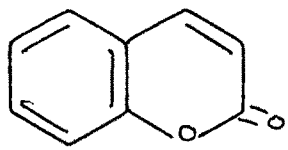
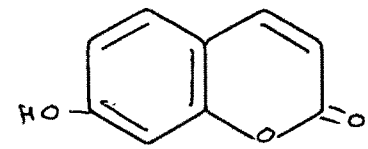
GENERAL INTRODUCTION

GENERAL INTRODUCTION

Coumarins or benzo-α-pyrones, are among the compounds most abundantly occurring in nature, either in free state or in combined state. Some of them are pharmacologically active anticoagulants, rodenticides and insecticides. Coumarin (I) is a sweet smelling constituent of white clover and is found in a large variety of plants. Umbelliferon (II), Scopoletin (III), Aesculetin (IV), Ayapin (V), Fraxetin (VI) and Daphnetin (VII) are the simple coumarins occurring in nature.



I



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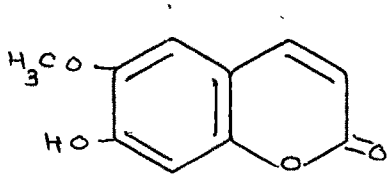

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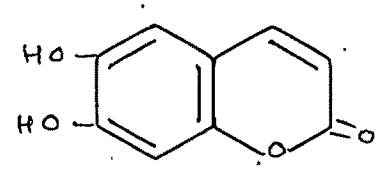

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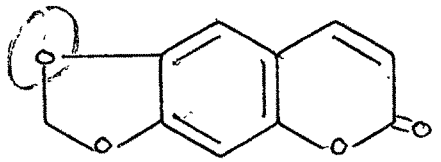

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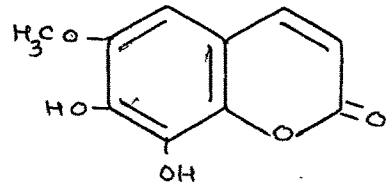
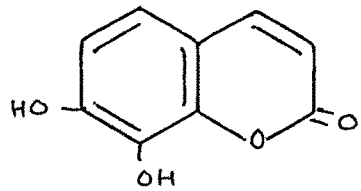
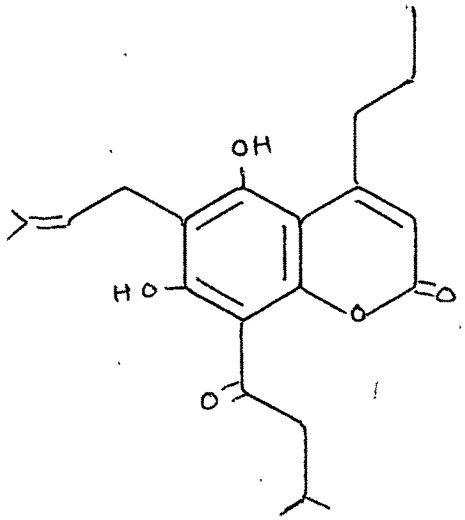


VI

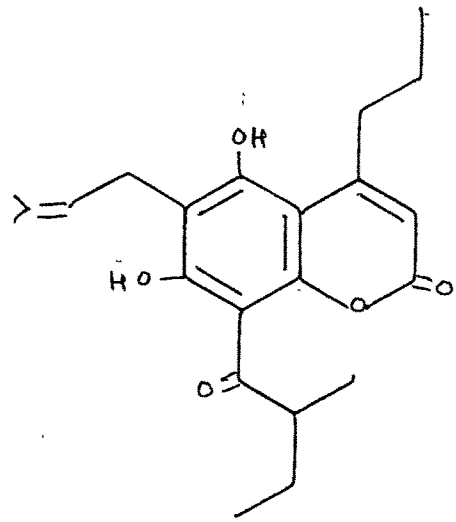


VII

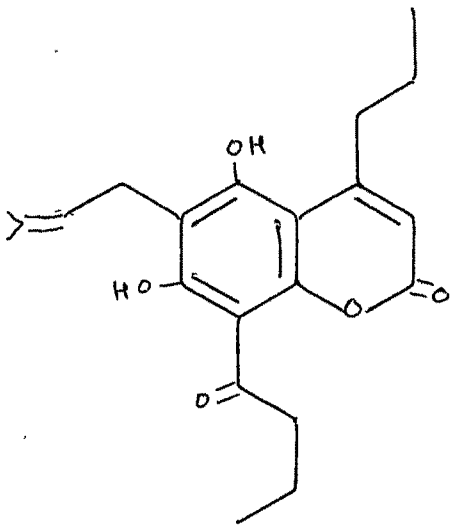
Among naturally occurring compounds, most of the derivatives of benzo-α-pyrones, a number of them are essentially non-terpenoid but have isoprene units present in them. The majority are components of higher plants and very few are metabolic products. Their wide distribution has been noticed earlier[1,2]. L.Crombie and co-workers[3] have isolated four different 4-alkylated coumarin derivatives, Mammea B/BA (VIII), Mammea B/BB (IX), Mammea B/BC (X) and Mammea C/BB (XI) from the seeds of the insecticide bearing plant Mammea Americana L. (Guttiferea).



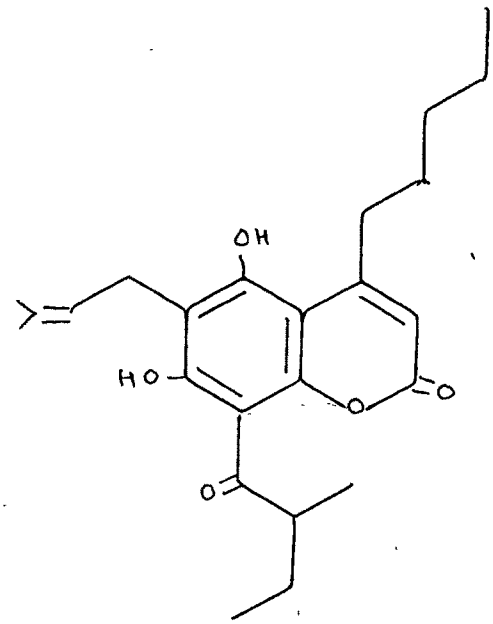
VIII



IX



X

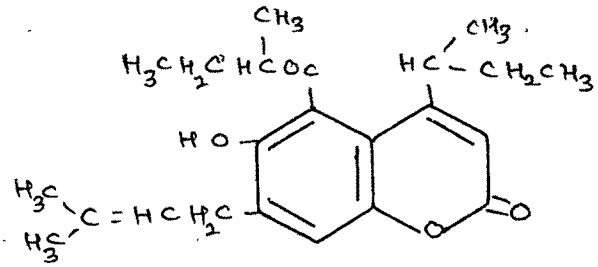


XI

Structures of these coumarin derivatives have been assigned by the spectral data.

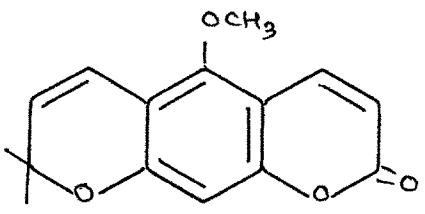
Govindachari, Pai and co-workers[4] isolated 4-alkylcoumarin derivative, ferruol-A, from the trunk-bark

of Mesua ferrea L. Structure of (XII) was established on the basis of IR, UV and NMR spectra and also by degradation methods.

