CHAPTER III

PRENYLATION OF 3-HYDROXYCOUMARINS

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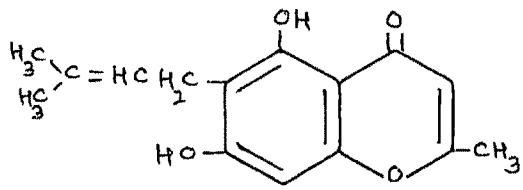
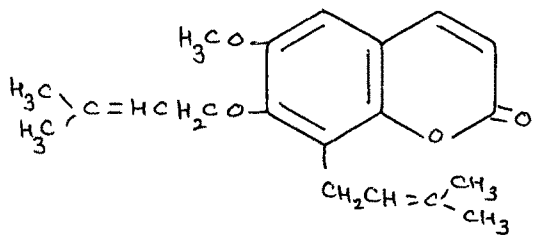
THEORETICAL

A large number of naturally occurring isoprenoids are directly linked to a nuclear carbon. Peucenin[1] (I) and Brayleyanin[2] (II) are among the many known examples of this type. Sometimes, the double bond in the dimethylallyl group gets oxidised forming either an epoxide as in Auropten[3] (III) or a Glycol, as in Toddalolactone[4] (IV).



I



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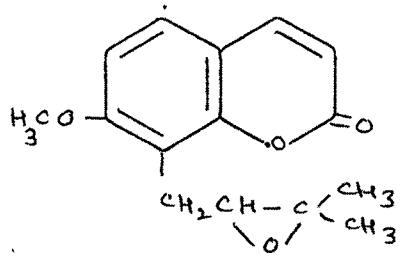
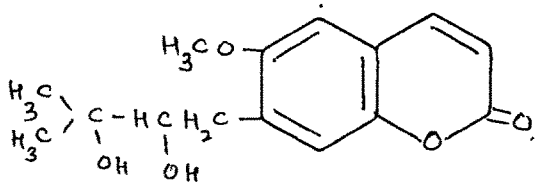
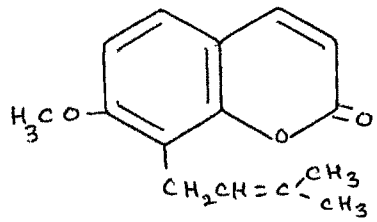


III



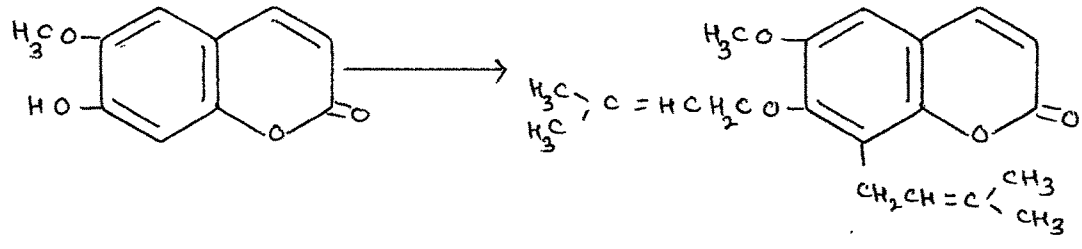
IV

Osthol (V) is one of the several coumarins in the rhizomes of Imperatoria Ostruthium and in the roots of Angelica archangelica L. Butenandt and Marten[5] and Spath and Pesta[6] established the structure of it. Spath and Holzen[7] synthesised osthol first by alkylating 2-hydroxy--4-methoxybenzaldehyde with γ,γ-dimethylallyl bromide and converting it into osthol by interaction with malonic acid followed by the decarboxylation of the product.



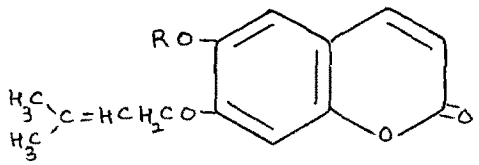
V

Brayleyanin (II), has isoprenoid groups both on oxygen and carbon, is obtained from Flindersia brayleyana. Anet Hughes and Ritchie[8] alkylated scopoletin (VI) in the 8-position with γ,γ-dimethylallyl bromide and then etherified the product with the same halide to obtain synthetic brayleyanin (II).

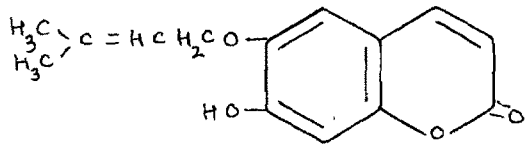


VI II

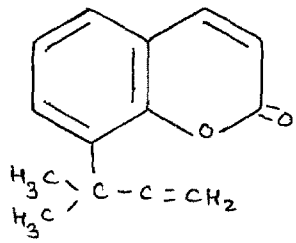
F.M.Dean et al.[9] reported some new coumarins from Ptaereroxylon obliquum having the following structures established on the basis of the spectral data.



VII



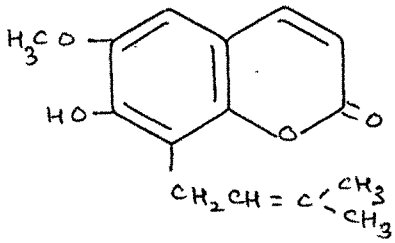
VIII



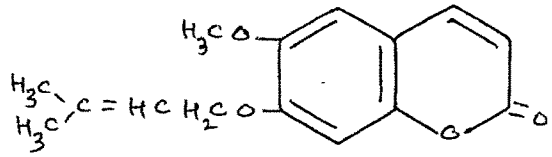
IX

Murray and Ballantyne[10] obtained obliquetin (X) by the Claisen rearrangement of 3,3-dimethylallylether of scopoletin (XI), alongwith nieshoutin (XII). They have also reported[11] the normal and abnormal Claisen rearrangement products in this case.

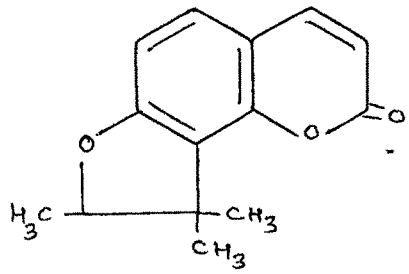
Seshadri et al.[12] isolated new coumarin compounds from H. Candicans and synthesised these compounds, tert-O-methylcandicanin[13] and tert-O-β-glycolide of heraclenol[14].



X

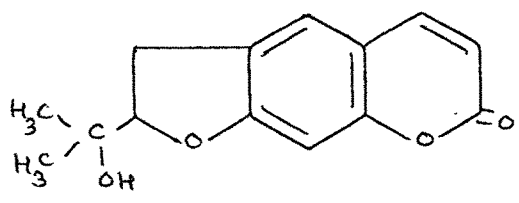


XI

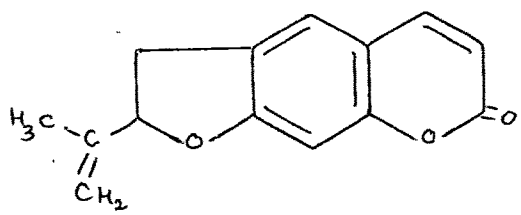


XII

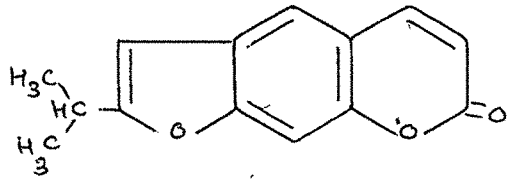
Cyclisation of the epoxide of type (III) or the glycol of type (IV) with an adjacent phenolic hydroxyl gives dihydrofuran type compounds like marmesin[15] (XIII). The loss of water leads to the isopropenyl dihydrofuran (XIV). The final dehydration of (XIII) yields an isomeric isopropyl-furan (XV) owing to the instability of the isopropenyl compound in the presence of acid.



XIII

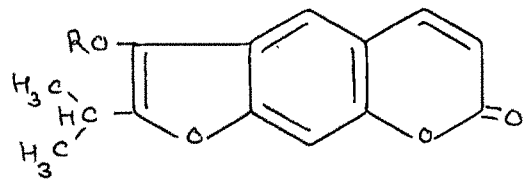


XIV



XV

Isopropylfuranocoumarins are also reported as the natural products. Oreoselone[16] (XVIa) and its methyl-ether peucedanin (XVIb) are of this type. Its formation is suggested by Spath et al.[16] from epoxide or the triol.



XVI

(a) R=H

(b) R=CH_3

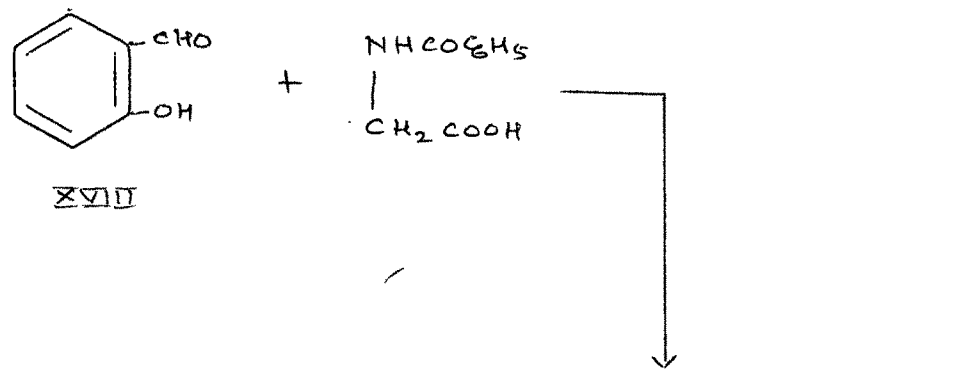
The present work, deals with the synthesis of 3-hydroxycoumarin derivatives so it is thought of interest to review some of the work done on 3-hydroxycoumarins.

3-Hydroxycoumarin derivatives were prepared according to the method of Shaw, McMillen and Armstrong[17]. Many 3-hydroxycoumarin derivatives have been synthesised by one or the other method.

In 1885, Plochi and Wolfrum[18] first synthesised 3-hydroxycoumarin (XVII). Godwin and Taves[19] showed an inhibiting effect on the growth of avena roots and

Rodighiero and Antonelio[20] observed that 3-aminocoumarin, from which 3-hydroxycoumarin can easily be obtained by the hydrolysis, are good antibacterial agents against staphylococcus Pyrogens, Salmonella, Shigella, etc.

Plochi and Wolfrum[18] synthesised 3-hydroxycoumarin by the condensation of salisaldehyde (XVIII) with hippuric acid in the presence of acetic anhydride. Erlenmeyer and Stadlin[21] then modified the method by allowing the mixture to react in the presence of acetic anhydride and sodium acetate on steam bath. The product obtained was hydrolysed with alkali giving 3-hydroxycoumarin.

