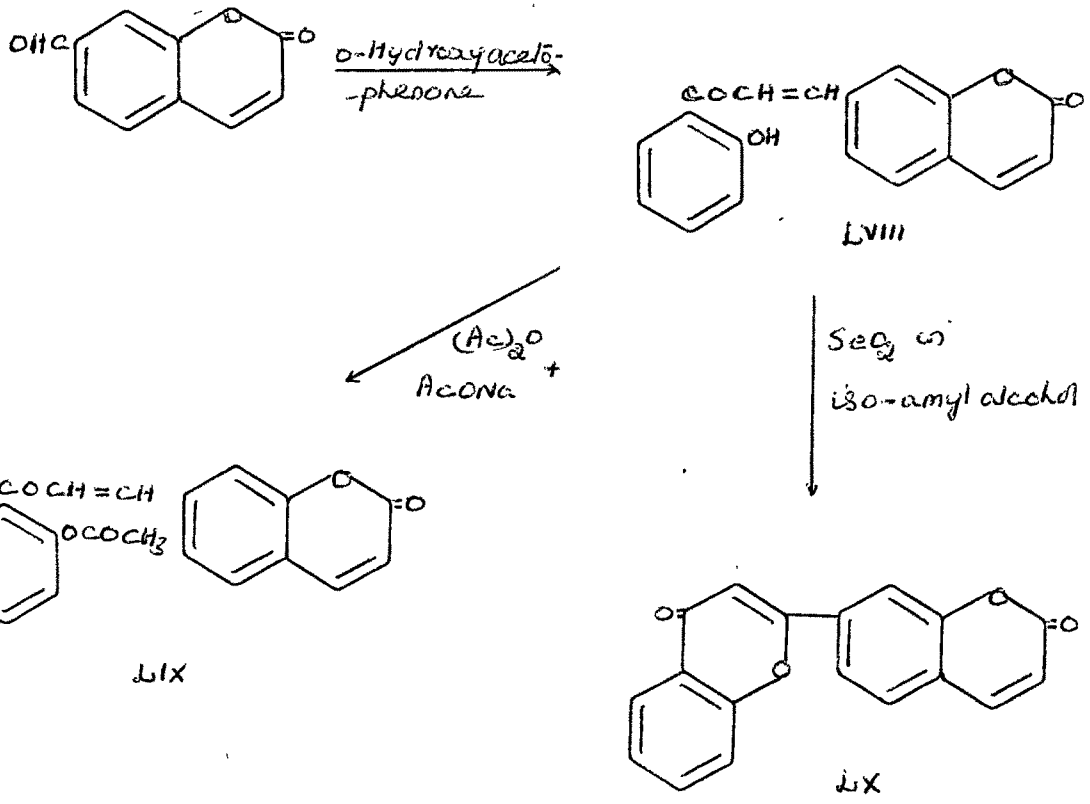
7-Methylcoumarin on bromination with N-bromosuccinimide in dry benzene gave 7-bromomethylcoumarin(LIV). It gave an acetoxy derivative (LV) on heating with acetic anhydride and sodium acetate. 7-Bromomethylcoumarin on heating with hexamine in acetic acid, afforded 7-formylcoumarin (LVI), characterised by the formation of a 2,4-dinitrophenylhydrazone derivative.

7-Formylcoumarin on Perkin acetylation with acetic anhydride and fused sodium acetate gave β-(7-coumarinyl)acrylic acid (LVII). It decolourised potassium permanganate solution and bromine water.



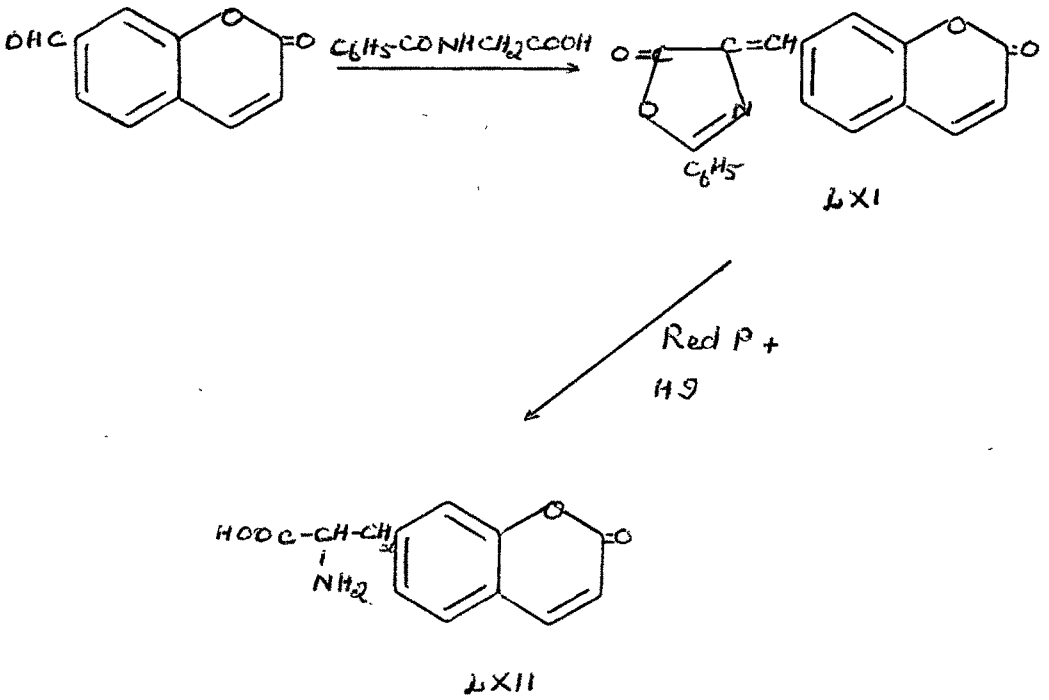
Synthesis of 7-(2'-chromonyl)coumarin (LX) :

7-Formylcoumarin on condensation with o-hydroxyacetophenone in presence of alcoholic potassium hydroxide solution yielded β-(7-coumarinyl)vinyl-o-hydroxyphenyl ketone (LVIII). It gave a red colour with concentrated sulphuric acid and a positive Wilson test. Further, it gave an acetoxy derivative (LIX) when heated with acetic anhydride and fused sodium acetate indicating the presence of a free hydroxyl group. The above ketone (LVIII) on refluxing with selenium dioxide in iso-amyl alcohol at 140-50° for 24 hours gave 7-(2'-chromonyl)coumarin (LX).