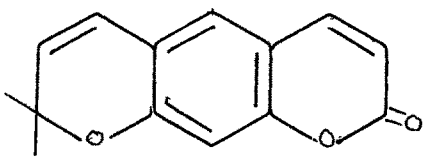


XII

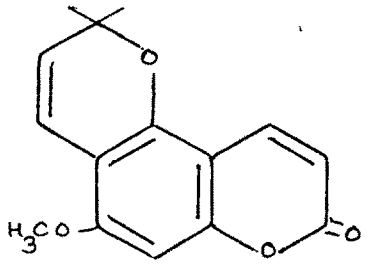
Chromenocoumarin derivatives are also a naturally occurring coumarin derivatives group. The first member of this group to be isolated was Xanthoxyletin (XIII) from Xanthoxylum Americannum D.Mill[5]. Xanthyletin (XIV), Alloxanthoxyletin (XV), Seselin (XVI) and Luvangetin (XVII) are the examples of 2,2-dimethylchromenocoumarin derivatives.



XIII



XIV



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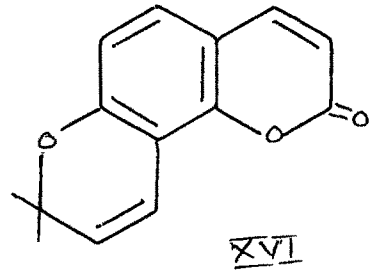

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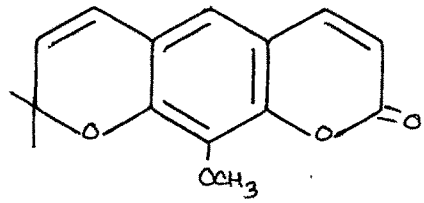
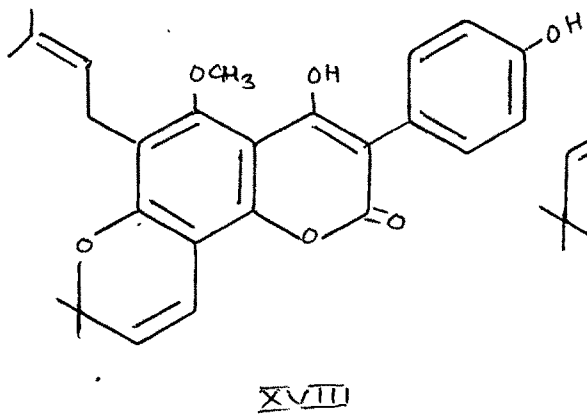
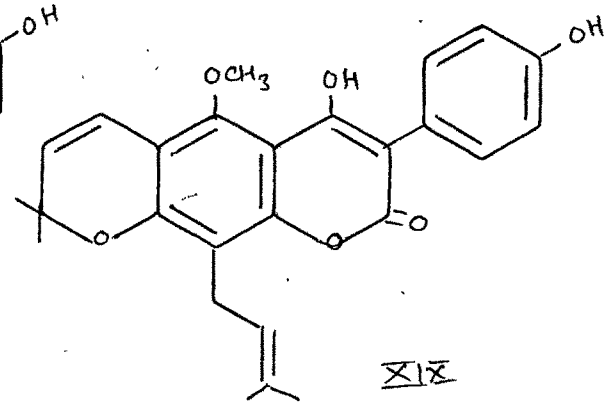


XVII

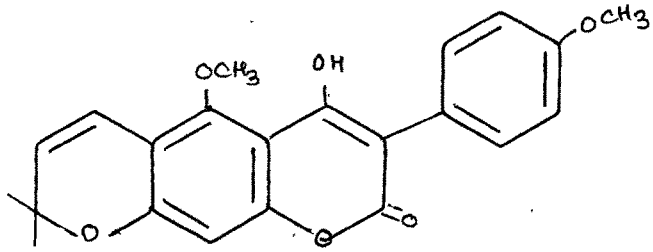
A new group of isoprenylated 4-hydroxy-3-phenyl-coumarins among the naturally occurring isoflavonoids, have been reported by Pelter and Stainton[6]. Scandenin (XVIII), Lochocarpic acid (XIX) and Robustic acid (XX) are the examples of this group, mainly isolated from the spacies of Derris.



XVIII

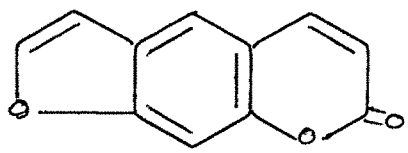


XIX

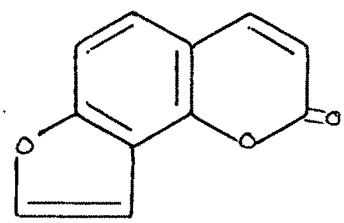


XX

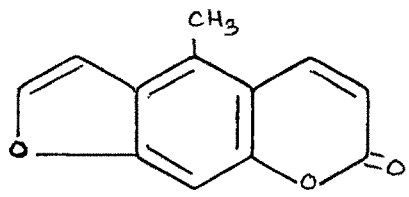
Yet, an another group of interesting naturally occurring coumarin derivatives are the furanocoumarins[7,8]. They are active as fish poisons, and insecticides. Plants of Rutaceae and Umbelliferae families are the principle sources of the many naturally occurring members of this group. Psoralene (XXI), Angelicin (XXII), Bergaptan (XXIII), Xanthotoxin (XXIV), Pimpinellin (XXV), Isopimpinellin (XXVI) and Oreoselone (XXVII) are a few members of this group.