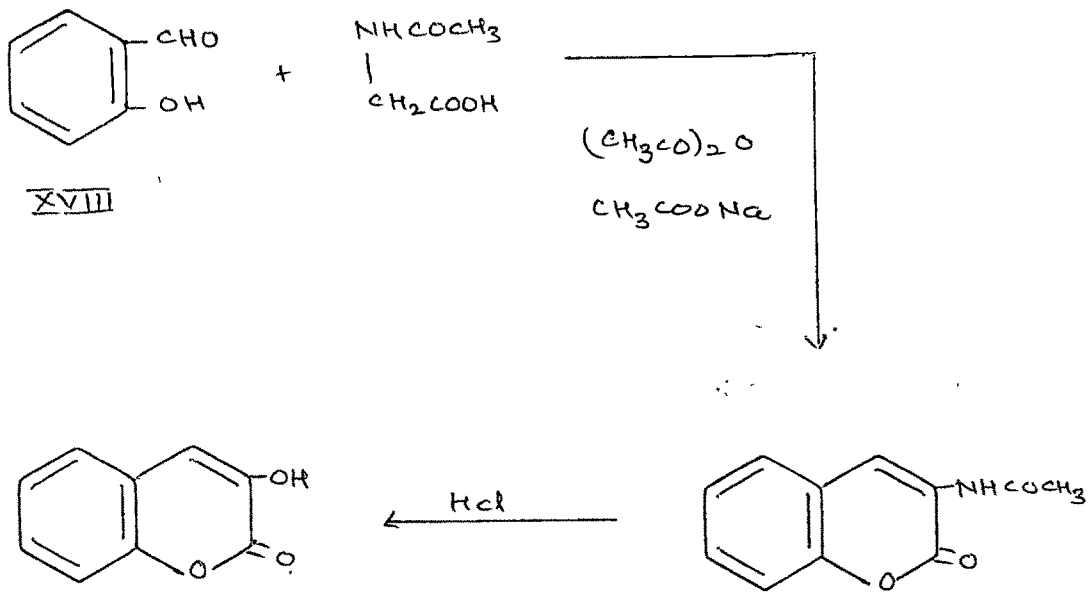


XVIII

XVII

Dey and Lakshminarayan[22] extended this method to the synthesis of 3-amino-5,6-benzocoumarin which on treatment with nitrous acid gave corresponding 3-hydroxy-coumarin derivative. Beer, et al.[23] synthesised 3-hydroxy-coumarin derivative via oxazole derivative by treating the 2-nitro-6-hydroxybenzaldehyde with aceturic acid in the presence of acetic anhydride and sodium acetate.

Shaw et al.[17] developed the experimental conditions for the synthesis of 3-acetamido- and 3-hydroxycoumarin. They condensed salisaldehyde (XVIII) with acetylglycine in the presence of acetic anhydride and sodium acetate on a steam bath. The resultant 3-acetamidocoumarin was then refluxed with hydrochloric acid (3 N) in nitrogen atmosphere to give 3-hydroxycoumarin in 83 % yield.

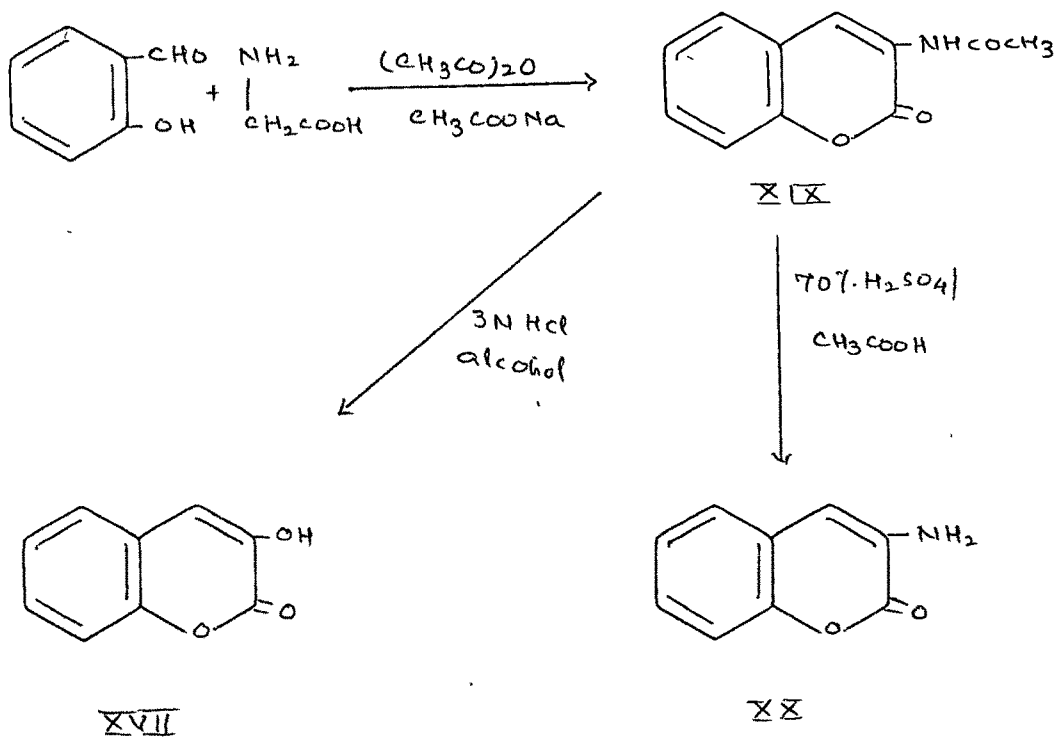


XVIII

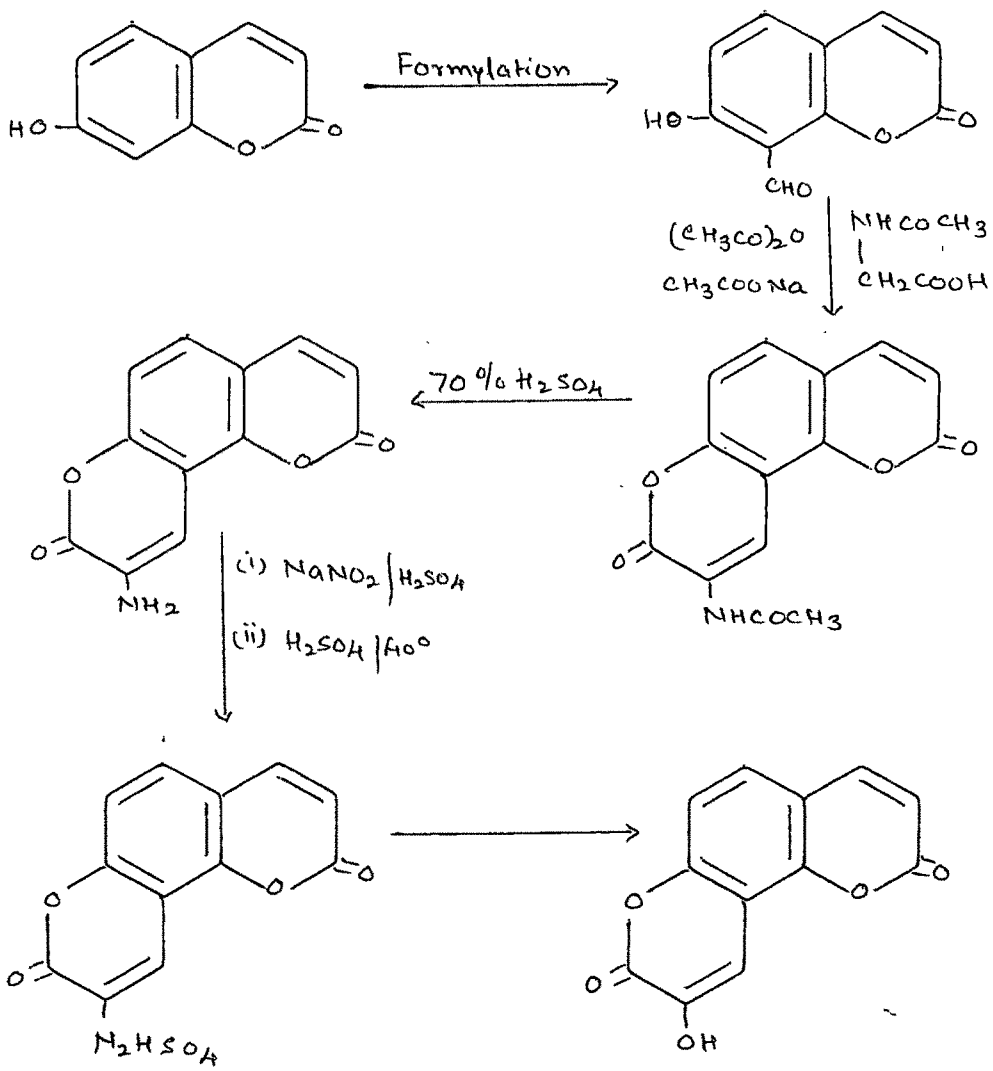
XVII

Trivedi and Sethna[24] synthesised several substituted 3-hydroxycoumarins and studied the pattern of substitution in 3-hydroxycoumarin. They synthesised 3-hydroxy--coumarin derivatives according to Shaw et al.[17].