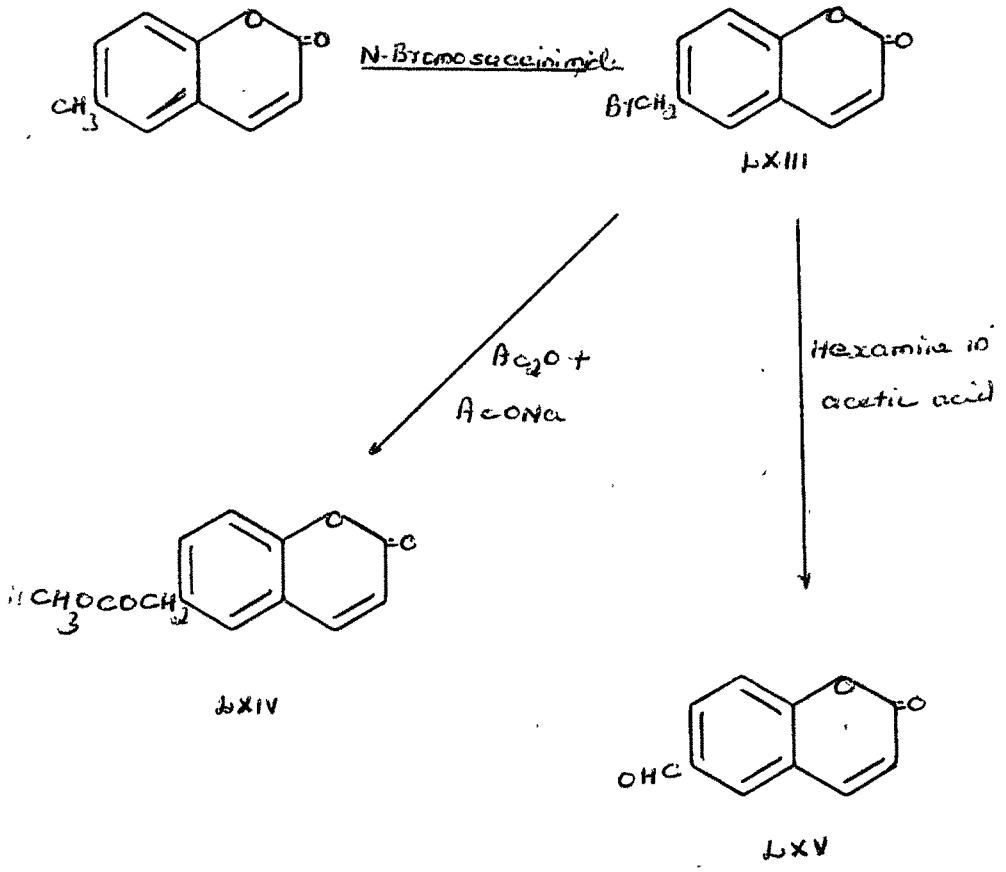
Synthesis of β-(7-coumarinyl)alanine (LXII) :

7-Formylcoumarin on condesnation with hippuric acid in presence of sodium acetate and acetic anhydride gave the corresponding azlactone (LXI). This on heating with red phosphorus and hydriodic acid in acetic anhydride solution afforded β-(7-coumarinyl)alanine(LXII).



Studies on 6-bromomethylcoumarin :

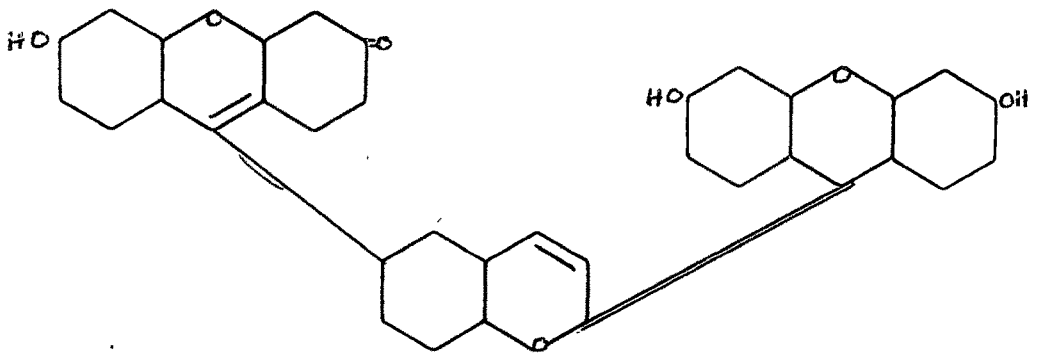
6-Bromomethylcoumarin (LXIII),prepared from 6-methylcoumarin according to Buu-Hoi and Lecocq[10], on heating with acetic anhydride and fused sodium acetate gave an acetoxy derivative (LXIV) which was found identical with the known 6-acetoxymethylcoumarin[21]. On Sommelet reaction with hexamine in glacial acetic acid 6-bromomethylcoumarin gave 6-formylcoumarin (LXV). The same formylcoumarin was also prepared by Sen and Chakravarti[22]


N-Bromosuccinimide
LXIII
Ac_2O +
AcONa
Hexamine in
acetic acid
LXIV
LXV

by the Reimer-Tiemann reaction on simple coumarin. These authors carried out several synthetical works with this formylcoumarin and these are mentioned below:

They found that 6-formylcoumarin underwent benzoin condensation giving a product which they named coumaroin. The condensation of 6-formylcoumarin with acetone and acetophenone in the presence of sodium hydroxide afforded dicoumaral acetone and coumaral acetophenone respectively.

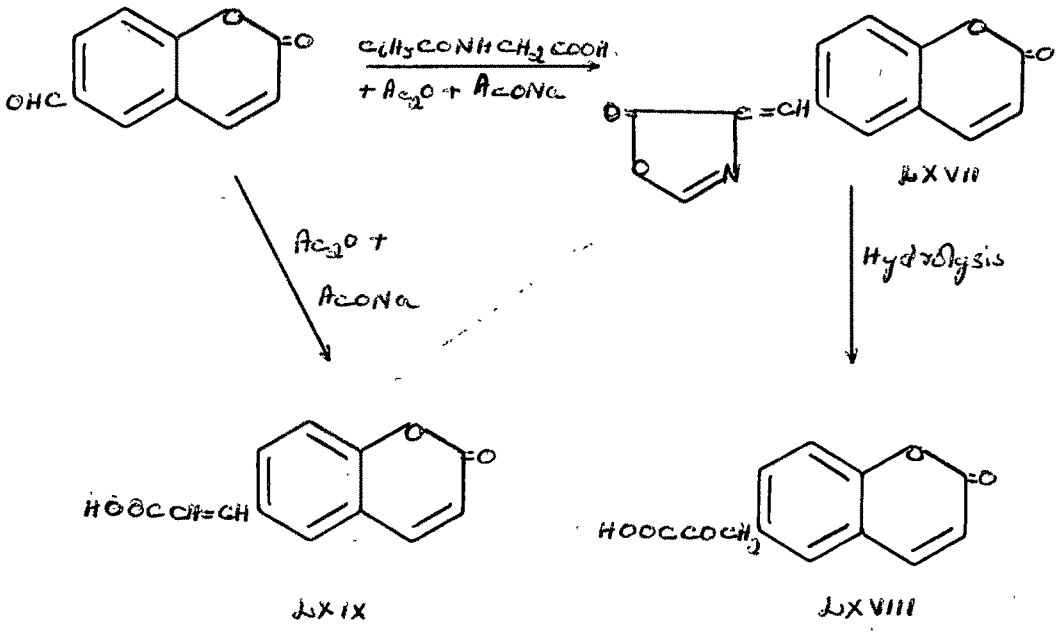
Several azomethine dyes were synthesised by the condensation of 6-formylcoumarin with (i) monoamines such as p-toluidine, B-naphthylamine, p-nitroaniline and aminoazobenzene, (ii) diamines such as benzidine, o-, m- and p-phenylene diamine and (iii) such dyes as rosaniline, chrysodine and safranine, which contain free amino group. Further, 6-formylcoumarin was condensed with resorcinol in the presence of sulphuric acid at a temperature of 120-30^{0} and the product obtained was assigned the structure (LXVI). No proof for this structure was given.



LXVI

The condensations of 6-formylcoumarin with B-naphthol and diethyl-m-aminophenyl have also been described.