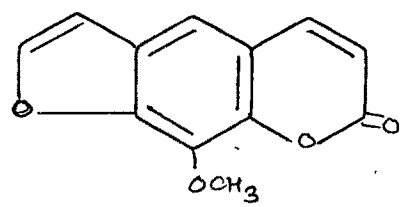
XXI



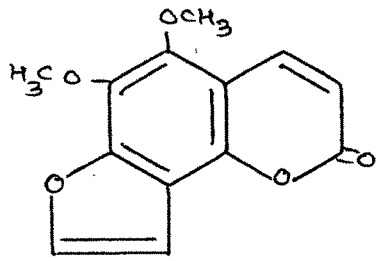
XXII



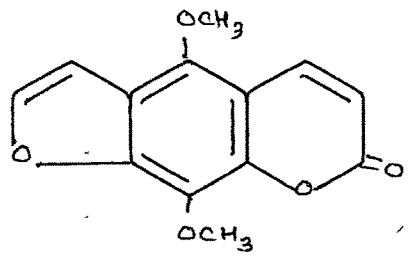
XXIII



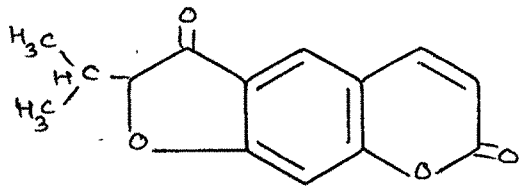
XXIV



XXV

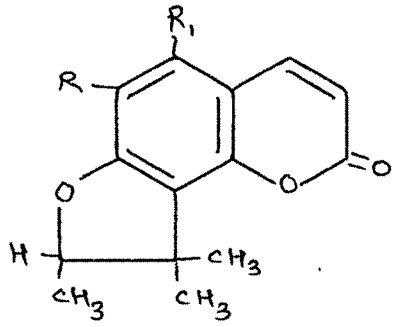


XXVI



XXVII

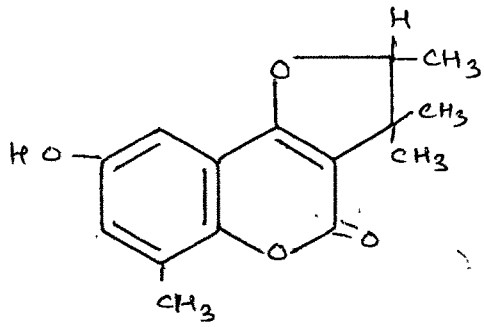
Murray et al.[9] isolated dihydrofurano compounds in the group of coumarins, e.g. Nieshoutol (XXVIIIa) and Nieshoutin (XXVIIIb) from the African sneez-wood, Ptaeroxylon obliquum. Irrie and co-workers[10] isolated similar type of dihydrofuranocoumarin derivative from rhizomes of G. Palmatum, e.g. Glaupalol (XXIX).



XXVIII

(a) R=H; R_1=OCH_3

(b) R=OCH_3; R_1=H



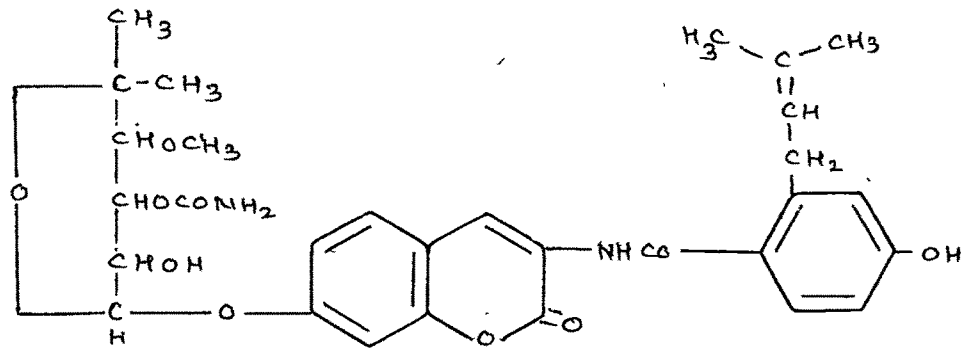
XXIX

The interest in coumarin derivatives has considerably increased in recent years because of the discovery of their varied biochemical properties, industrial uses and analytical applications.

Many natural coumarins affect the living cells of plants and animals in various ways. Bose[11] has reviewed the biochemical properties of natural coumarins.

Link et al.[12] discovered that the haemorrahagic principle of the spoiled sweet clover was 3,3'-methylene--bis(4-hydroxycoumarin), also known as dicoumarol. This has led to the preparation and testing of several 4-hydroxy-coumarin derivatives as anticoagulant drugs and a number of very effective drugs of this group, such as, warfarin, tromexan, coumachlor and marcoumar are on the market. It is interesting to note that some simple coumarins have the opposite effect. Herniarin and ayapin have been found to possess remarkable haemostatic property and are active both in vitro and vivo[13].

Novobiocin[14], an antibiotic, isolated from streptomyces sp., has been found to be a coumarin derivative having the structure (XXX). The antibacterial spectrum of this antibiotic corresponds generally with that of penicillin and erythromycin, but in vitro, is less potent than penicillin and erythromycin.



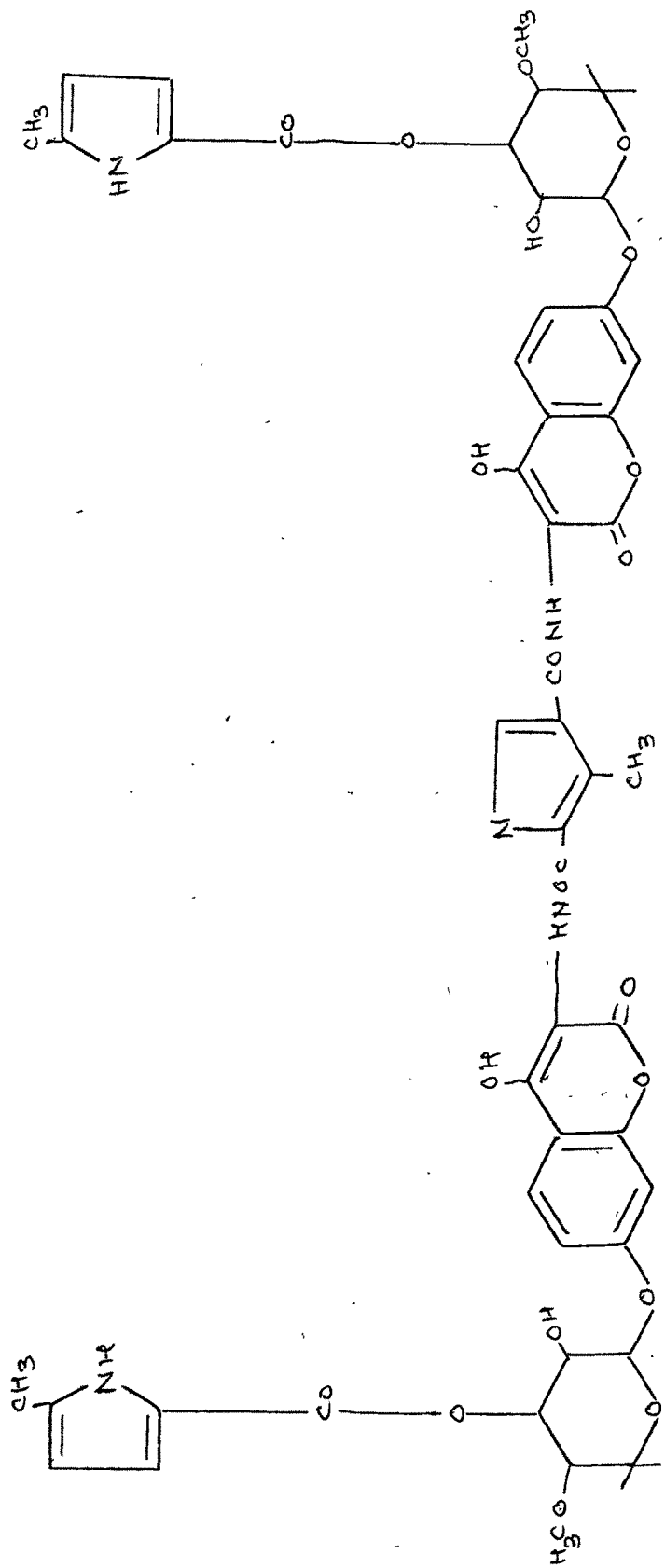
XXX

Kawaguchi and co-workers[15] have obtained a new coumarin derivative, an antibiotic coumermycin, from the filtrate (pH 5) residue of the fermentation beers of streptomyces rishiriensis having the structure (XXXI).