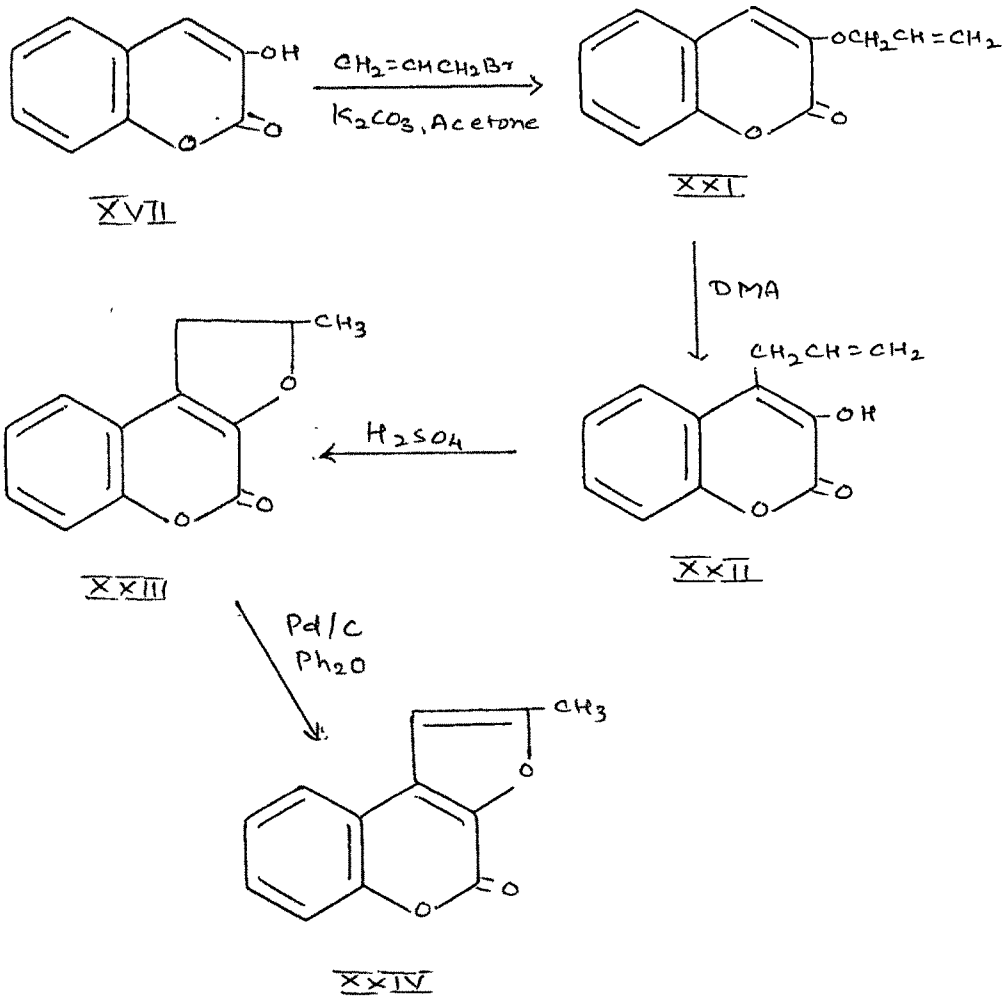
Chakravarti and co-workers[25] synthesised a number of 3-amino- and 3-hydroxycoumarins which have been found to possess good bacteriastatic and fungistatic properties. They condensed o-hydroxyaldehydes with glycine in the presence of acetic anhydride and sodium acetate. The intermediate 3-acetamido derivative (XIX) on treatment with alcoholic hydrochloric acid gave corresponding 3-hydroxycoumarin derivative and (XIX) on treating with sulphuric acid (70 %) and acetic acid at 50-60° gave the 3-aminocoumarin derivative (XX).



Shaikh and Trivedi[26] have synthesised few 3-hydroxycoumarin derivatives in order to prepare 3-hydroxy-pyranobenzopyran derivatives. They formylated the different hydroxycoumarins and these o-hydroxyformylcoumarins were condensed with acetylglycine in the presence of acetic anhydride and sodium acetate. The resultant acetamido derivatives were hydrolysed by sulphuric acid to give 3-aminocoumarins which, subsequently, were diazotised and hydrolysed to give 3-hydroxycoumarin derivatives.



As mentioned in Chapter I, furanocoumarins of type (D) have been synthesised for the first time by Shaikh and Trivedi[26]. 3-Hydroxycoumarin (XVII) was allylated with allyl bromide to 3-allyloxycoumarin (XXI). This on Claisen migration gave 4-allyl-3-hydroxycoumarin (XXII). This was further cyclised to 2-methyl-9-oxo-9H-2,3-dihydrofurano-(2,3-c)benzopyran (XXIII) with concentrated sulphuric acid, which was subsequently dehydrogenated by palladised charcoal (10 %) to 2-methyl-9-oxo-9H-furano(2,3-c)benzopyran (XXIV). They have also prepared the substituted furanocoumarins of this type.



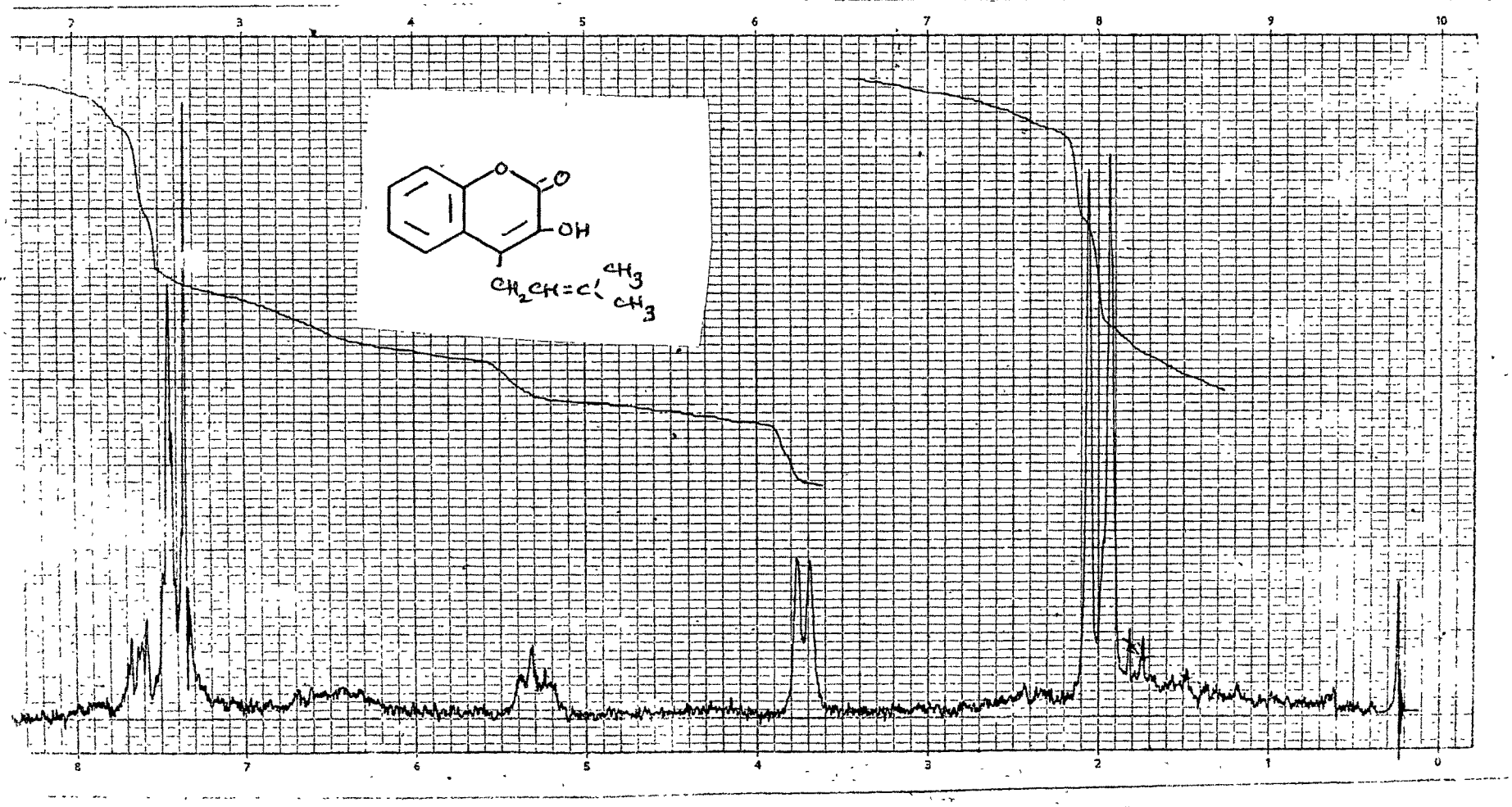
XVII XXI XXII XXIII XXIV

Several C-prenylated 3-hydroxycoumarin derivatives and isopropylfuranocoumarin derivatives from 3-hydroxycoumarins are described in this Chapter.

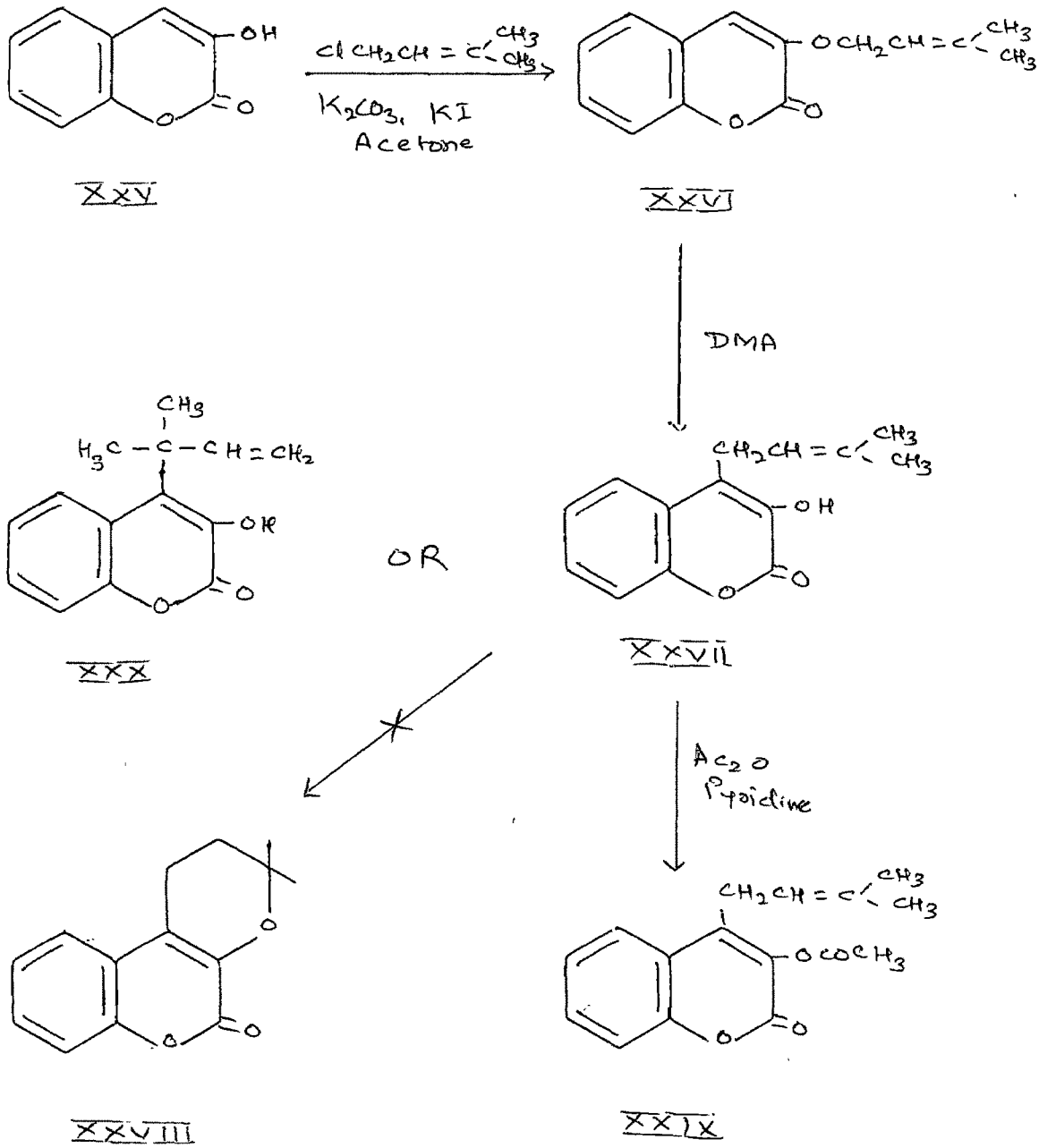
Synthesis of 3-acetoxy-4-prenylcoumarin

3-Hydroxycoumarin[17] (XXV) on prenylation with prenyl chloride (1-chloro-3-methyl-but-2-ene) in the presence of anhydrous potassium carbonate and potassium iodide in dry acetone afforded 3-prenyloxycoumarin (XXVI). The IR spectrum in nujol showed the bands at 1720 $cm.^{-1}$ for α-pyrone carbonyl stretching frequency and 1370 $cm.^{-1}$ for a geminal dimethyl group stretching. (XXVI) on refluxing with dimethylaniline underwent Claisen rearrangement to give 3-hydroxy-4-prenyl-coumarin (XXVII). The structure of this compound was confirmed by its IR and NMR spectra. The IR spectrum in nujol showed the bands at 3340 $cm.^{-1}$ for a hydroxyl group, 1710 $cm.^{-1}$ for α-pyrone carbonyl stretching and 1360 $cm.^{-1}$ for a geminal dimethyl group.