Banerjee[23] in his attempt to synthesise phenanthracoumarin condensed 6-formylcoumarin with hippuric acid in the presence of sodium acetate and acetic anhydride and obtained the azlactone (LXVII). This was hydrolysed to the coumarin-6-pyruvic acid (LXVIII).

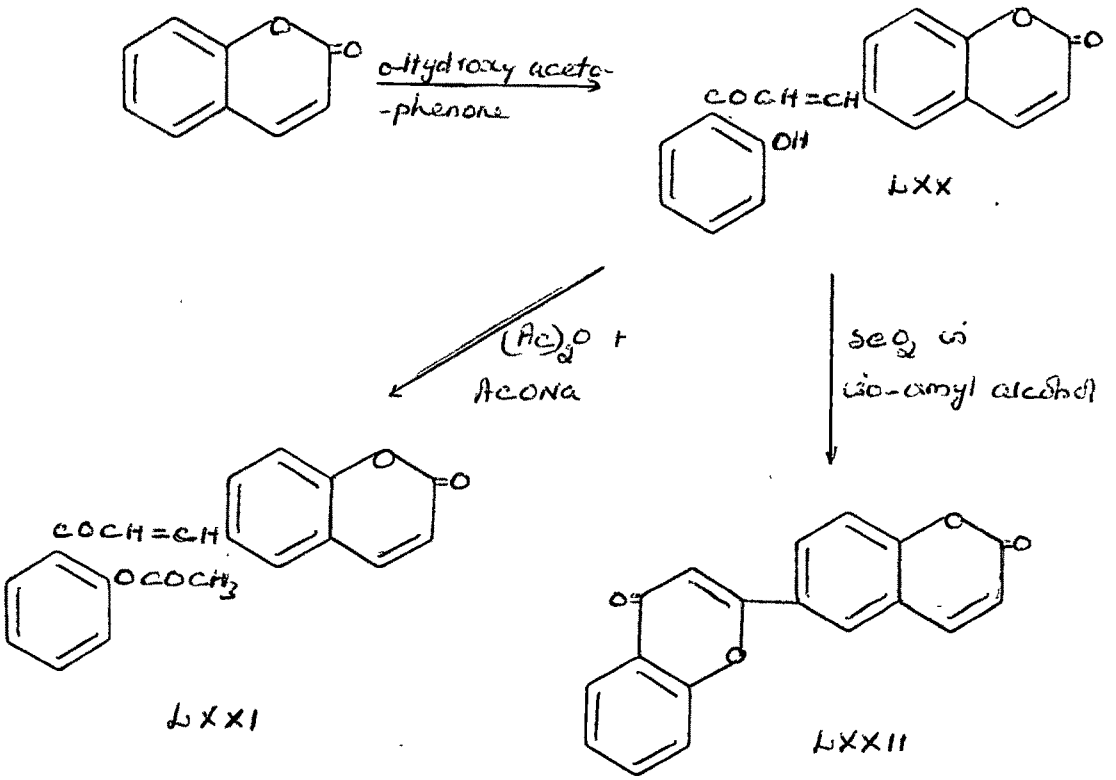


The azlactone (LXVII) was then condensed with p-toluidine, α-naphthylamine and aniline and substituted amides were obtained.

In the course of the present work, 6-formyl-coumarin was subjected to Perkin reaction by heating with acetic anhydride and freshly fused sodium acetate and β-(6-coumarinyl) acrylic acid (LXIX) was obtained.

Synthesis of 6-(2'-chromonyl)coumarin (LXXII) :

6-Formylcoumarin was condensed with o-hydroxy-acetophenone in the presence of alcoholic potassium hydroxide. The yellow product obtained on acidification of the reaction mixture gave red colour with concentrated sulphuric acid and a positive Wilson test showing the presence of a free hydroxyl group. Moreover, it gave an acetoxy derivative (LXXI) by heating with acetic anhydride and sodium acetate. β-(6-Coumarinyl) vinyl-o-hydroxy phenyl ketone structure (LXX) was therefore assigned to this product. This ketone on refluxing with selenium dioxide in iso-amyl alcohol was cyclised to 6-(2'-chromonyl) coumarin (LXXII).



The use of bromomethylcoumarins for the synthesis of various furocoumarins and coumarino-α-pyrones is described in chapter III.

EXPERIMENTAL

Chloromethylation of 4,6-dimethylcoumarin : 4,6-Dimethyl-3-chloromethylcoumarin :

Paraformaldehyde (0.6 g.) was dissolved in acetic acid (10 ml.) by passing hydrogen chloride gas. 4,6-Dimethylcoumarin (1 g.) was then added and this was followed by fused zinc chloride (0.1 g.). Hydrogen chloride gas was passed at 70° for 4 hours. The reaction mixture was then kept overnight and the solid which separated crystallised from benzene-petroleum ether in white plates (0.4 g.), m.p. 128°.

Analysis : Found : C,64.45 ; H,4.81 ; Cl,16.09 %.
$C_{12}H_{11}O_2Cl$ requires : C,64.86 ; H,4.95 ; Cl,15.81 %.

3,4,6-Trimethylcoumarin :

4,6-Dimethyl-3-chloromethylcoumarin (0.5 g.) was dissolved in acetic acid and zinc dust (2 g.) was added. This was followed by hydrochloric acid (con.5 ml.) portionwise. The reaction mixture after heating for 1 hour on a steam bath was filtered. The filtrate on dilution provided 3,4,6-trimethylcoumarin. It was crystallised from alcohol. M.P. 165°. Mixed m.p. with 3,4,6-trimethylcoumarin obtained by Pechmann reaction between p-cresol with ethyl-α-methylacetoacetate was not depressed. Chakravarti[25] reported the m.p. 165°.

4,6-Dimethyl-3-acetoxymethylcoumarin :

The chloromethyl derivative (0.5 g.) was refluxed with acetic anhydride (5 ml.) and fused sodium acetate (2 g.) for 1 1/2 hours. The reaction mixture was poured in water and the product obtained crystallised from dilute acetic acid in white needles, m.p. 136°.

Analysis : Found : C,68.14 ; H,5.62 %.

$C_{14}H_{14}O_4$ requires : C,68.29 ; H,5.69 %.

Attempted preparation of 4,6-dimethyl-3-formylcoumarin by Sommelet reaction :

A mixture of 4,6-dimethyl-3-chloromethylcoumarin (0.5 g.) and hexamine (2 g.) in glacial acetic acid (25 ml.) was heated directly on a wire gauze for 30 minutes. Hydrochloric acid (10 ml. ; 1:1) was then added and heating continued for futher 10 minutes. The product separating on pouring the reaction mixture in cold water crystallised from dilute acetic acid in pale yellow needles, m.p. 189°. It did not give a 2,4-dinitro phenylhydrazone. Its analysis : C,76.26 ; H,5.1 %.

4,6-Dimethyl-3-formylcoumarin requires C,71.29 ; H,4.95 %.

4,6-Dimethyl-3-(morpholinomethyl)coumarin :

4,6-Dimethyl-3-chloromethylcoumarin (0.5 g.) was dissolved in minimum amount of dry benzene and morpholine (2 ml.) was added. The reaction mixture was refluxed on a steam bath for 2 hours. Benzene was removed

and the product crystallised from benzene-petroleum ether in white needles, m.p.137°.