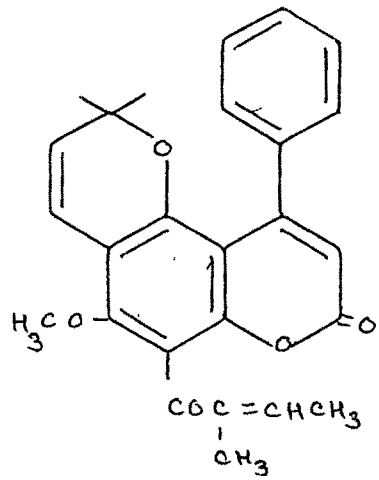
Coumermycin A, inhibits the growth of gram positive, gram negative and acid fast bacteria and against staphylococai. It is about 30 times more potent than novobiocin.

Callophylloid, a naturally occurring 4-phenyl-coumarin isolated from Callophyllum inophyllum (XXXII), was found to have anticoagulant activity in rabbits[16].

There are number of methods available for the synthesis of coumarin derivatives. These have been reviewed by Sethna and Shah[8] and Wawzonek[17].



XXXI



XXXII

The coumarin derivatives have also been subjected to various substitution reactions such as chlorination[18-21], bromination[22-30], iodination[31-32], chloromethylation[33], nitration[26,28,34-37], Fries and Friedel-Crafts reactions[27,38-42], formylation[43-45], sulphonation[26,48,49] and other reactions.

The present work deals with the isoprenylated coumarins having an isoprenyl unit, which may be attached either to oxygen or to carbon or cyclised as a neighbouring hydroxyl groups forming a furan ring or a chromene ring.

Chapter I deals with the studies in the synthesis of some 5-oxo-5H-2,2-dimethylpyrano(3,2-c)benzopyran derivatives, furanocoumarins formed by an abnormal Claisen rearrangement and some other furanocoumarin derivatives, starting with different 4-hydroxycoumarins.

Chapter II deals with the synthesis of some pyrano-

-coumestan derivatives, furanocoumarins and pyranofurano-coumarins and difuranocoumarin derivatives.

In Chapter III, different 3-hydroxycoumarins are condensed with different isoprenylating reagents giving furanocoumarin derivatives or acyclic isoprenylated coumarin derivatives.

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CHAPTER I

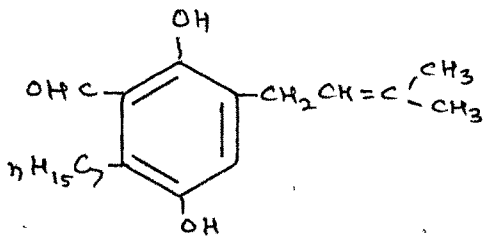
PRENYLATION OF 4-HYDROXYCOUMARINS

CHAPTER I

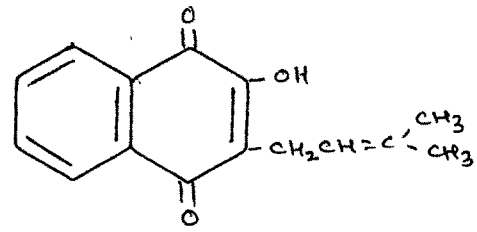
PRENYLATION OF 4-HYDROXYCOUMARINS

THEORETICAL

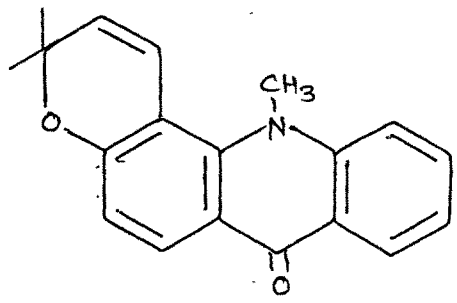
Among natural products, a number of compounds are essentially non-terpenoid but have isoprene units present in them. Such compounds belong to diverse molecular type. The majority are components of higher plants, a few, however, are mould metabolic products. Their wide distribution has earlier been described by Geissmann[1] and Robinson[2]. Most of them are derivatives of benzopyrones, though there are number of examples which are derivatives of benzene, naphthalene and also of quinoline. Some of them are represented below :-



Flavoglucin

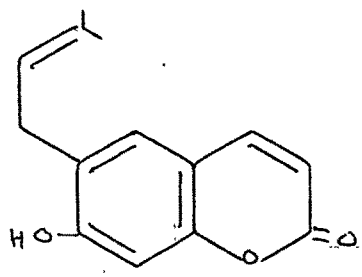


Lapachol

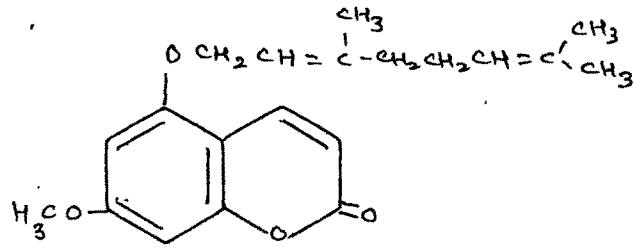


Acronycin

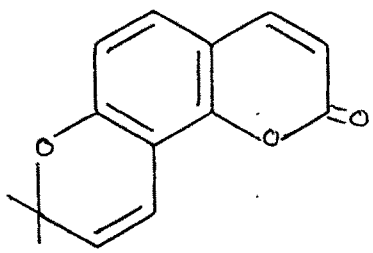
About ninety coumarins or benzo-α-pyrones compose one of the most important group of natural products[3-5]. Majority of them are derived from plants, especially Leguminosae, Orchidaceae, Rutaceae and Umbelliferae, the other coming from animals or micro-organisms. Among the coumarins, many are with isoprenoid chains of one, two or three isoprene units. The isoprene unit may be linked to an oxygen atom forming an ether, or to a nuclear carbon of the main skeleton. The unit has been encountered in several modifications differing in state of oxidation and also involved in ring formation by combination with an adjacent hydroxyl. Few examples of such isoprenoids are Suberosin (I), 5-Geranyl-7-methoxycoumarin (II), Seselin (III), Nieshoutin (IV).