The NMR spectrum in $CDCl_3$ showed two singlets at δ 1.70 and 1.82 for a geminal dimethyl group. It showed a doublet at δ 3.50 for a $-CH_2-$ group and triplet at δ 5.07 for a proton adjacent to methylene group (Fig. 1). The up-field doublet at δ 3.50 indicates that the $-CH_2$ group of the side chain is attached to an aromatic ring. If a doublet would be around δ 5.50, the $-CH_2$ group of the side chain would be at the end and the structure of the compound be given (XXX).



(Fig. 1) : 3-Hydroxy-4-prenylcoumarin



XXV XXVI XXX XXVII XXVIII XXIX

Thus the rearrangement of 3-prenyloxycoumarin (XXVI) is an abnormal Claisen rearrangement giving the product (XXVII) , and the normal Claisen product (XXX),

could not be isolated. Here the formation of the abnormal Claisen product can be explained by the formation of spirocyclopropylhexadienone as an intermediate in the reaction and the mechanism of it is already discussed in Chapter I. Chamberlain and Grundon[27] have shown this type of rearrangement and have reported the normal and abnormal Claisen products in the case of quinoline and have also given the NMR spectra for the structures assigned to the compounds. Grundon et al.[28] have also confirmed the structure of peucenin on the basis of the NMR spectra, which is also a case of abnormal Claisen rearrangement.

Attempts to cyclise (XXVII) to give corresponding furano- or pyranocoumarin (XXVIII) with different cyclising reagents such as conc. sulphuric acid, polyphosphoric acid, DDQ, etc. failed.

(XXVII) was reacted with acetic anhydride in the presence of pyridine to give 3-acetoxy-4-prenylcoumarin (XXIX).

Synthesis of 3-acetoxy-6-methyl-4-prenylcoumarin

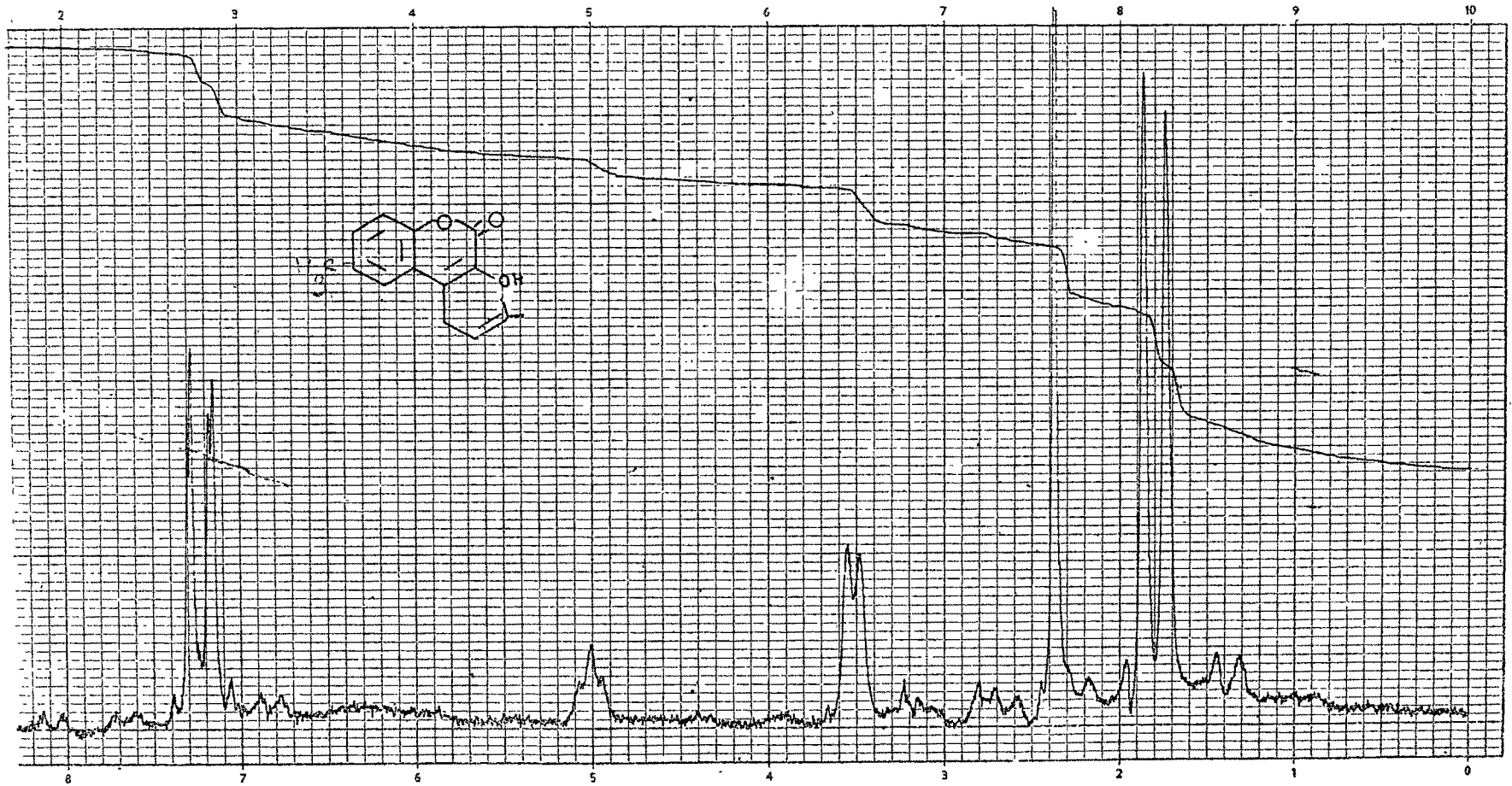
3-Hydroxy-6-methylcoumarin (XXXI) was prenylated with 1-chloro-3-methyl-but-2-ene in the presence of anhydrous potassium carbonate and potassium iodide in dry acetone to give 3-prenyloxy-6-methylcoumarin (XXXII). Its IR spectrum in nujol showed the bands at 1732 $cm.^{-1}$ for α-pyrone carbonyl stretching, 1365 $cm.^{-1}$ for a geminal dimethyl group stretching and 975 $cm.^{-1}$ for aliphatic >C=C< stretching. The NMR

spectrum in $CDCl_3$ showed the following signals :- δ 1.78, singlet, geminal dimethyl group; 2.38, singlet, methyl group at position-6; 4.58, doublet, J=8Hz, two protons, of $O-\underline{CH_2}-CH$ group at position-3; 5.50, triplet, J=8Hz, one proton of $O-CH_2-\underline{CH}$ group at position-3; 6.75, singlet, one proton aromatic at position-4 and 7.15, singlet, three protons aromatic.

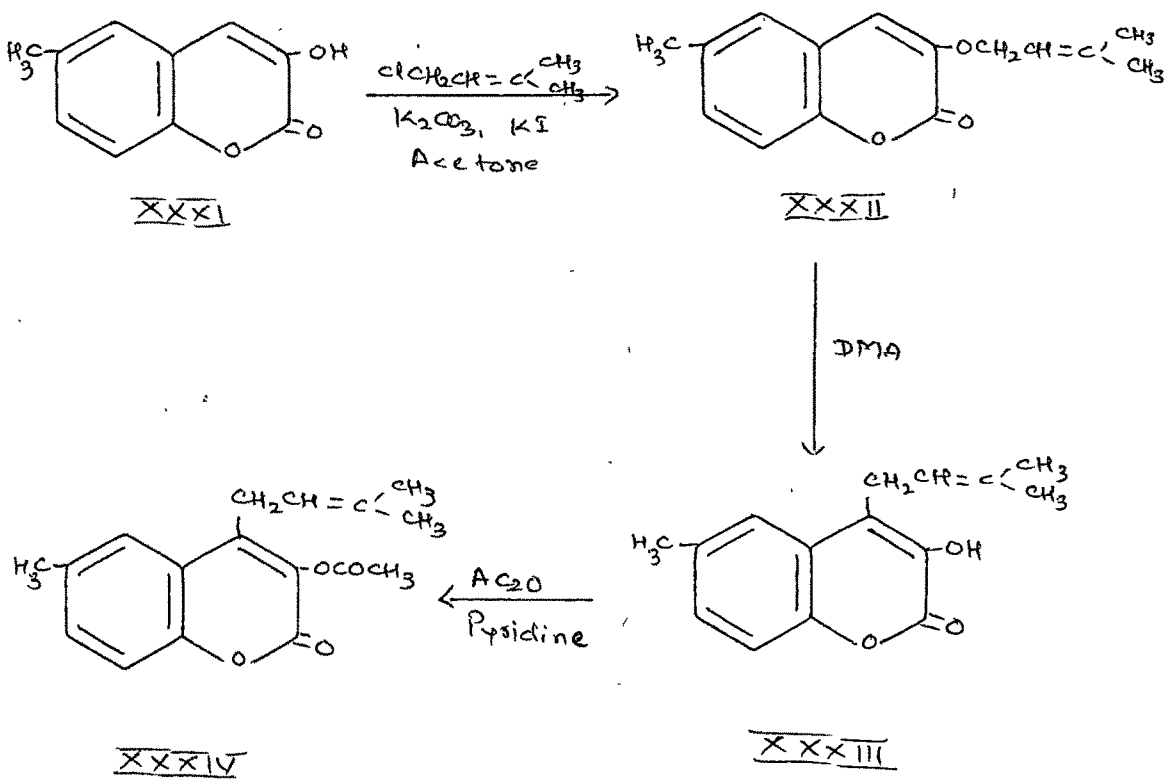
(XXXII) on refluxing with dimethylaniline yielded 3-hydroxy-4-prenyl-6-methylcoumarin (XXXIII). The structure of this compound is confirmed by its IR and NMR spectra.
IR (nujol) : 1700 $cm.^{-1}$ (α-pyrone carbonyl stretching frequency), 1630 $cm.^{-1}$ (aromatic -C=C- stretching frequency) and 1360 $cm.^{-1}$ (geminal dimethyl group stretching frequency).
NMR ($CDCl_3$) : δ 1.75 and 1.85, two singlets, geminal dimethyl group; 2.38, singlet, methyl group at position-6; 3.50, doublet, two protons of $-\underline{CH_2}-CH$ group at position-4; 5.00, triplet, one proton of $-CH_2-\underline{CH}$ group at position-4 and 7.15-7.40, multiplet, three protons aromatic (Fig. 2).