Analysis : Found : C,69.23 ; H,6.89 ; N,5.32 %.
$C_{16}H_{19}O_3N$ requires : C,69.44 ; H,7.17 ; N,5.28 %.

4,6-Dimethyl-3-(dimethylaminomethyl)coumarin :

4,6-Dimethyl-3-chloromethylcoumarin (0.5 g.) was dissolved in minimum amount of dry benzene and dimethylamine (2 ml.) was added and the reaction mixture refluxed on a steam bath for 2 hours. Benzene was then removed and the product crystallised from benzene-petroleum ether in white needles, m.p.123-26°.

Analysis : Found : C,72.52 ; H,7.21 ; N,5.86 %.
$C_{14}H_{17}O_2N$ requires : C,72.73 ; H,7.35 ; N,6.06 %.

4,6-Dimethyl-3-cyanomethylcoumarin :

A solution of 4,6-dimethyl-3-chloromethylcoumarin (1 g.) in alcohol was mixed with an aqueous solution of potassium cyanide (1 g.) and the reaction mixture refluxed on a steam bath for 3 hours. The product separating on dilution of the reaction mixture with water crystallised from dilute alcohol in light pink needles, m.p. 156°.

Analysis : Found : C,73.19 ; H,4.99 ; N,6.26 %.
$C_{13}H_{11}O_2N$ requires : C,73.23 ; H,5.16 ; N,6.57 %.

4,6-Dimethylcoumarin-3-acetic acid :

The above cyanomethylcoumarin was dissolved in 70 % sulphuric acid and heated on a water bath for 2 hours. This was then diluted. The separated product was taken

in sodium bicarbonate solution. On acidification of the bicarbonate extract the acid obtained was crystallised from dilute acetic acid in white needles, m.p. 180°.

Analysis : Found : C,67.00 ; H,5.08 %.

$C_{13}H_{12}O_4$ requires : C,67.23 ; H,5.17 %.

Ethyl-4,6-dimethylcoumarin-3-acetate :

The above acid (1 g.) was dissolved in ethyl alcohol (50 ml.) and concentrated sulphuric acid (4 ml.) was added. The mixture was heated on a steam bath for 6 hours. The product separating on dilution of the reaction mixture with water was washed with sodium bicarbonate solution and crystallised from dilute methyl alcohol in white needles, m.p. 108°.

Analysis : Found : C,68.93 ; H,6.27 %.

$C_{15}H_{16}O_4$ requires : C,69.29 ; H,6.15 %.

Attempted synthesis of 4,6-dimethyl-3,3'-bicoumarinyl :

A solution of ethyl-4,6-dimethylcoumarin-3-acetate (0.8 g.) was mixed with salicylaldehyde (0.3 g.) and four drops of piperidine. The reaction mixture was heated on a steam bath for 8 hours. The solid obtained on pouring the reaction mixture in cold hydrochloric acid was washed with dilute sodium hydroxide solution and crystallised from dilute alcohol in white needles, m.p. 108°. Mixed m.p. with the original ester was not depressed.

Chloromethylation of 4,7-dimethylcoumarin : 4,7-Dimethyl-3-chloromethylcoumarin :

Paraformaldehyde (0.6 g.) was dissolved in acetic acid (10 ml.) by passing dry hydrogen chloride gas. The solution was then mixed with 4,7-dimethylcoumarin (1 g.) and fused zinc chloride (0.1 g.) and hydrogen chloride gas was passed for 4 hours at 70°. On keeping the reaction mixture overnight at room temperature a solid separated. It crystallised from benzene-petroleum ether in white needles (0.5 g.) m.p. 142°.

Analysis : Found : C, 64.55 ; H, 4.76 ; Cl, 16.16 %.

$C_{12}H_{11}O_2Cl$ requires : C, 64.86 ; H, 4.95 ; Cl, 15.81 %.

3,4,7-Trimethylcoumarin :

The above chloromethyl derivative (0.5 g.) was dissolved in acetic acid and zinc dust (2 g.) was added. This was followed by concentrated hydrochloric acid (5 ml.) portionwise. The reaction mixture was then heated on a steam bath for 1 hour. The product which separated on dilution of the reaction mixture with water crystallised from alcohol in white needles, m.p. 114°. Mixed m.p. of this product with 3,4,7-trimethylcoumarin prepared from m-cresol and ethyl-α-methyl acetoacetate by Pechmann reaction, was not depressed. Fries and Klostermann[24] reported the same melting point.

Attempted preparation of 4,7-dimethyl-3-formylcoumarin by Sommelet reaction :

A mixture of 4,7-dimethyl-3-chloromethylcoumarin (0.5 g.) and hexamine (2 g.) in glacial acetic acid (25 ml.)

was refluxed directly on a wire gauze for 30 minutes. Hydrochloric acid (10 ml. ; 1:1) was then added and heating continued for further 10 minutes. The product separating on pouring the reaction mixture in cold water crystallised from dilute acetic acid in white needles, m.p. 193°. It did not give a 2,4-dinitro phenyl hydrazone. Analysis : C,76.00 ; H,4.93 %. 4,7-Dimethyl-3-formylcoumarin requires C,71.29 ; H,4.95 %.

4,7-Dimethyl-3-morpholinomethylcoumarin :

4,7-Dimethyl-3-chloromethylcoumarin (0.5 g.) was dissolved in dry benzene and morpholine (2 ml.) was added. This was heated on a steam bath for 3 hours. After the removal of benzene the solid which separated was crystallised from benzene-petroleum ether in shining white needles, m.p. 137°.

Analysis : Found : C,69.11 ; H,6.94 ; N,4.87 %.

$C_{16}H_{19}O_3N$ requires : C,69.44 ; H,7.17 ; N,5.28 %.

4,7-Dimethyl-3-dimethylaminomethylcoumarin :

A solution of 4,7-dimethyl-3-chloromethyl-coumarin (0.5 g.) in dry benzene was mixed with dimethyl-amine (2 ml.) and heated on a steam bath for 3 hours. The solid separating on removal of benzene crystallised from benzene-petroleum ether in white prims, m.p. 108°.

Analysis : Found : C,72.35 ; H,6.99 ; N,6.13 %.

$C_{19}H_{17}O_2N$ requires : C,72.73 ; H,7.35 ; N,6.06 %.

4,7-Dimethyl-3-cyaromethylcoumarin :

4,7-Dimethyl-3-chloromethylcoumarin (1 g.) was dissolved in alcohol and mixed with a solution of potassium cyanide (2 g.) in water. The reaction mixture was refluxed on a steam bath for 3 hours. The product separating on pouring the reaction mixture in water crystallised from dilute alcohol in white needles, m.p. 160°.

Analysis : Found : C,73.03 ; H,4.99 ; N,6.38 %.
$C_{13}H_{11}O_2N$ requires : C,73.23 ; H,5.16 ; N,6.57 %.

4,7-Dimethylcoumarin-3-acetic acid :

The above cyanomethylcoumarin (0.5 g.) was dissolved in 70 % sulphuric acid and heated on a steam bath for 2 hours. It was then poured in water. The solid which separated was dissolved in sodium bicarbonate. The solid separating on acidification of the bicarbonate extract crystallised from dilute acetic acid in white needles, m.p. 193°.

Analysis : Found : C,67.16 ; H,5.14 %.
$C_{13}H_{12}O_4$ rdquires : C,67.23 ; H,5.17 %.