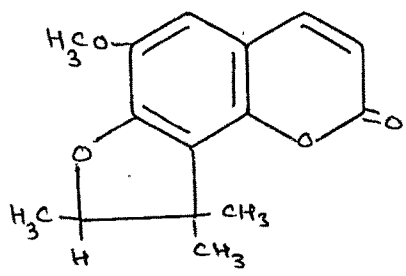
I



II

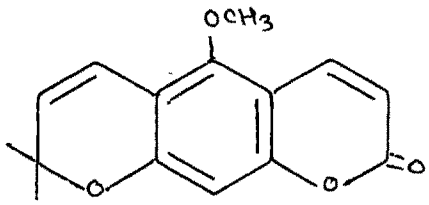


III

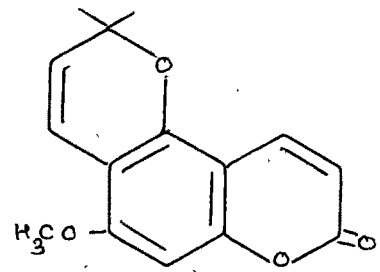


IV

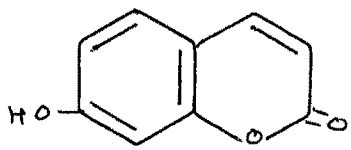
The first member to be isolated was Xanthoxyletin (V) from Xanthoxylum Americannum Mill[6]. Subsequently one of the angular isomerides, alloxanthoxyletin[7] (VI) and the parent member of the series, Xanthyletin[8] (VII), were isolated from the same source. Gordin[6a] found that the xanthoxyletin (V) contains a methoxyl group but no hydroxyl or keto group. The complete structure has been established by Robertson and his colleagues[9,10]. Xanthyletin (VII) has been synthesised by Späth[11] in low yield by the condensation of 2-methyl-but-3-yne-2-ol (IX) with 7-hydroxycoumarin (umbelliferon) (VIII).



V

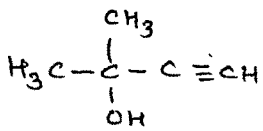


VI

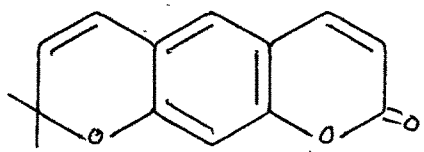


VIII

+

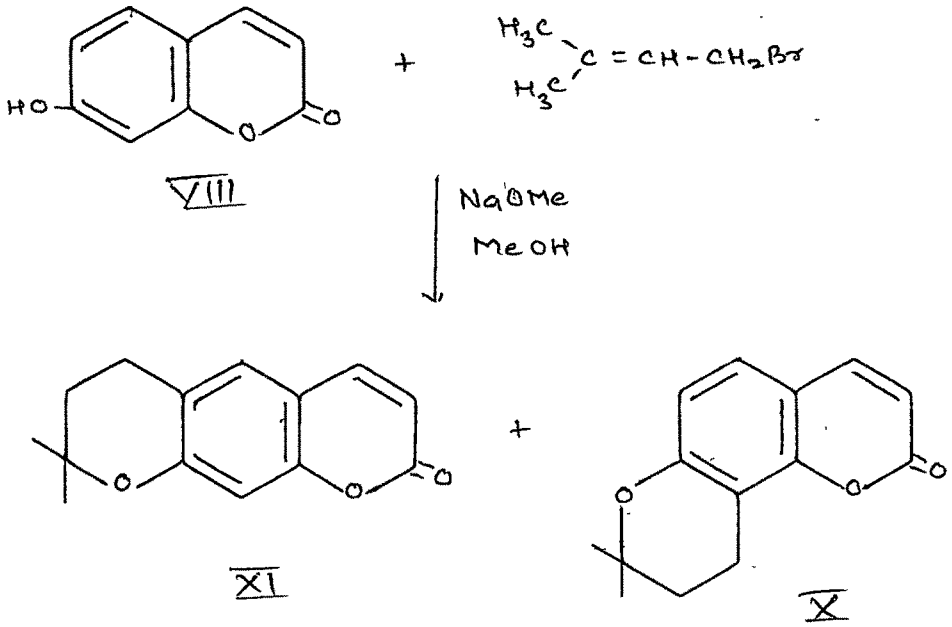


IX



VII

Seshadri and Austin[12] treated sodium salt of umbelliferon (VIII) with γ,γ-dimethylallyl bromide. The neutral fraction yielded two compounds, one is dihydroseselin (X) and dihydroxanthyletin (XI). Dehydrogenation of these compounds with DDQ, according to Cardillo[13], yielded seselin (III) and xanthyletin (VII).

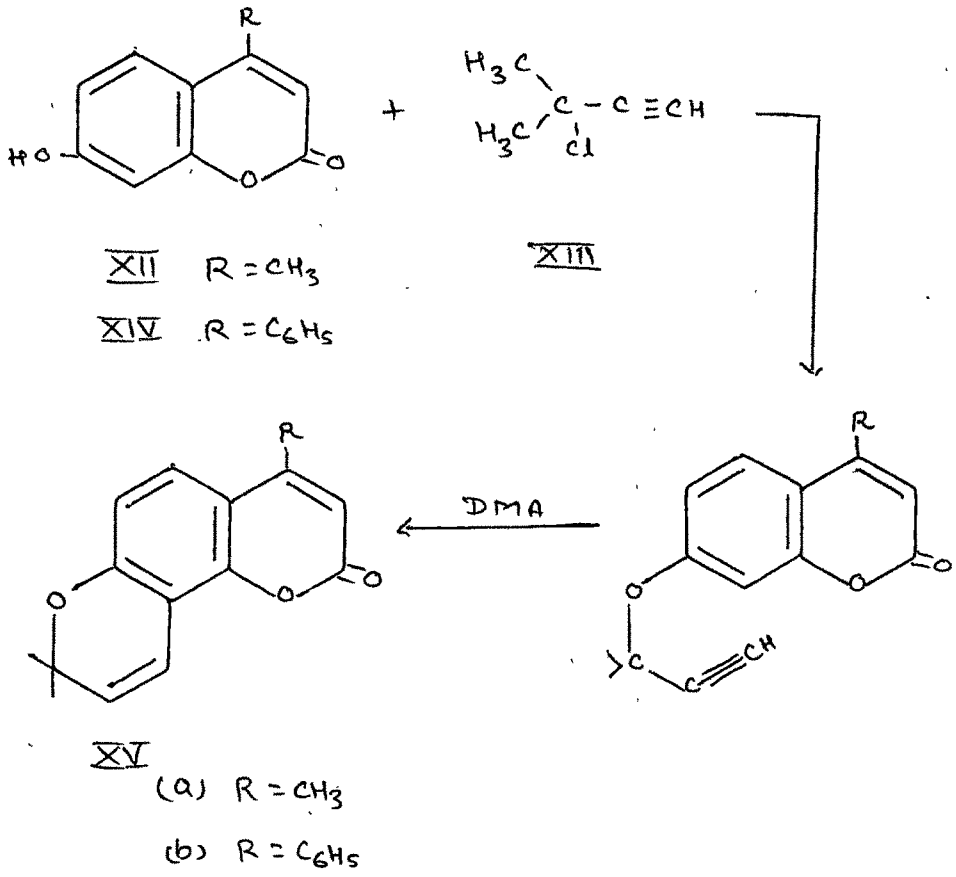


VIII

XI

X

Seshadri et al.[14] also synthesised 2,2-dimethyl-chromenocoumarins by the condensation of 4-methylumbelliferon (XII) and 4-phenylumbelliferon (XIV) with 3-chloro-3-methyl--but-1-yne (XIII), according to the method of Hlubuck et al[15]. The resultant propargylether was rearranged by boiling with dimethylaniline according to the Claisen method, giving chromenocoumarins (XVa and XVb).