(XXXIII) on acetylation with acetic anhydride in the presence of pyridine gave 3-acetoxy-6-methyl-4-prenyl-coumarin (XXXIV).

Attempts to cyclise (XXXIII) met with failure when it was treated with conc. sulphuric acid, polyphosphoric acid, DDQ, etc.



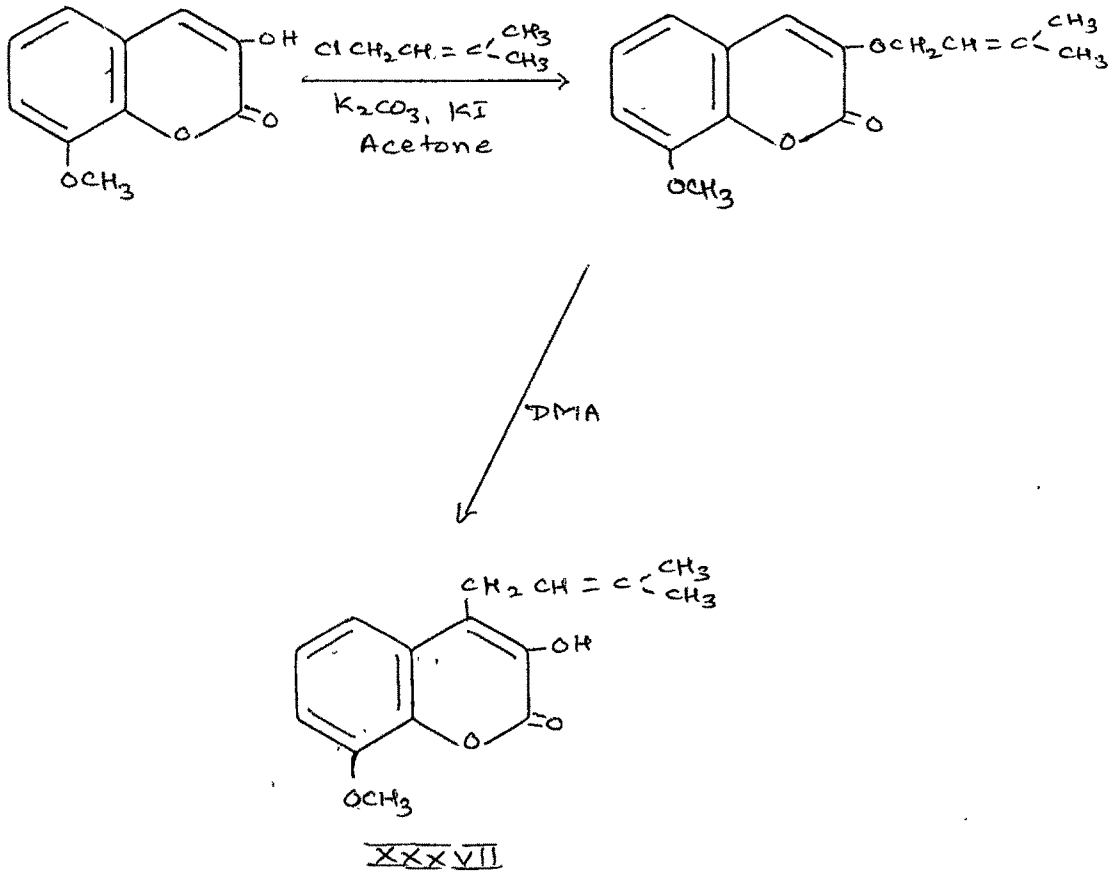
(Fig. 2) : 3-Hydroxy-4-prenyl-6-methylcoumarin



XXXI XXXII XXXIII XXXIV

Synthesis of 3-hydroxy-8-methoxy-4-prenylcoumarin

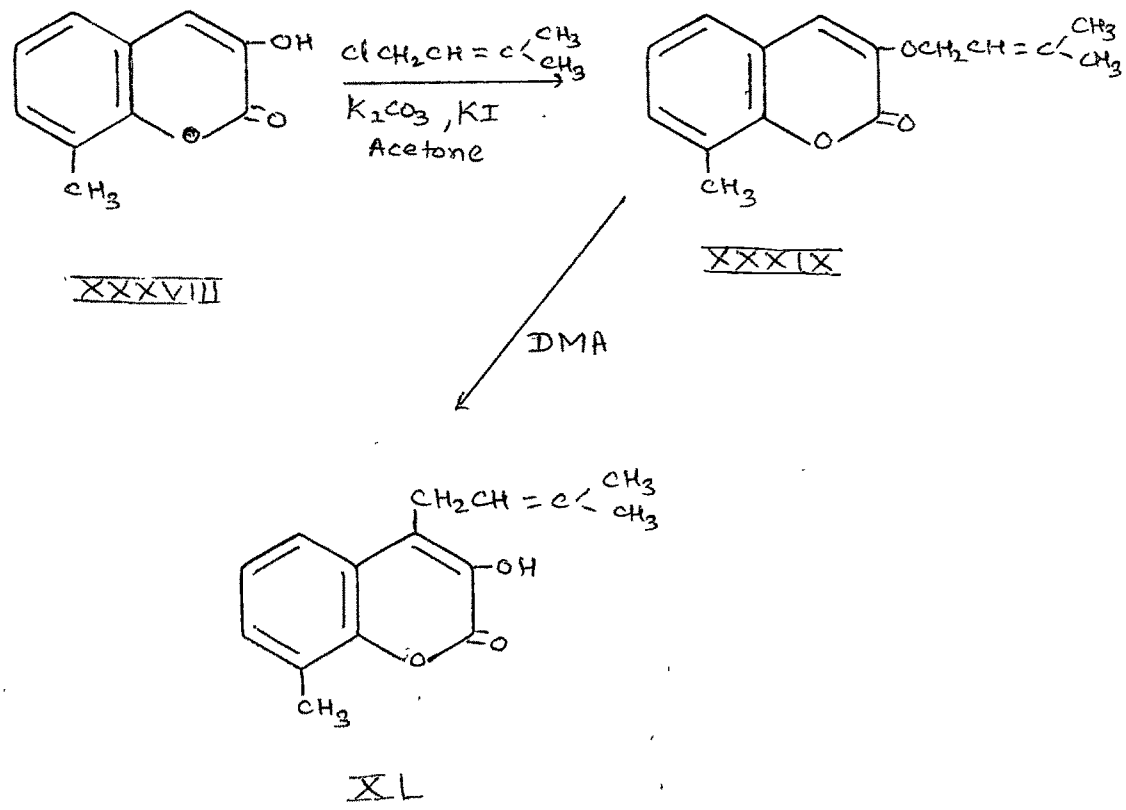
3-Hydroxy-8-methoxycoumarin (XXXV) was prenylated with 1-chloro-3-methyl-but-2-ene in the presence of anhydrous potassium carbonate and potassium iodide to give 8-methoxy--3-prenyloxycoumarin (XXXVI). This was further refluxed with dimethylaniline to give 3-hydroxy-8-methoxy-4-prenylcoumarin (XXXVII). It was attempted to cyclise with above mentioned reagents which ultimately failed to give corresponding cyclised product. (XXXVII) was reacted with acetic anhydride in the presence of pyridine which gave an oily product.



XXXVII

Synthesis of 3-hydroxy-8-methyl-4-prenylcoumarin

3-Hydroxy-8-methylcoumarin (XXXVIII) was condensed with 1-chloro-3-methyl-but-2-ene in the presence of anhydrous potassium carbonate, potassium iodide in acetone to give 8-methyl-3-prenyloxycoumarin (XXXIX) which on Claisen migration in boiling with dimethylaniline gave 3-hydroxy-8--methyl-4-prenylcoumarin (XL). Attempts to cyclise (XL) did not succeed.

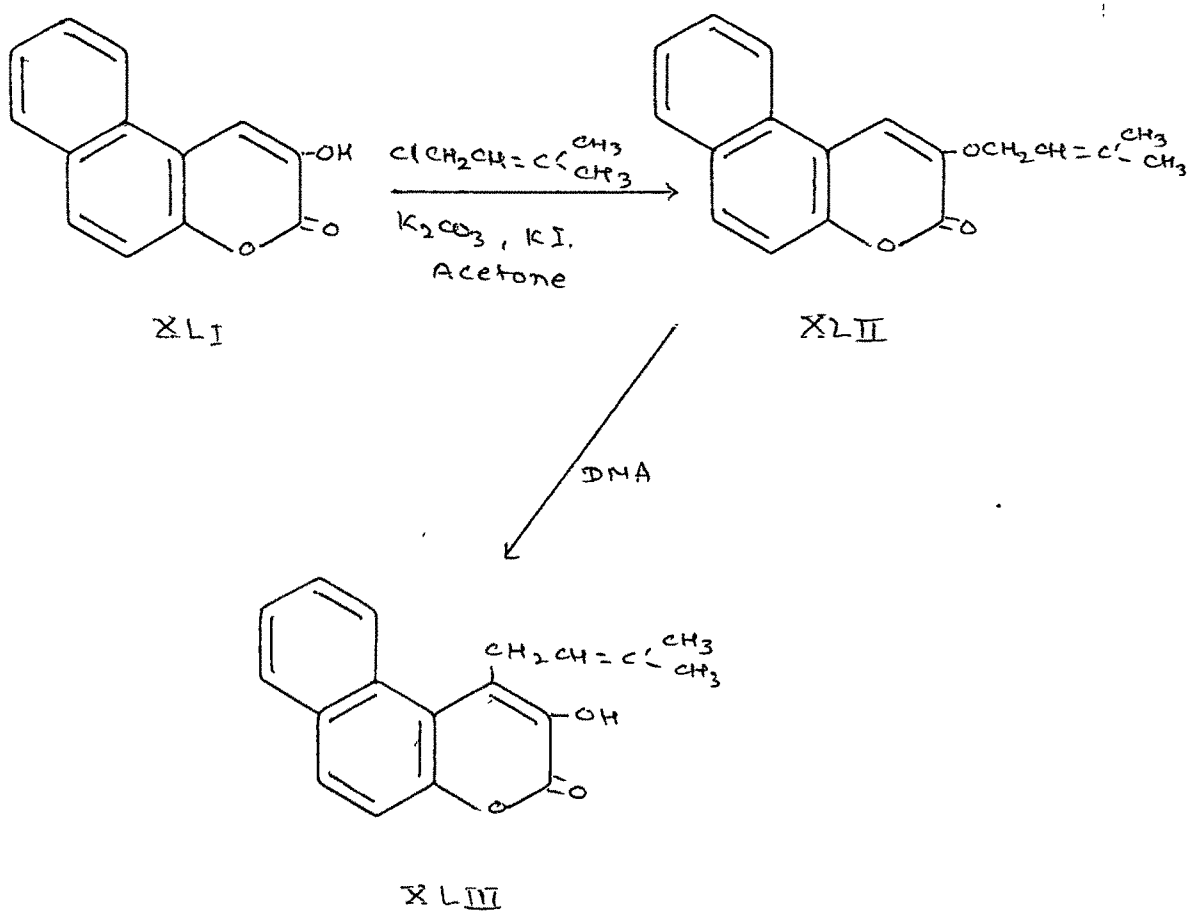


XXXVIII XXXIX

XL

Synthesis of 3-hydroxy-4-prenyl-5,6-benzocoumarin

3-Hydroxy-5,6-benzocoumarin (XLI) was condensed with 1-chloro-3-methyl-but-2-ene in the presence of anhydrous potassium carbonate and potassium iodide in acetone to give 3-prenyloxy-5,6-benzocoumarin (XLII). This was refluxed with dimethylaniline to give 3-hydroxy-4-prenyl--5,6-benzocoumarin (XLIII). Attempts to cyclise this compound failed.