Ethyl-4,7-dimethylcoumarin-3-acetate :

A solution of 4,7-dimethylcoumarin-3-acetic acid (1 g.) in ethyl alcohol was heated under reflux with concentrated sulphuric acid (4 ml.) for 5-6 hours. The reaction mixture was then poured into water and the separated solid was washed with sodium bicarbonate solution. It crystallised from dilute methyl alcohol in shining white

needles, m.p. 98°.

Analysis : Found : C,68.82 ; H,5.85 %.

$C_{15}H_{16}O_4$ requires : C,69.23 ; H,6.15 %.

Attempted synthesis of 4,7-dimethyl-3,3'-bicoumarinyl :

The above ester (0.5 g.) was dissolved in absolute alcohol and mixed with salicylaldehyde (0.2 g.) and 3 drops of piperidine. It was heated on a steam bath for 8 hours. The solid obtained on pouring the reaction mixture in ice cold hydrochloric acid was washed with dilute sodium hydroxide solution. It crystallised from dilute methyl alcohol in white needles, m.p. 98°. Mixed m.p. with the ethyl-4,7-dimethylcoumarin-3-acetate was not depressed.

4-Methyl-6-acetoxymethylcoumarin :

A mixture of 4-methyl-6-bromomethylcoumarin[10] (0.5 g.), fused sodium acetate (1.5 g.) and acetic anhydride (10 ml.) was heated gently for 1 1/2 hours. The solid separating on addition of the reaction mixture in water crystallised from dilute alcohol in white plates, m.p.134°.

Analysis : Found : C,67.67 ; H,5.30 %.

$C_{13}H_{12}O_4$ requires : C,67.23 ; H,5.17 %.

4-Methyl-6-formylcoumarin :

4-Methyl-6-bromomethylcoumarin (1 g.) was mixed with hexamine (2.5 g.) and acetic acid (25 ml.). This reaction mixture was then refluxed gently for 30 minutes. Hydrochloric acid (10 ml. ; 1:1) was then added and heating continued for further 10 minutes. The product obtained on

dilution of the reaction mixture with water crystallised from acetic acid in pale yellow needles, m.p.211°. Yield 0.5 g.

Analysis : Found : C,70.18 ; H,4.37 %.
$C_{11}H_8O_3$ requires : C,70.21 ; H,4.24 %.

The 2,4-dinitrophenylhydrazone :

It was prepared by heating a mixture of the above formyl derivative in alcohol and 2,4-dinitrophenylhydrazine hydrochloride in alcohol on a steam bath for 30 minutes. It was crystallised from nitrobenzene in orange needles, m.p. 322°.

Analysis : Found : N, 15.34 %.
$C_{17}H_{12}O_6N_4$ requires : N, 15.23 %.

β-(4-Methyl-6-coumarinyl)acrylic acid :

The above formyl derivative (0.5 g.) was heated under reflux with fused sodium acetate and acetic anhydride at 170-80° for 12 hours. The solid obtained on diluting the reaction mixture with water was taken in sodium bicarbonate solution and the sodium bicarbonate extract was acidified. The product obtained crystallised from acetic acid in small white needles (0.2 g.), m.p. 303°. It decolourised neutral potassium permanganate solution and bromine water.

Analysis : Found : C,67.66 ; H,4.11 %.
$C_{13}H_{10}O_4$ requires : C,67.82 ; H,4.34 %.

4-Methyl-6-morpholiromethylcoumarin :

A solution of 4-methyl-6-promomethylcoumarin (0.5 g.) in dry benzene was mixed with morpholine(2 ml.) and heated on a steam bath for 3 hours. The solid obtained after the removal of benzene crystallised from benzene-petroleum ether in white needles, m.p. 105°.

Analysis : Found : C,69.66 ; H,6.55 ; N,5.49 %.

$C_{15}H_{17}O_3N$ requires : C,69.50 ; H,6.56 ; N,5.40 %.

4-Methyl-6-dimethylaminomethylcoumarin :

4-Methyl-6-bromomethylcoumarin (1 g.) mixed with dimethylamine (2 ml.) in dry benzene was heated on a steam bath for 3 hours. Benzene was removed and the separated solid crystallised from petroleum ether in white needles, m.p.85°.

Analysis : Found : C,72.35 ; H,7.12 ; N,6.21 %.

$C_{13}H_{15}O_2N$ requires : C,71.88 ; H,6.91 ; N,6.45 %.

4-(4'-Methyl-6'-coumarinal)2-phenyl-5-oxazolone :

An intimate mixture of 4-methyl-6-formylcoumarin (1 g.) hippuric acid (2 g.),fused sodium acetate (2 g.) and acetic anhydride (15 ml.) was heated on a steam bath for 1 hour. This mixture was then cooled and mixed with alcohol (20 ml.). This was then again heated on a steam bath for 30 minutes to removed acetic anhydride. The yellow product separating on cooling was filtered,washed with boiling water and cold alcohol successively. It crystallised from nitrobenzene in yellow needles,m.p.241°. Yield 0.9 g.

Analysis : Found : C,72.40 ; H,3.59 ; N,3.98 %.

$C_{20}H_{13}O_4N$ requires : C,72.51 ; H,3.92 ; N,4.23 %.

B-(4-Methyl-6-coumarinyl)alanine :

A mixture of the above azlactone (1 g.),red phosphorus (0.8 g.), acetic anhydride (5 ml.) and hydriodic acid (5 ml. ; 50 %) was refluxed for 3 hours. The reaction mixture was cooled,filtered and the residue was washed with two 5 ml. portions of glacial acetic acid and then with excess water. The water extract gave a product on concentration. This was again dissolved in water and made just neutral with dilute ammonia solution. The product obtained on concentrating the solution was crystallised from minimum water in white granules (0.4 g.)m.p.245-50°.

Analysis : Found : C,62.86 ; H,5.55 ; N,5.51 %.

$C_{13}H_{13}O_4N$ requires: C,63.15 ; H,5.26 ; N,5.66 %.

α-Benzamido-β-(4-methyl-6-coumarinyl)acrylic acid :

A solution of the above azlactone (0.8 g.) in ethyl alcohol was mixed with sulphuric acid (10 ml.; 10 %) and heated until the reaction mixture became colourless. This was then diluted with water. The solid obtained was extracted with sodium bicarbonate solution. The bicarbonate extract on acidification gave the acid which was crystallised from acetic acid. M.P. 256°.

Analysis : Found : C,68.50 ; H,4.00 ; N,3.99 %.

$C_{20}H_{15}O_5N$ requires: C,68.77 ; H,4.29 ; N,4.01 %.

Ethyl-α-benzamido-β-(4-methyl-6-coumarinyl)acrylate :

The insoluble residue in the above hydrolysis which was the ethyl ester of the above acid crystallised from acetic acid in white wooly needles, m.p.186°.

Analysis : Found : C,69.68 ; H,5.14 ; N,3.47 %.

$C_{22}H_{19}O_5N$ requires: C,70.03 ; H,5.04 ; N,3.71 %.

The above acid (0.8 g.) was refluxed with red phosphorus (0.6 g.), acetic anhydride (4 ml.) and hydriodic acid (4 ml. ; 50 %) for 3 hours. The reaction mixture was filtered after cooling. The residue was washed with two 5 ml. portions of glacial acetic acid. The product separating on cooling the filtrate was dissolved in water and treated with ammonium hydroxide until the solution was neutral. This on concentration gave a product which crystallised from water in white granules (0.3 g.), m.p. 245-48°. Mixed m.p. with β-(4-methyl-6-coumarinyl)alanine described above was not depressed.