XII R = CH_3

XIV R = C_6H_5

XIII

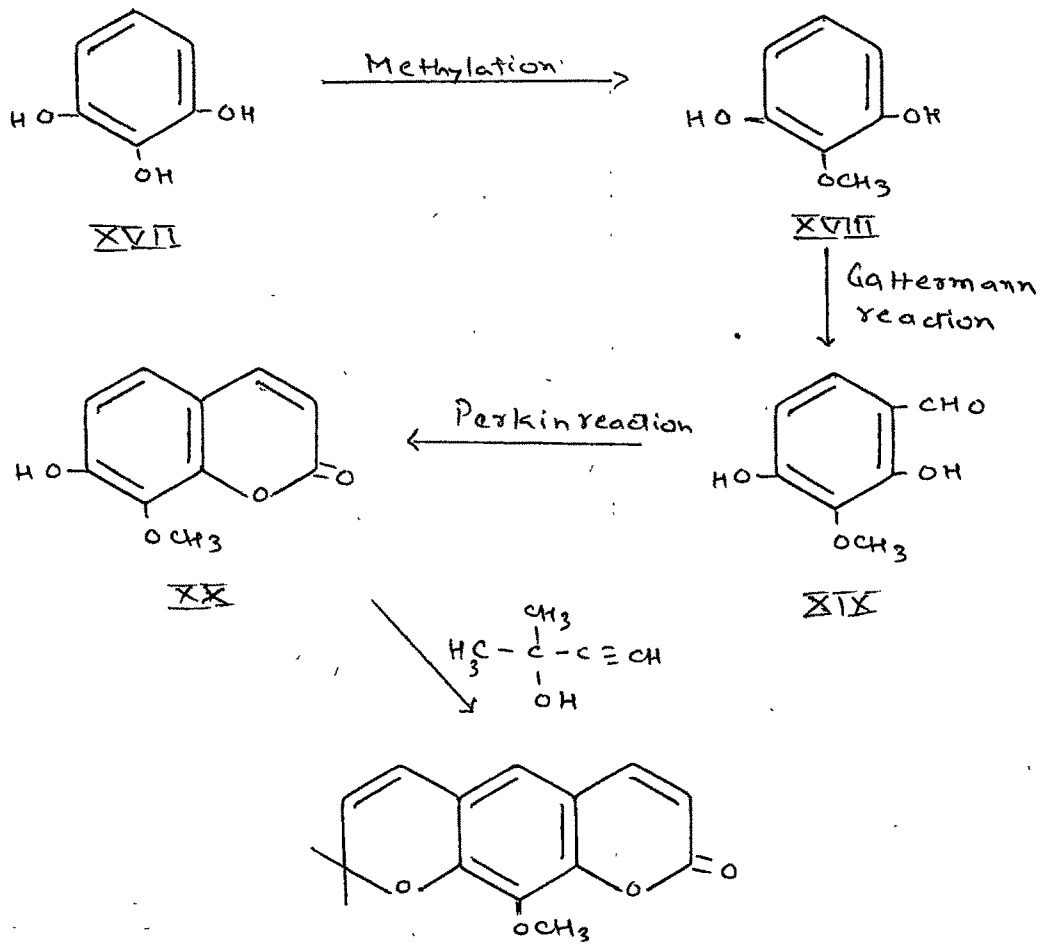
XV

(a) R = CH_3

(b) R = C_6H_5

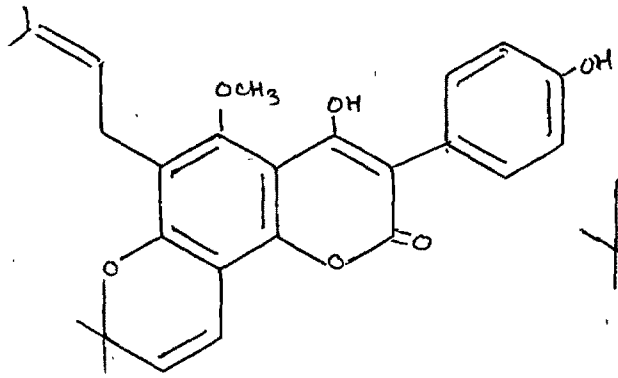
Seselin[16,17] (III) occurs in Seseli indicum Wight and Skimmia Japonica thunb. Seselin has been synthesised by the condensation of umbelliferon and 2-methyl-but-3-yne-2-ol. Luvangetin[18] (XVI) occurs in the fruits of Luvanga Scandens Ham; alongwith isopimpinellin, xanthotoxin and xanthyletin. Spath and Schmid[19] synthesised luvangetin (XVI) by methylating pyrogallol (XVII) to 2-methylether of pyrogallol (XVIII) and converting it by the application of Gattermann reaction to an aldehyde (XIX). This aldehyde was cyclised to form 8-methoxyumbelliferon (XX)

by Perkin reaction. This 8-methoxyumbelliferon was reacted with 2-methyl-but-3-yne-2-ol to give luvangetin (XVI) in very low yield.

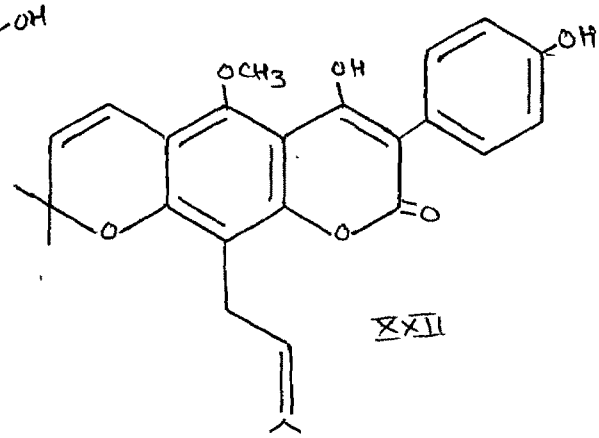


Recently Pelter and Stainton[20] discovered a group of 4-hydroxy-3-phenylcoumarins among the naturally occurring isoflavonoids in nature. Seven of the eight natural ones possess isoprene units either in the acylic or heterocyclic form or both. They have been isolated mainly from two species of Derris[21,22]. The roots of D.Scandens[23-25]

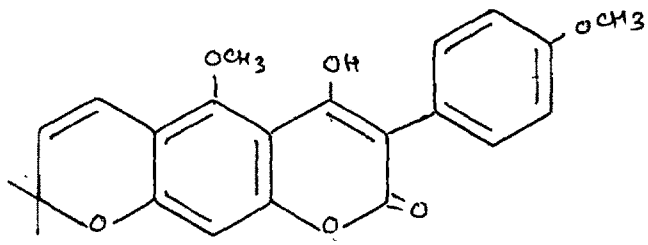
contain scandenin (XXI), lonchocarpic acid (XXII) and lonchocarpenin, whereas those of D.Robusta[23,26,27] yielded robustic acid (XXIII), methylrobustate, robustin and 4'-O-methylrobustin. In nature, isoprenylation may occur at coumarin ring stage or before the formation of coumarin ring.