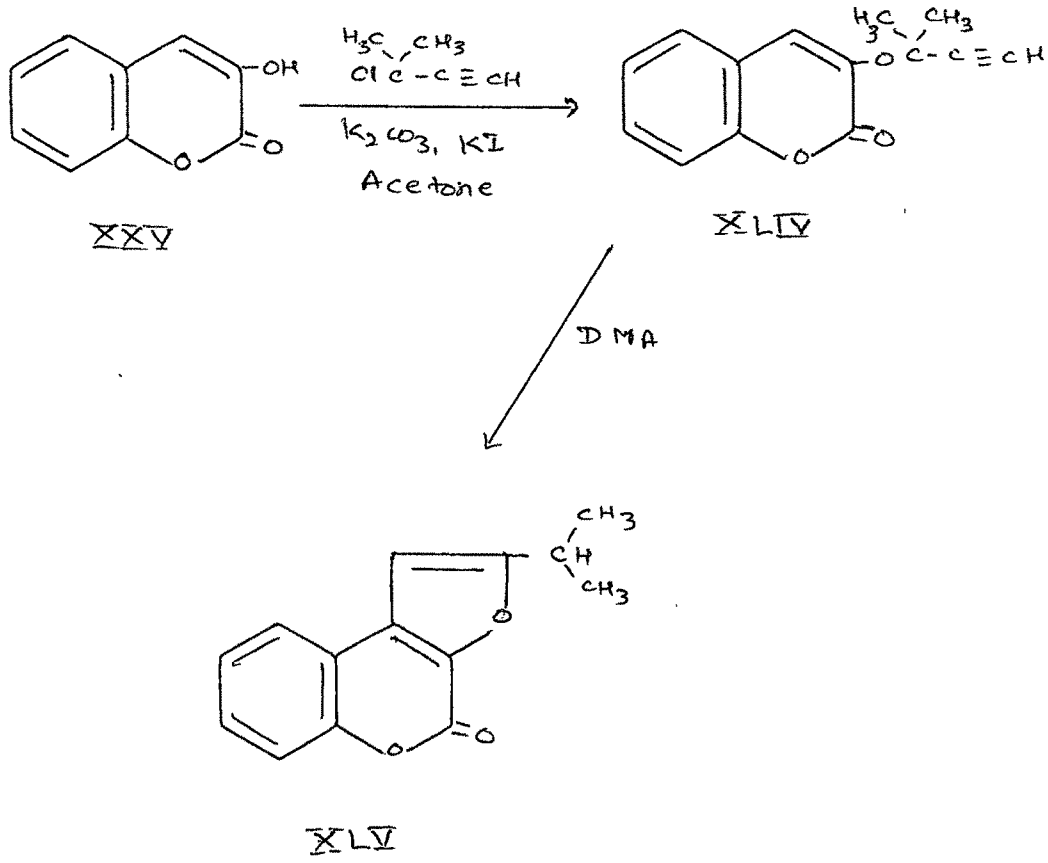
XLI XLII XLIII

As above method failed to give either the furan derivative or pyran derivatige, next method of prenylation with 3-chloro-3-methyl-but-1-yne was tried which gave good results.

Synthesis of 9-oxo-9H-2-isopropylfurano(2,3-c)benzopyran

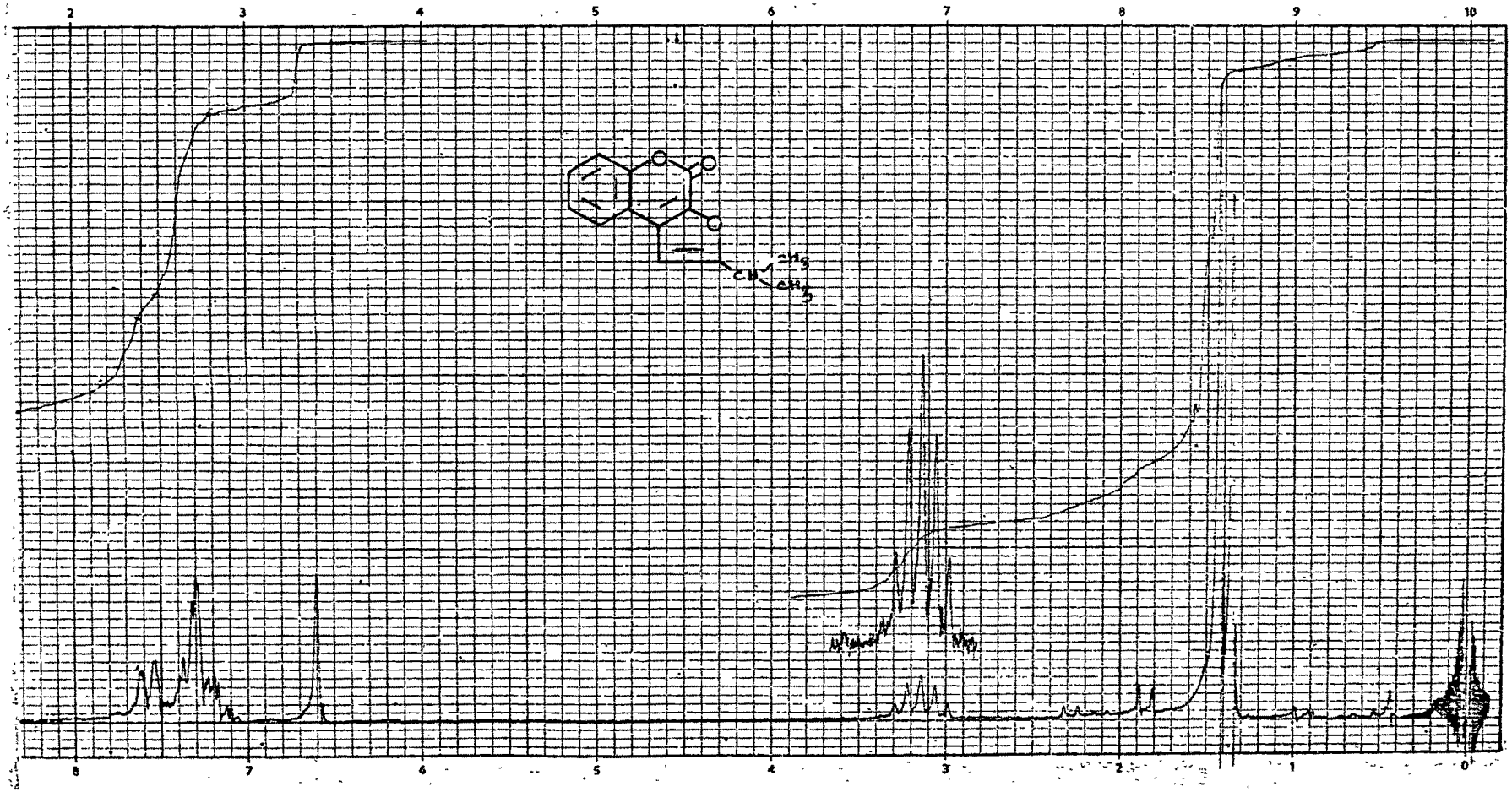
3-Hydroxycoumarin (XXV) was condensed with 3-chloro-3-methyl-but-1-yne in the presence of anhydrous potassium carbonate and potassium iodide in acetone to give

3-propargyloxycoumarin (XLIV). This was further refluxed with dimethylaniline to give 9-oxo-9H-2-isopropylfurano-(2,3-c)benzopyran (XLV).



The structure of (XLV) was confirmed by its IR and NMR spectra. The IR spectrum showed following bands :- 1725 $cm.^{-1}$ (α-pyrone carbonyl stretching frequency), 1610 $cm.^{-1}$ (aromatic -C=C- stretching frequency) and 1370 $cm.^{-1}$ (geminal dimethyl group stretching frequency).