Condensation of 4-methyl-6-formylcoumarin with o-hydroxyacetophenone : β-(4-Methyl-6-coumarinyl)vinyl-o-hydroxyphenyl ketone :

A solution of 4-methyl-6-formylcoumarin (1 g. ; 1 mole) in alcohol was mixed with o-hydroxyacetophenone (0.7 g. ; 1 mole) and potassium hydroxide (10 g. in 10 ml. water). After keeping overnight, the reaction mixture was diluted with ice water and acidified. The precipitated

yellow product crystallised from acetic acid in yellow needles (0.5 g.), m.p. 218°.

Analysis : Found : C,74.69 ; H,4.41 %.

$C_{19}H_{14}O_4$ requires : C,74.50 ; H,4.57 %.

The acetoxy derivative :

The above chalcone (0.5 g.) was heated with acetic anhydride (5 ml.) and fused sodium acetate (2 g.) for 1 1/2 hours. It crystallised from dilute alcohol in light yellow plates, m.p. 151°.

Analysis : Found : C,72.69 ; H,4.59 %.

$C_{21}H_{16}O_5$ requires : C,72.41 ; H,4.59 %.

4-Methyl-6-(2-chromonyl)coumarin :

A mixture of the above ketone (1 g.) in iso amyl alcohol and selenium dioxide (2.5 g.) was refluxed at 140-50° for 24 hours. It was filtered hot. The solid obtained on cooling the filtrate crystallised from acetic acid in tiny white needles (0.4 g.), m.p. 300°.

Analysis : Found : C,74.80 ; H,3.91 %.

$C_{19}H_{12}O_4$ requires : C,74.99 ; H,3.94 %.

4-Methyl-7-acetoxymethylcoumarin :

A mixture of 4-methyl-7-bromomethylcoumarin(5 g.) fused sodium acetate (2 g.) and acetic anhydride (5 ml.) was refluxed gently for 1 1/2 hours. The product separating on dilution of the reaction mixture was crystallised from

benzene-petroleum ether in white needles, m.p.118°

Analysis : Found : C,67.39 ; H,5.15 %.

$C_{13}H_{10}O_4$ requires : C,67.23 ; H,5.17 %.

Sommelet reaction on 4-methyl-7-bromomethylcoumarin :

4-Methyl-7-formylcoumarin :

4-Methyl-7-bromomethylcoumarin (1 g.) was mixed with hexamine (2.5 g.) and acetic acid (25 ml.) and refluxed gently for 30 minutes. Hydrochloric acid was then added (10 ml. ; 1:1) and heating continued for further 10 minutes. The product obtained on adding the reaction mixture in water was crystallised from acetic acid in pale yellow needles, m.p. 201°. Yield 0.3 g.

Analysis : Found : C,70.38 ; H,4.34 %.

$C_{11}H_8O_3$ requires : C,70.21 ; H,4.24 %.

The 2,4-dinitrophenyl hydrazone :

This was prepared by refluxing a solution of 4-methyl-7-formylcoumarin and 2,4-dinitrophenylhydrazine hydrochloride in alcohol on a steam bath for 15 minutes. The hydrazone crystallised from nitrobenzene in orange yellow needles.It decomposed at 310°.

Analysis : Found : N,15.17 %.

$C_{17}H_{12}O_6N_4$ requires : N,15.22 %.

β-(4-Methyl-7-coumaryl)acrylic acid :

A mixture of 4-methyl-7-formylcoumarin (0.8 g.), fused sodium acetate (2.4 g.) and acetic anhydride (8 ml.) was refluxed at 170-80° for 12 hours in an oil bath. The reaction mixture was then added to water and kept overnight.

The precipitated product crystallised from acetic acid in white needles, m.p. 315°. It was soluble in sodium bicarbonate with effervescence. It decolourised neutral potassium permanganate solution and bromine water.

Analysis : Found : C,67.41 ; H,4.25 %.
$C_{13}H_{10}O_4$ requires : C,67.82 ; H,4.34 %.

4-Methyl-7-morpholiromethylcoumarin :

A solution of 4-methyl-7-bromomethylcoumarin (0.5 g.) in dry benzene was mixed with morpholine (2 ml.) and refluxed on a steam bath for 3 hours. The solid obtained on removal of benzene crystallised from petroleum ether in white needles, m.p. 85°.

Analysis : Found : C,69.26 ; H,6.50 ; N,5.34 %.
$C_{15}H_{17}O_3N$ requires : C,69.50 ; H,6.56 ; N,5.40 %.

4-Methyl-7-dimethylamiromethylcoumarin :

A mixture of 4-methyl-7-bromomethylcoumarin (0.5 g.) in dry benzene and dimethylamine (2 ml.) was refluxed on a steam bath for 3 hours. Benzene was then removed . The solid obtained crystallised from petroleum ether in white needles, m.p. 75°.

Analysis : Found : C,72.07 ; H,7.13 ; N,6.16 %.
$C_{13}H_{15}O_2N$ requires : C,71.88 ; H,6.91 ; N,6.45 %.

4-(4'-Methyl-7'-coumarinal)2-phenyl-5-oxazolone :

An intimate mixture of 4-methyl-7-formyl-coumarin (2 g.), hippuric acid (4 g.),fused sodium acetate (2 g.) and acetic anhydride (15 ml.) was heated on a steam bath for 1 hour. It was then cooled and

alcohol (20 ml.) was added. The heating on the steam bath was continued for further 1/2 hour. The yellow product separating on cooling the reaction mixture was washed with water and cold alcohol successively. It crystallised from nitrobenzene in yellow needles, m.p. 263°. Yield 0.8 g.

Analysis : Found : C,72.10 ; H,3.99 ; N,4.55 %.
$C_{20}H_{13}O_4N$ requires : C,72.51 ; H,3.92 ; N,4.23 %.

β-(4-Methyl-7-coumarinyl)alanine :

A mixture of the above azlactone (1 g.), red phosphorus (0.8 g.), acetic anhydride (5 ml.) and hydriodic acid (5 ml. ; 50 %) was refluxed for 3 hours. It was then cooled and filtered. The residue was washed with 5 ml. portions of glacial acetic acid. The solid obtained on cooling the filtrate was dissolved in water and just neutralised with ammonium hydroxide solution. This solution, on evaporation afforded a solid which crystallised from water in tiny white needles (0.4 g.), m.p. 255°. It is soluble in sodium bicarbonate solution and hydrochloric acid.

Analysis : Found : C,62.78 ; H,5.48 ; N,5.79 %.
$C_{13}H_{13}O_4N$ requires : C,63.15 ; H,5.26 ; N,5.68 %.

α-Benzamido-β-(4-methyl-7-coumarinyl)acrylic acid :

The azlactone (0.5 g.) in ethyl alcohol was refluxed with sulphuric acid (5 ml. ; 10 %) until the colour of the solution changed. The product separating on dilution of the reaction mixture with water was

treated with sodium bicarbonate solution. The bicarbonate extract on acidification gave the acid. It crystallised from acetic acid in white needles, m.p. 258°.

Analysis : Found : C,68.30 ; H,4.47 ; N,4.44 %.

$C_{20}H_{15}O_5N$ requires : C,68.77 ; H,4.29 ; N,4.01 %.