XXI



XXII



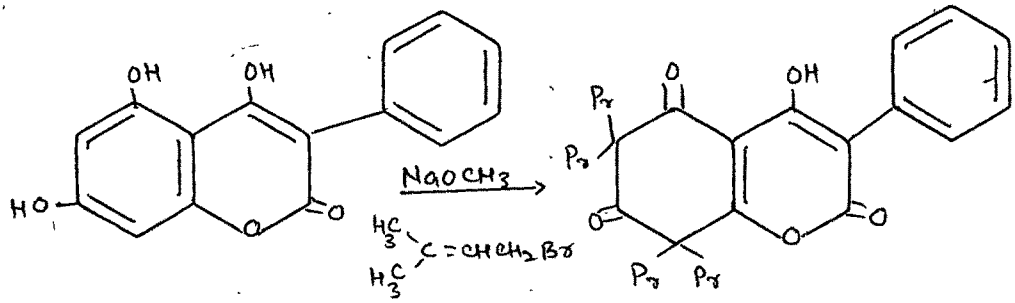
XXIII

Clarke[28] isolated scandenin from Derris together with lonchocarpic acid. Subba Rao and Seshadri[29], also isolated scandenin from an Indian species of D.Scandens but were unable to extract lonchocarpic acid.

Rao and Seshadri[30] isolated robustic acid together with robustenin. Johnson and Pelter[25] proved the

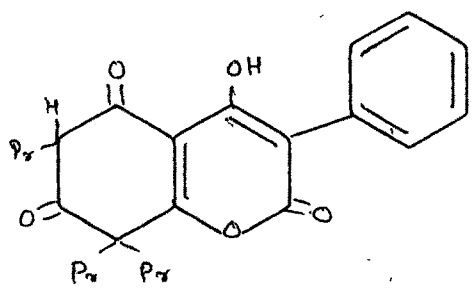
structure of robustic acid by mass spectral data and chemical degradation.

Johnson et al.[23] obtained dichromans in the condensation of 4,5,7-trihydroxycoumarin with prenyl bromide in the presence of borontrifluoride etherate in diglyme. Jain and Jain[31] condensed 3-phenyl-4,5,7-trihydroxycoumarin (XXIV) with prenyl bromide in the presence of methanolic sodium methoxide, which ultimately afforded two solid compounds, one was tetraprenyl derivative (XXV) and the second was the triprenyl derivative (XXVI). They confirmed the structures of these compounds by spectral data.



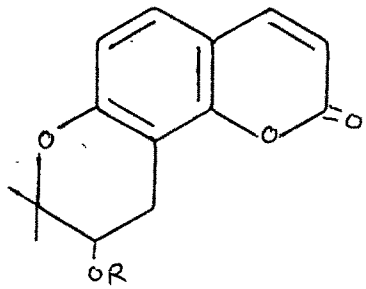
XXIV XXV

+



XXVI

Seshadri et al.[32] isolated selinidin (XXVII) from the roots of Selinum Vaginatum, as a glucoside. They synthesised the same by the cyclisation of 8-prenyl-7-hydroxycoumarin with perbenzoic acid[32-34].

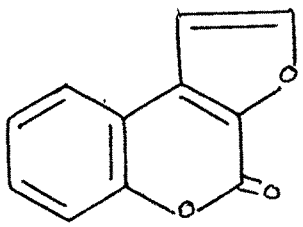


XXVII

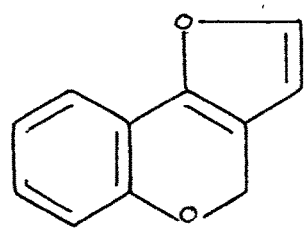
R = angelate

FURANOCOUMARINS :

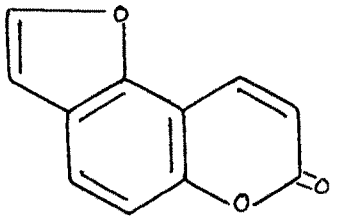
The furanocoumarins[35,36] are fish poisons and insecticides. Plants of the Rutaceae and Umbelliferae families are the principle source of the many naturally occurring members of this group. Eight isomeric linear and angular furanocoumarins are theoretically possible, but only two of them have been found to occur in nature. The two catagories are : Furano(3,2-g)benzopyran-2-one, psoralene derivative (F) and Furano(2,3-h)benzopyran-2-one, angelicin derivative (G).