NMR (CCl_4) : δ 1.40, doublet, J=7Hz, two methyl groups of isopropyl side chain at position-2; 3.15, quintate, J=7Hz

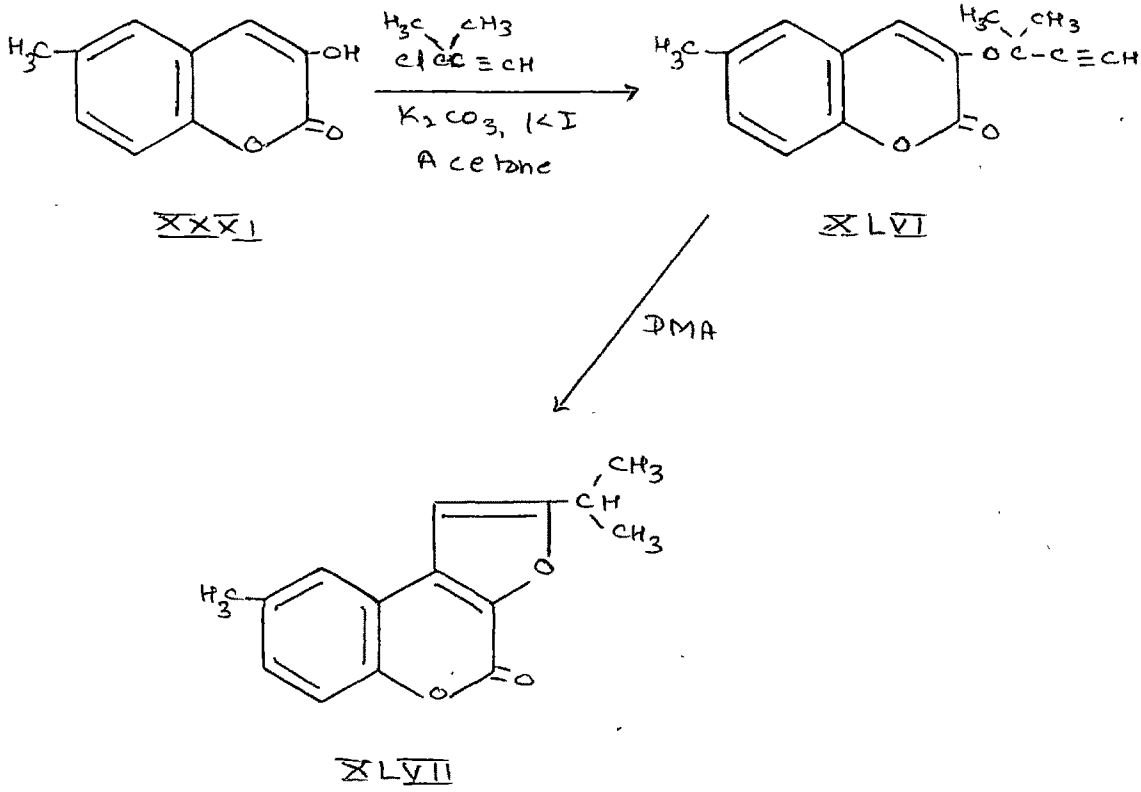


(Fig. 3) : 9-Oxo-9H-2-isopropylfurano(2,3-c)benzopyran

one proton of isopropyl group at position-2; 6.60, singlet, one proton at position-3 and 7.10-7.60, multiplet, four protons aromatic (Fig. 3).

Synthesis of 9-oxo-9H-2-isopropyl-5-methylfurano-(2,3-c)benzopyran

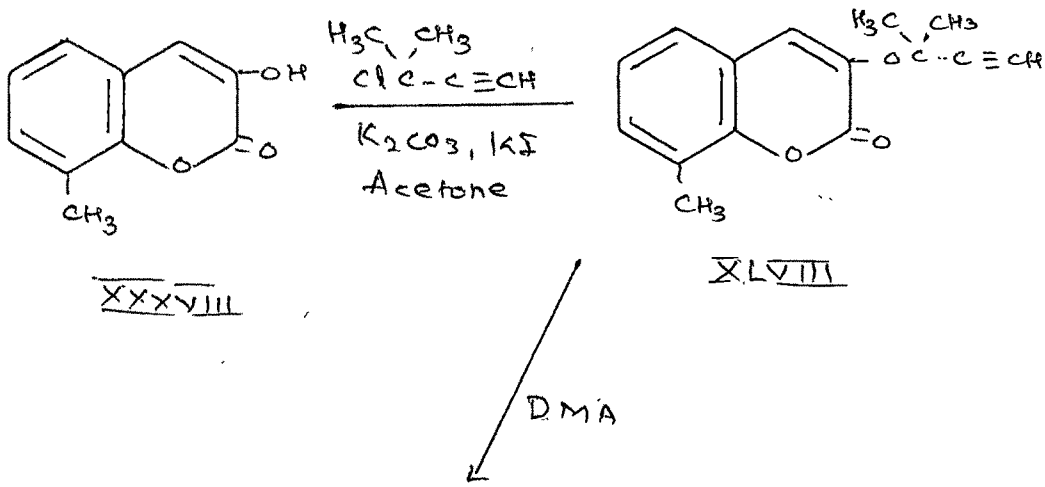
3-Hydroxy-6-methylcoumarin (XXXI) was condensed with 3-chloro-3-methyl-but-1-yne in the presence of anhydrous potassium carbonate and potassium iodide in acetone to give 3-propargyloxy-6-methylcoumarin (XLVI). This on refluxing with dimethylaniline gave 9-oxo-9H-2-isopropyl-5-methylfurano(2,3-c)-benzopyran (XLVII).



XXXI XLVI XLVII

Synthesis of 9-oxo-9H-2-isopropyl-7-methylfurano-(2,3-c)benzopyran

3-Hydroxy-8-methylcoumarin (XXXVIII) was condensed with 3-chloro-3-methyl-but-1-yne in the presence of anhydrous potassium carbonate and potassium iodide in acetone to give 3-propargyloxy-8-methylcoumarin (XLVIII), which on boiling with dimethylaniline gave 9-oxo-9H-2-isopropyl-7-methylfurano(2,3-c)benzopyran (XLIX).



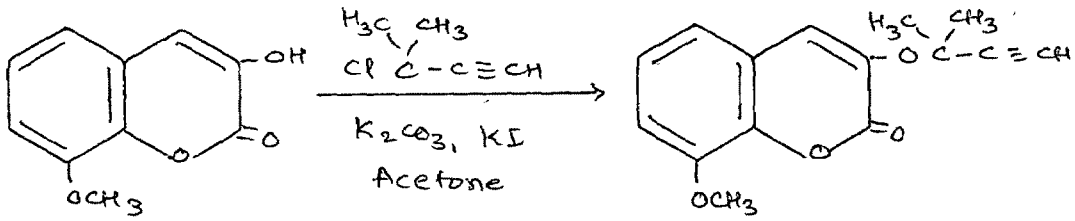
XXXVIII

XLVIII

XLIX

Synthesis of 8-methoxy-3-propargyloxycoumarin

3-Hydroxy-8-methoxycoumarin (XXXV) was condensed with 3-chloro-3-methyl-but-1-yne in the presence of anhydrous potassium carbonate and potassium iodide to give 8-methoxy--3-propargyloxycoumarin (L). As the yield of (L) was low, it was not possible to carry out its Claisen migration.



XXXV L

Attempted prenylation of 3-hydroxycoumarin with 2-methyl-but-3-en-2-ol

3-Hydroxycoumarin (XXV) was condensed with 2-methyl--but-3-en-2-ol in the presence of BF_3-etherate in dioxan. The product obtained after working up the reaction mixture gave an oily product which could not be further purified or identified.

Similarly, 3-hydroxy-6-methyl-, 3-hydroxy-8-methyl- and 3-hydroxy-8-methoxycoumarin failed to give prenylated coumarin derivatives with 2-methyl-but-3-en-2-ol in the presence of BF_3-etherate.

EXPERIMENTAL

3-Acetoxy-4-prenylcoumarin (XXIX) : 3-Prenyloxycoumarin (XXVI) :

3-Hydroxycoumarin (1.0 g.) was refluxed with anhydrous potassium carbonate (3.0 g.), potassium iodide (1.0 g.) and 1-chloro-3-methyl-but-2-ene (1 ml.) in acetone (100 ml.) for 12 hr. on a water bath. Acetone was distilled off and water was added to the residue. The solid separated was filtered and washed with dilute sodium hydroxide solution. The solid did not develope green colouration with ferric chloride solution. The solid, 3-prenyloxycoumarin, crystallised from alcohol as yellow plates, m.p. 116°. Yield 0.4 g.

Analysis : Found : C, 73.38 ; H, 5.84 %

$C_{14}H_{14}O_3$ requires : C, 73.04 ; H, 6.09 %.

Claisen migration of 3-prenyloxycoumarin : 3-Hydroxy-4-prenylcoumarin (XXVII) :

3-Prenyloxycoumarin (0.5 g.) was refluxed in dimethylaniline (5 ml.) for 2 hr. The solution was cooled and added to an ice-cold hydrochloric acid. The solid separated was passed over alumina and eluted with benzene. The solid, after evaporation of solvent, crystallised from petroleum ether as 3-hydroxy-4-prenylcoumarin, which gave green colouration with ferric chloride solution, m.p. 112°. Yield 0.4 g.

Analysis : Found : C, 72.98 ; H, 5.82 %

$C_{14}H_{14}O_3$ requires : C, 72.04 ; H, 6.09 %.

3-Acetoxy-4-prenylcoumarin (XXIX) :

3-Hydroxy-4-prenylcoumarin (0.2 g.), acetic anhydride (0.4 ml.) and pyridine (2 drops) were heated on a water bath for 4 hr. The reaction mixture was added to ice-cold dilute hydrochloric acid solution and the solid separated was filtered and crystallised from benzene-petroleum ether mixture, as 3-acetoxy-4-prenylcoumarin, m.p. 234°. Yield 0.1 g.

Analysis : Found : C, 70.26 ; H, 5.87 %

$C_{16}H_{16}O_4$ requires : C, 70.58 ; H, 5.88 %.

3-Acetoxy-6-methyl-4-prenylcoumarin (XXXIV) : 6-Methyl--3-prenyloxycoumarin (XXXII) :

3-Hydroxy-6-methylcoumarin (1.2 g.) was refluxed with anhydrous potassium carbonate (3.0 g.), potassium iodide (1.0 g.) and 1-chloro-3-methyl-but-2-ene (1 ml.) in acetone (100 ml.) for 10 hr. The acetone was distilled off and the water was added to the residue. The solid separated was filtered and washed with dilute sodium hydroxide solution. It did not give green colouration alcoholic ferric chloride solution. The solid, 6-methyl-3-prenyloxycoumarin, crystallised from petroleum ether, m.p. 114°. Yield 0.5 g.

Analysis : Found : C, 73.30 ; H, 6.32 %

$C_{15}H_{16}O_3$ requires : C, 73.77 ; H, 6.56 %.

Claisen migration of 6-methyl-3-prenyloxycoumarin :

3-Hydroxy-6-methyl-4-prenylcoumarin (XXXIII) :

6-Methyl-3-prenyloxycoumarin (0.5 g.) was refluxed in dimethylaniline (5 ml.) for 2 hr. The solution was cooled and added to an ice-cold hydrochloric acid solution. The solid separated was filtered, washed and crystallised from benzene-petroleum ether mixture, as 3-hydroxy-6-methyl-4-prenylcoumarin, m.p. 159-60°. Yield 0.35 g.

It gave green colouration with alcoholic ferric chloride solution.

Analysis : Found : C, 73.31 ; H, 6.65 %

$C_{15}H_{16}O_3$ requires : C, 73.77 ; H, 6.56 %.

3-Acetoxy-6-methyl-4-prenylcoumarin (XXXIV) :

3-Hydroxy-6-methyl-4-prenylcoumarin (1.0 g.) was heated on a water bath with acetic anhydride (2 ml.) and pyridine (2 drops) for 4 hr. The solution was then added to the ice-cold hydrochloric acid solution and the solid separated was filtered, washed with dilute sodium hydroxide solution and crystallised from petroleum ether, as 3-acetoxy-6-methyl-4-prenylcoumarin, m.p. 98-9°. Yield 1.0 g.