Ethyl-α-benzamido-β-(4-methyl-7-coumarinyl)acrylate :

The part which was insoluble in sodium bicarbonate in the above hydrolysis crystallised from acetic acid in white shining needles, m.p. 221°.

Analysis : Found : C,69.69 ; H,5.18 ; N,3.67 %.

$C_{22}H_{19}O_5N$ requires : C,70.03 ; H,5.04 ; N,3.71 %.

A mixture of α-benzamido-β-(4-methyl-7-coumarinyl)acrylic acid (1 g.), red phosphorus (0.8 g.), acetic anhydride (5 ml.) and hydriodic acid (5 ml. ; 50 %) was refluxed for 3 hours. The cold reaction mixture was then filtered and the residue was washed with minimum amount of acetic acid. The total filtrate on cooling gave a product. This was dissolved in water and just neutralised with ammonium hydroxide solution. This solution on concentration afforded the amino acid which crystallised from water in tiny white needles (0.5 g.), m.p.255°. Mixed m.p. with β-(4-methyl-7-coumarinyl) alanine described earlier was not depressed.

Condensation of 4-methyl-7-formylcoumarin with o-hydroxy acetophenone : β-(4-Methyl-7-coumarinyl)vinyl-o-hydroxy-phenyl ketone :

A solution of 4-methyl-7-formylcoumarin (1 g.) in alcohol was kept overnight with o-hydroxy-acetophenone (0.7 g.) and potassium hydroxide (10 g. in 10 ml. water). It was then diluted and acidified. The precipitated yellow product was washed with sodium bicarbonate solution and crystallised from acetic acid in dark yellow needles (0.8 g.), m.p. 214°. It was sparingly soluble in sodium hydroxide solution. It gave a red colour with concentrated sulphuric acid and a positive Wilson test.

Analysis : Found : C, 74.71 ; H, 4.80 %.

$C_{19}H_{14}O_4$ requires : C, 74.50 ; H, 4.57 %.

The acetoxy derivative :

It was prepared by heating a mixture of the above ketone (0.5 g.), fused sodium acetate (2 g.) and acetic anhydride (5 ml.) for 2 hours. It crystallised from dilute acetic acid in yellow needles, m.p. 156°.

Analysis : Found : C, 72.06 ; H, 4.52 %.

$C_{21}H_{16}O_5$ requires : C, 72.40 ; H, 4.59 %.

4-Methyl-7-(2'-chromonyl)coumarin :

The above hydroxy ketone (0.5 g.) dissolved in iso-amyl alcohol (50 ml.) was mixed with selenium dioxide (1.25 g.) and refluxed at 140-50° for 24 hours.

The solution was filtered hot. The product obtained on cooling crystallised from nitrobenzene in pale yellow cubes, m.p. 262°.

Analysis : Found : C,75.09 ; H,3.79 %.
$C_{19}H_{12}O_4$ requires : C,74.99 ; H,3.94 %.

Bromination of 7-methylcoumarin with N-bromosuccinimide : 7-Bromomethylcoumarin :

N-Bromosuccinimide (1 g.) in dry benzene was mixed with a solution of 7-methylcoumarin (1 g.) in dry benzene. Benzoyl peroxide (0.01 g.) was then added. After refluxing the reaction mixture on a steam bath for 6 hours, the solution became colourless. Benzene was removed and the solid was washed with hot water to remove any unreacted N-bromosuccinimide. It crystallised from acetic acid in colourless needles (0.6 g.), m.p.182°.

Analysis : Found : Br, 33.45 %.
$C_{10}H_7O_2Br$ requires : Br, 33.47 %.

7-Acetoxymethylcoumarin :

A mixture of 7-bromomethylcoumarin (0.5 g.), fused sodium acetate (1.5 g.) and acetic anhydride(5 ml.) was heated for 1 1/2 hours. The solid separating on adding the reaction mixture to water crystallised from dilute alcohol, m.p. 104°.

Analysis : Found : C,65.86 ; H,4.68 %.
$C_{12}H_{10}O_4$ requires : C,66.06 ; H,4.58 %.

7-Formylcoumarin :

A mixture of 7-bromomethylcoumarin (1 g.) and hexamine (3 g.) in glacial acetic acid (50 ml.) was refluxed for 30 minutes. Hydrochloric acid (10 ml. ; 1:1) was then added and heating continued for further 10 minutes. The reaction mixture was then added to cold water and the product obtained crystallised from acetic acid in pale yellow needles (0.4 g.), m.p.205°.

Analysis : Found : C,68.93 ; H,3.62 %.

$C_{10}H_6O_3$ requires : C,68.98 ; H,3.44 %.

2,4-Dintrophenylhydrazone :

It was prepared as described earlier. It crystallised from nitrobenzene in yellow needles, m.p. > 300°.

Analysis : Found : N,15.63 %.

$C_{16}H_{10}O_6N_4$ requires : N,15.82 %.

β-(7-Coumarinyl)acrylic acid :

A mixture of 7-formylcoumarin (0.5 g.),fused sodium acetate (1.5 g.) and acetic anhydride (5 ml.) was heated at 170-80° for 12 hours. It was then added to water. The solid obtained crystallised from acetic acid in yellow cubes (0.3 g.)m.p.275°. It decolourised potassium permanganate solution and bromine water.

Analysis : Found : C,66.58 ; H,3.72 %.

$C_{12}H_8O_4$ requires : C,66.67 ; H,3.70 %.

Condensation of 7-formylcoumarin with o-hydroxyaceto-phenone : β-(7-Coumarinyl)viryl-o-hydroxyphenyl ketone :

A solution of 7-formylcoumarin (1 g.) in alcohol (25 ml.) was mixed with o-hydroxyacetophenone (2 ml.) and potassium hydroxide (10 g. in 10 ml.water) and kept at room temperature for 24 hours. This mixture was then diluted and acidified. The yellow product which separated was washed with sodium bicarbonate solution. It crystallised from acetic acid in yellow needles (0.5 g.) m.p.204-6°. This was soluble in sodium hydroxide solution. It gave a red colouration with concentrated sulphuric acid and a positive Wilson test.

Analysis : Found : C,74.37 ; H,3.94 %.

$C_{18}H_{12}O_4$ requires : C,73.98 ; H,4.11 %.

The acetoxy derivative :

A mixture of the above ketone (0.5 g.), fused sodium acetate (2 g.) and acetic anhydride (5 ml.) was refluxed for 1 1/2 hours. The reaction mixture was poured in water and the product crystallised from dilute alcohol in pale yellow shining plates. M.P. 130°.

Analysis : Found : C,71.81 ; H,4.26 %.

$C_{20}H_{14}O_5$ requires : C,71.86 ; H,4.19 %.

7-(2'-Chromonyl)coumarin :

The above hydroxy ketone (0.8 g.) in iso-amyl alcohol (50 ml.) was refluxed with selenium dioxide (2 g.) at 140-50° for 24 hours. This solution was filtered hot

and the product obtained on cooling the filtrate, crystallised from dilute acetic acid in pale yellow powder (0.5 g.), m.p. 250°.

Analysis : Found : C,74.09 ; H,3.12 %.

$C_{18}H_{10}O_4$ requires : C,74.49 ; H,3.44 %.

Condensation of 7-formylcoumarin with hippuric acid : 4-(7'-Coumarinal)2-phenyl-5-oxazolone :

A mixture of 7-formylcoumarin (2 g.), hippuric acid (4 g.), fused sodium acetate (2 g.) and acetic anhydride (20 ml.) was warmed till a clear solution was formed. This was then refluxed for 1 hour. The reaction mixture was cooled and alcohol (20 ml.) was added. It was heated for further 30 minutes. The yellow solid which separated on cooling was washed with boiling water and cold alcohol successively. It crystallised from nitrobenzene in yellow plates (2 g.), m.p.230°.

Analysis : Found : C,71.55 ; H,3.55 ; N,4.53 %.

$C_{19}H_{12}O_4N$ requires : C,71.69 ; H,3.77 ; N,4.40 %.

β-(7-Coumarinyl)alanine :

The above azlactone (1.5 g.) was heated under reflux with red phosphorus (1.2 g.), acetic anhydride (7 ml.) and hydriodic acid (5 ml. ; 50 %) for 3 hours. The reaction mixture was cooled and filtered. The solid obtained from the filtrate on cooling was dissolved in water and neutralised with ammonium hydroxide solution. The solid separating on concentration of the solution , crystallised from water in white needles (0.5 g.),

m.p. 280° (decomp.). It was soluble in sodium bicarbonate solution and hydrochloric acid.

Analysis : Found : C,61.45 ; H,4.66 ; N,5.50%:
$C_{12}H_{11}O_4N$ requires : C,61.80 ; H,4.72 ; N,6.00 %.

6-Acetoxymethylcoumarin :

A mixture of 6-bromomethylcoumarin (0.5 g.), fused sodium acetate (1.5 g.) and acetic anhydride (5 ml.) was heated under reflux for 1 1/2 hours. The reaction mixture was then added to water and the separated solid crystallised from methyl alcohol in white flat needles, m.p. 108°. Stoermer and Oetker[21] reported the melting point 108-9°.

Sommelet reaction on 6-bromomethylcoumarin : 6-Formylcoumarin :

A mixture of 6-bromomethylcoumarin (2 g.) and hexamine (5 g.) in glacial acetic acid (50 ml.) was refluxed directly on a wire gauze for 30 minutes. Hydrochloric acid (20 ml. 1:1) was then added and heating continued for further 15 minutes. The white solid obtained on diluting the reaction mixture with ice cold water, crystallised from acetic acid in white plates (0.8 g.), m.p. 189°. Sen and Chakravarti[22] reported the same melting point.

β-(6-Coumarinyl)acrylic acid :

A mixture of 6-formylcoumarin (1 g.), fused sodium acetate (3 g.) and acetic anhydride (10 ml.) was heated in an oil bath at 175-80° for 10 hours. The

solid obtained on pouring the reaction mixture to ice cold water was taken in sodium bicarbonate solution. The sodium bicarbonate extract on acidification gave the acid which crystallised from acetic acid in white needles (0.7 g.), m.p. 306°. It decolourised potassium permanganate solution and bromine water.

Analysis : Found : C,66.40 ; H,3.91 %.

$C_{12}H_8O_4$ requires : C,66.67 ; H,3.70 %.

Condensation of 6-formylcoumarin with o-hydroxy-acetophenone : β-(6-Coumarinyl)vinyl-o-hydroxyphenyl ketone :

A solution of 6-formylcoumarin (2 g.) in alcohol was kept for 24 hours with o-hydroxy acetophenone (4 ml.) and potassium hydroxide (20 ml. ; 100 %). The yellow solid obtained on dilution and acidification of the reaction mixture was washed with sodium bicarbonate solution. It crystallised from acetic acid in yellow plates (0.8 g.), m.p. 218°. It is soluble in sodium hydroxide solution and gives red colour with concentrated sulphuric acid and a positive Wilson test.

Analysis : Found : C,74.24 ; H,4.25 %.

$C_{18}H_{12}O_4$ requires : C,73.98 ; H,4.11 %.

The acetoxy derivative :

Prepared by heating the above ketone (0.5 g.) with fused sodium acetate (1.5 g.) and acetic anhydride (5 ml.) for 1 1/2 hours. The solid separated on diluting

the reaction mixture with water crystallised from dilute alcohol in light yellow shining prisms, m.p. 157°.

Analysis : Found : C,71.64 ; H,4.43 %.

$C_{20}H_{14}O_5$ requires : C,71.86 ; H,4.19 %.

6-(2'-Chromonyl)-coumarin :

The above hydroxy ketone (0.6 g.) in iso-amyl alcohol was refluxed with selenium dioxide (2 g.) at 145-50° for 24 hours. It was filtered hot and the separated product from the cold filtrate crystallised from acetic acid in brown needles (0.3 g.), m.p. 260°.

Analysis : Found : C,74.67 ; H,3.31 %.

$C_{18}H_{10}O_4$ requires : C,74.49 ; H,3.44 %.

REFERENCES

1. M.Kruger., Ber., 56B, 480 (1923).
2. K.G.Naik and A.D.Patel., J.Chem.Soc., 1043, (1934).
3. V.D.N.Sastri and T.R.Seshadri., Proc.Indian Acad.Sci., 9A, 22 (1939).
4. T.R.Seshadri and P.S.Rao., Proc.Indian Acad.Sci., 4A, 162 (1936).
5. R.N.Sen and D.Chakravarti., J.Indian Chem.Soc., 6, 843 (1929).
6. T.J.Thompson and R.H.Edee., J.Amer.Chem.Soc., 47, 2556 (1925).
7. P.L.De Benneville and R.Connor., J.Amer.Chem.Soc., 62, 3067 (1940).
8. B.B.Dey and H.Dalal., J.Chem.Soc., 123, 3384 (1923).
9. B.B.Dey and K.K.Row., J.Chem.Soc., 123, 3375 (1923).
10. J.Lecocq and N.P.Buu-Hoi., Compt.rend., 224, 937 (1947).
11. J.Lecocq., Ann.Chim., 3, 62 (1948).
12. P.C.Taunk, S.K.Jain and R.L.Mital., Ann.Soc.Sci., Bruxelles., Ser.1, 84(3), 383 (1971).
13. Fuson and Mc.Keever., Organic reactions., Vol. 1, John Wiley and Sons., New York., 1942, p. 63.
14. Olah and Tolgyesi., Ch. 21, Friedel Crafts and related reactions edited by Olah, interscience publishers, New York., 1964.
15. S.S.Lele ; N.C.Sawant and S.Sethna., J.Org.Chem., 25, 1713 (1960).

16. S.S.Lele, N.G.Sawant and S.Sethna., J.Indian Chem. Soc., 38, 975 (1961).

17. B.B.Dey and K.Radhabai., J.Chem.Soc., 11, 635 (1934).

18. P.Da Re, L.Borsla, I.Setnikar and M.J.Magistretti., Experientia., 18, 387 (1962) ; C.A., 57, 11811 (1962).

19. B.B.Dey and Y.Sankaranarayanan., J.Chem.Soc., 11, 687 (1934).

20. C.L.Wilson, J.Amer.Chem.Soc., 61, 2303 (1939).

21. R.Stoermer and Ed.Oetker., Ber., 37, 192 (1904).

22. R.N.Sen and D.Chakravarti., J.Amer.Chem.Soc., 50, 2428 (1928).

23. S.K.Banerjee., J.Indian Chem.Soc., 9, 479 (1932).

24. K.Fries and W.Klostermann., Ber., 39, 871 (1906).

25. D.Chakravarti., J.Indian Chem.Soc., 9, 25 (1932).