NMR ($CDCl_3$) : 1.69, singlet, geminal dimethyl group; 2.35, singlet, methyl group of $-COCH_3$; 2.40, singlet, methyl group at position-6; 5.00, doublet, two protons of $-CH_2-CH$; 6.20, triplet, one proton of $-CH_2-CH$; and 7.20, multiplet, three protons aromatic.

Analysis : Found : C, 71.41 ; H, 6.36 %

$C_{17}H_{18}O_4$ requires : C, 71.32 ; H, 6.29 %.

3-Hydroxy-8-methoxy-4-prenylcoumarin (XXXVII) : 8-Methoxy--3-prenyloxycoumarin (XXXVI) :

3-Hydroxy-8-methoxycoumarin (1.2 g.) was refluxed with anhydrous potassium carbonate (3.0 g.), potassium iodide (1.0 g.) and 1-chloro-3-methyl-but-2-ene (1 ml.) in acetone (100 ml.) for 10 hr. The solvent was removed by distillation and the residue was diluted with water. The solid separated was filtered, washed with dilute sodium hydroxide solution and crystallised from benzene-petroleum ether mixture, as 8-methoxy-3-prenyloxycoumarin, m.p. 83-4°. Yield 0.15 g.

Analysis : Found : C, 68.79 ; H, 5.85 %

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

Claisen migration of 8-methoxy-3-prenyloxycoumarin : 3-Hydroxy-8-methoxy-4-prenylcoumarin (XXXVII) :

8-Methoxy-3-prenyloxycoumarin (0.5 g.) was refluxed with dimethylaniline (5 ml.) for 2 hr. The solution was cooled and poured into the ice-cold hydrochloric acid solution. The solid separated was filtered and crystallised from benzene-petroleum ether mixture, as 3-hydroxy-8-methoxy--4-prenylcoumarin, m.p. 168-70°. Yield 0.3 g.

Analysis : Found : C, 69.11 ; H, 6.04 %

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

3-Hydroxy-8-methyl-4-prenylcoumarin (XL) : 8-Methyl-3--prenyloxycoumarin (XXXIX) :

3-Hydroxy-8-methylcoumarin (1.1 g.) was refluxed with anhydrous potassium carbonate (3.0 g.), potassium iodide (1.0 g.) and 1-chloro-3-methyl-but-2-ene (1 ml.)in acetone (100 ml.) for 10 hr. Acetone was distilled off and the residue was washed with water, filtered and then washed with sodium hydroxide solution. The solid, thus obtained was crystallised from benzene-petroleum ether mixture, as 8-methyl-3-prenyloxycoumarin, m.p. 122°. Yield 0.3 g.

Analysis : Found : C, 73.60 ; H, 6.42 %

$C_{15}H_{16}O_3$ requires : C, 73.77 ; H, 6.56 %.

Claisen migration of 8-methyl-3-prenyloxycoumarin : 3-Hydroxy--8-methyl-4-prenylcoumarin (XL) :

8-Methyl-3-prenyloxycoumarin (0.5 g.) was refluxed with dimethylaniline (5 ml.) for 2 hr. The solution was cooled and added to ice-cold hydrochloric acid solution. The solid separated was filtered, washed with water and crystallised from petroleum ether, as 3-hydroxy-8-methyl-4-prenylcoumarin, m.p. 142-44°. Yield 0.4 g.

Analysis : Found : C, 73.27 ; H, 6.49 %

$C_{15}H_{16}O_3$ requires : C, 73.77 ; H, 6.56 %.

3-Hydroxy-4-prenyl-5,6-benzocoumarin (XLIII) : 3-Prenyloxy--5,6-benzocoumarin (XLII) :

3-Hydroxy-5,6-benzocoumarin (1.3 g.) was refluxed with anhydrous potassium carbonate (3.0 g.), potassium iodide (1.0 g.) and 1-chloro-3-methyl-but-2-ene (1 ml.) in acetone (100 ml.) for 12 hr. The solvent was then evaporated and the residue was diluted with water. The solid was filtered, washed with sodium hydroxide solution and crystallised from petroleum ether, as 3-prenyloxy-5,6-benzocoumarin, m.p. 65-66°. Yield 0.4 g.

The analysis of this compound did not agree with with the molecular formula but the structure is quite agreeable with its NMR spectrum.

NMR (CCl_4) : δ 1.75 and 1.80, two singlets, geminal dimethyl group; 4.65, doublet, two protons of $-CH_2-CH$; 5.45, triplet, one proton of $-CH_2-CH$: and 7.05-7.90, multiplet, six protons aromatic.

Claisen migration of 3-prenyloxy-5,6-benzocoumarin : 3-Hydroxy-4-prenyl-5,6-benzocoumarin (XLIII) :

3-Prenyloxy-5,6-benzocoumarin (0.5 g.) was refluxed with dimethylaniline (5 ml.) for 2 hr. The solution was cooled and added to the ice-cold hydrochloric acid solution. The solid separated was filtered, washed with water and crystallised from petroleum ether, as 3-hydroxy--4-prenyl-5,6-benzocoumarin, m.p. 83-84°. Yield 0.3 g. It gave green colouration with alcoholic ferric chloride solution.

Analysis : Found : C, 77.49 ; H, 5.38 %

$C_{18}H_{16}O_3$ requires : C, 77.12 ; H, 5.75 %.

9-Oxo-9H-2-isopropylfurano(2,3-c)benzopyran (XLV) :

3-Propargyloxycoumarin (XLIV) :

3-Hydroxycoumarin (1.0 g.), anhydrous potassium carbonate (3.0 g.), potassium iodide (1.0 g.) and 3-chloro--3-methyl-but-1-yne (3 ml.) were refluxed in acetone (100 ml.) for 50 hr. The mixture was diluted with water, after distilling of the solvent and extracted with ether. The ethereal solution, after evaporation of the solvent, examined on TLC (chloroform) showed two compounds. Elution with petroleum ether-benzene (2:1) yielded an unidentifiable liquid and elution with benzene gave a solid, 3-propargyloxycoumarin, crystallised from petroleum ether, m.p. 82°. Yield 0.1 g.

Analysis : Found : C, 74.13 ; H, 5.05 %

$C_{14}H_{12}O_3$ requires : C, 73.68 ; H, 5.26 %.

Claisen migration of 3-propargyloxycoumarin : 9-Oxo-9H--2-isopropylfurano(2,3-c)benzopyran (XLV) :

3-Propargyloxycoumarin (0.2 g.) was refluxed with dimethylaniline (5 ml.) for 4 hr. The mixture was added to an ice-cold hydrochloric acid solution and extracted with ether. The residue was chromatographed over alumina and eluted with benzene. The solid, 9-oxo-9H-2-isopropyl-furano(2,3-c)benzopyran, crystallised from petroleum ether, m.p. 93-94° . Yield 0.15 g.

Analysis : Found : C, 73.77 ; H, 5.08 %

$C_{14}H_{12}O_3$ requires : C, 73.68 ; H, 5.26 %.

9-Oxo-9H-2-isopropyl-5-methylfurano(2,3-c)benzopyran (XLVII):

6-Methyl-3-propargyloxycoumarin (XLVI) :

3-Hydroxy-6-methylcoumarin (1.1 g.), anhydrous potassium carbonate (3.0 g.), potassium iodide (1.0 g.) and 3-chloro-3-methyl-but-1-yne (3 ml.) were refluxed in acetone (100 ml.) for 50 hr. The solvent distilled off and the water was added to the residue and extracted with ether. The ethereal solution was evaporated and the residue was chromatographed on silica gel. The solid, 6-methyl-3-propargyloxycoumarin, crystallised from benzene-petroleum ether mixture, m.p. 119-21°. Yield 0.07 g.

Analysis : Found : C, 73.87 ; H, 6.27 %

$C_{15}H_{14}O_3$ requires : C, 74.36 ; H, 5.83 %.

Claisen migration of 6-methyl-3-propargyloxycoumarin : 9-Oxo-9H-2-isopropyl-5-methylfurano(2,3-c)benzopyran (XLVII) :

6-Methyl-3-propargyloxycoumarin (0.2 g.) was refluxed with dimethylaniline (5 ml.) for 4 hr.. The solution was cooled and added to the ice-cold hydrochloric acid solution. The solution extracted with ether and the residue was chromatographed over alumina. Elution with benzene gave a solid, 9-oxo-9H-2-isopropyl-5-methylfurano(2,3-c)benzopyran, crystallised from benzene-petroleum ether mixture, m.p. 182-83°. Yield 0.1 g.

Analysis : Found : C, 74.18 ; H, 5.70 %

$C_{15}H_{14}O_3$ requires : C, 74.36 ; H, 5.83 %.

9-Oxo-9H-2-isopropyl-7-methylfurano(2,3-c)benzopyran (XLIX) :

8-Methyl-3-propargyloxycoumarin (XLVIII) :

3-Hydroxy-8-methylcoumarin (1.1 g.), anhydrous potassium carbonate (3.0 g.), potassium iodide (1.0 g.) and 3-chloro-3-methyl-but-1-yne (3 ml.) were refluxed in acetone (100 ml.) on a water bath for 50 hr. The solvent was distilled off and the water was added to the residue. The solution was then extracted with ether and the ethereal layer was evaporated. The residue was passed over silica gel and elution with benzene gave a solid, 8-methyl-3-propargyloxy-coumarin, crystallised from benzene-petroleum ether, m.p. 174-76°. Yield 0.09 g.

Analysis : Found : C, 74.73 ; H, 6.07 %

$C_{15}H_{14}O_3$ requires : C, 74.36 ; H, 5.83 %.

Claisen migration of 8-methyl-3-propargyloxycoumarin :

9-Oxo-9H-2-isopropyl-7-methylfurano(2,3-c)benzopyran (XLIX) :

8-Methyl-3-propargyloxycoumarin (0.2 g.) was refluxed in dimethylaniline (5 ml.) for 4 hr. The solution was cooled and added to the ice-cold hydrochloric acid solution. The solid, 9-oxo-9H-2-isopropyl-7-methylfurano(2,3-c)benzo-pyran, separated was filtered and crystallised from petroleum ether, m.p. 171-73°. Yield 0.1 g.

Analysis : Found : C, 74.80 ; H, 6.17 %

$C_{15}H_{14}O_3$ requires : C, 74.36 ; H, 5.83 %.

8-Methoxy-3-propargyloxycoumarin (L) :

3-Hydroxy-8-methoxycoumarin (1.2 g.) was refluxed with anhydrous potassium carbonate (3.0 g.), potassium iodide (1.0 g.) and 3-chloro-3-methyl-but-1-yne (3 ml.) in acetone (100 ml.) for 60 hr. The solvent was distilled off and water was added to the residue. The solution was extracted with ether and the solid obtained, after the evaporation of the solvent, 8-methoxy-3-propargyloxycoumarin, crystallised from petroleum ether, m.p. 115-16°. Yield 0.02 g.

Analysis : Found : C, 69.39 ; H, 5.52 %

$C_{15}H_{14}O_4$ requires : C, 69.76 ; H, 5.42 %.

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