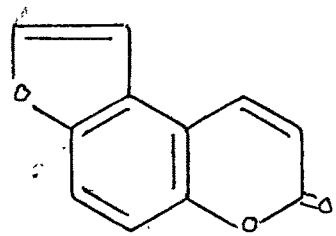
A



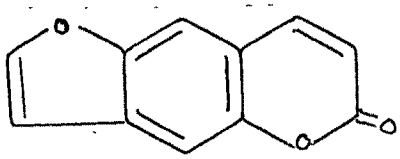
B



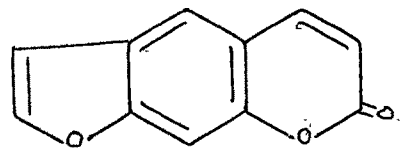
C



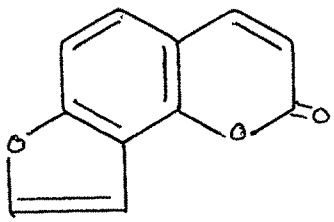
D



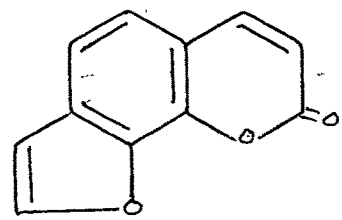
E



F



G

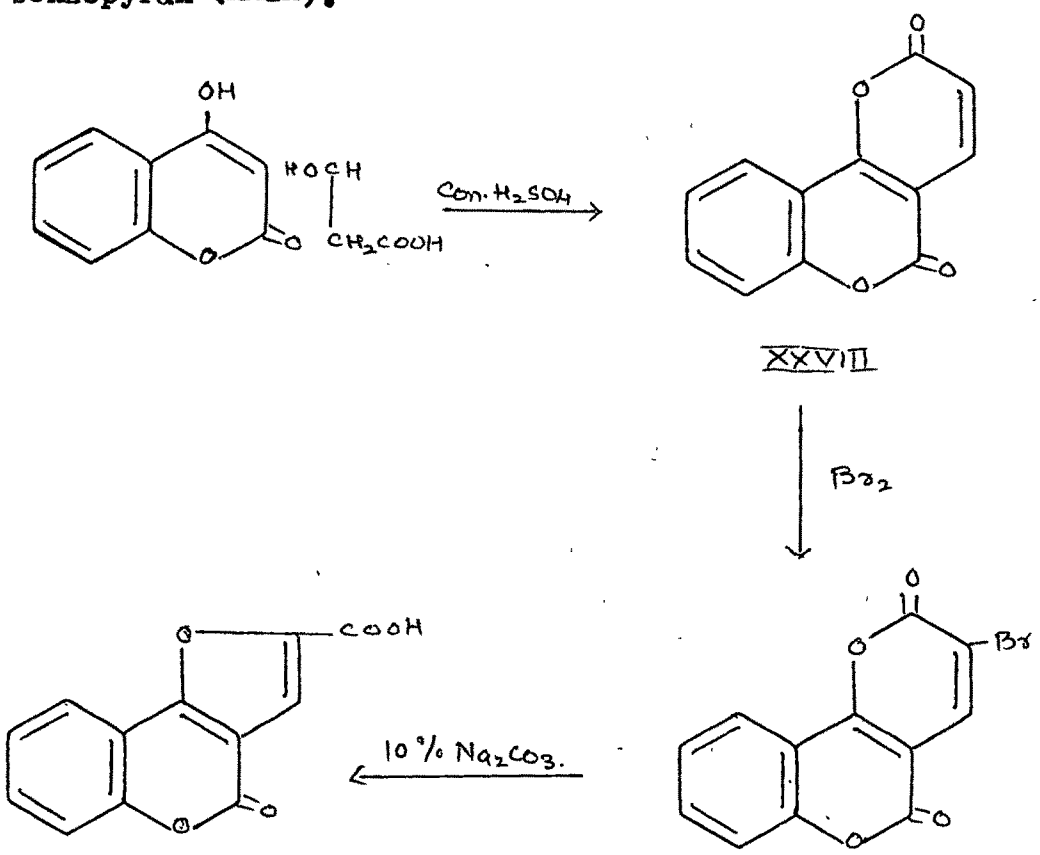


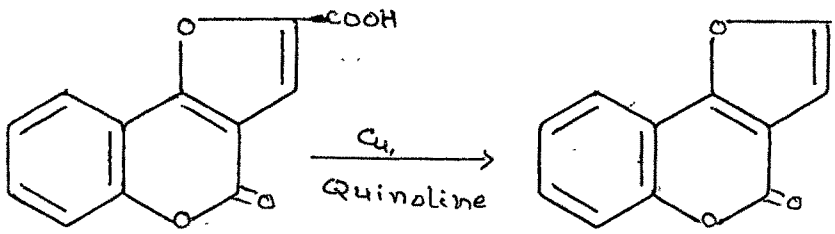
H

Spath[35] in his review of naturally occurring coumarins, enumerated compounds having C_5 units and the furanocoumarins.

Furanocoumarins of type of (A) are discussed in Chapter III.

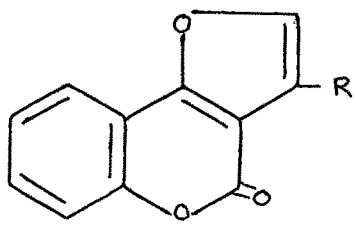
Furanocoumarins of type (B) have been synthesised by Dholakia and Trivedi[36]. Pechmann condensation of 4-hydroxycoumarin with malic acid yielded 2,5-dioxo-2H, 5H-pyrano(3,2-c)benzopyran (XXVIII) which on bromination gave 3-bromo derivative. This on hydrolysis with 10 % sodium carbonate solution and subsequent decarboxylation with copper and quinoline yielded 4-oxo-4H-furano(3,2-c)-benzopyran (XXIX).





XIX

Similarly, 3-methyl-4-oxo-4H-furano(3,2-c)-benzopyran (XXXa) and 3-phenyl-4-oxo-4H-furano(3,2-c)-benzopyran (XXXb) were synthesised. Here the acid obtained after the hydrolysis of 3-bromo derivative by 10 % sodium carbonate solution was cyclised by refluxing with hydrochloric acid. Usgaonkar and Patel[37] also synthesised this by the hydrolysis of 3-bromo derivative with alcoholic potassium hydroxide and decarboxylating the product by directly heating in a metal bath at 300°.

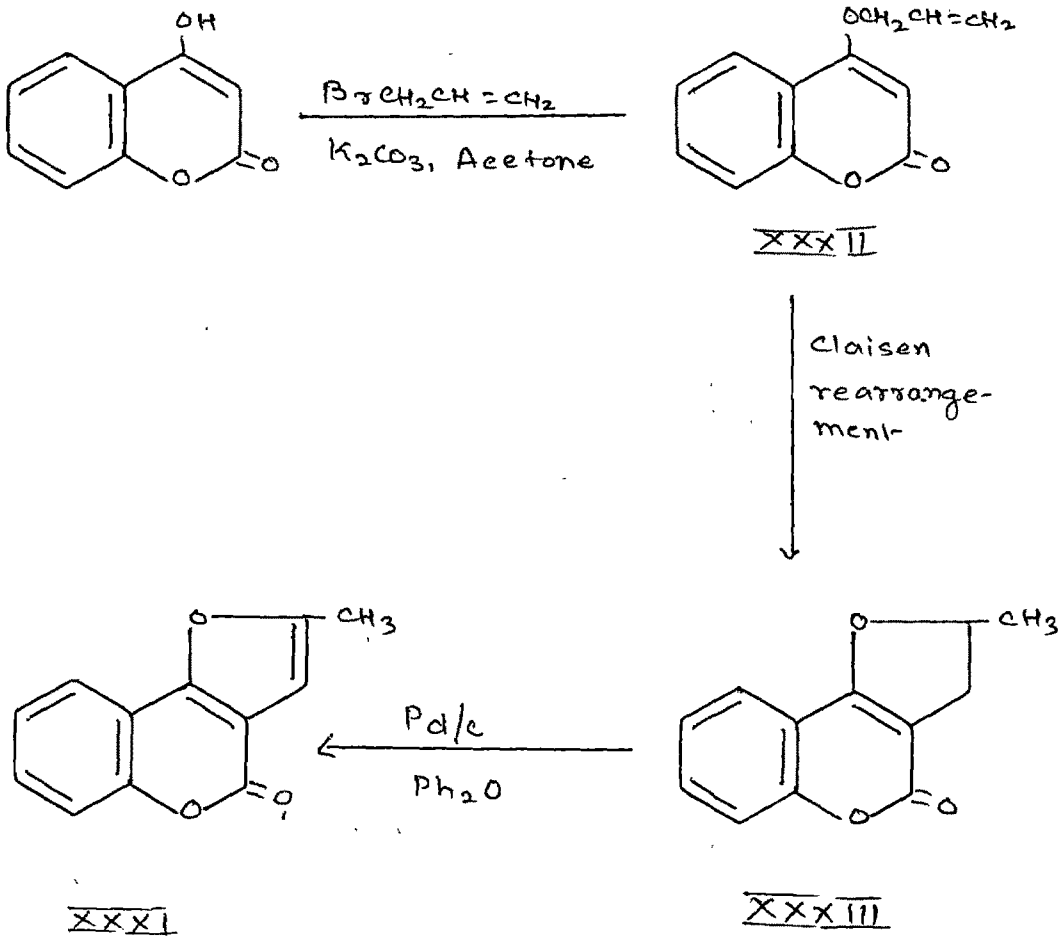


XXX

(a) R = CH_3

(b) R = C_6H_5

They have also synthesised 2-methyl-4-oxo-4H-furano(3,2-c)benzopyran (XXXI). 4-Hydroxycoumarin on allylation with allyl bromide gave 4-allyloxycoumarin (XXXII) which on Claisen migration gave 2,3-dihydrofurano-(3,2-c)benzopyran (XXXIII). Dehydrogenation of this was carried out by palladised charcoal (10 %) to give 2-methyl-4-oxo-4H-furano(3,2-c)benzopyran (XXXI).



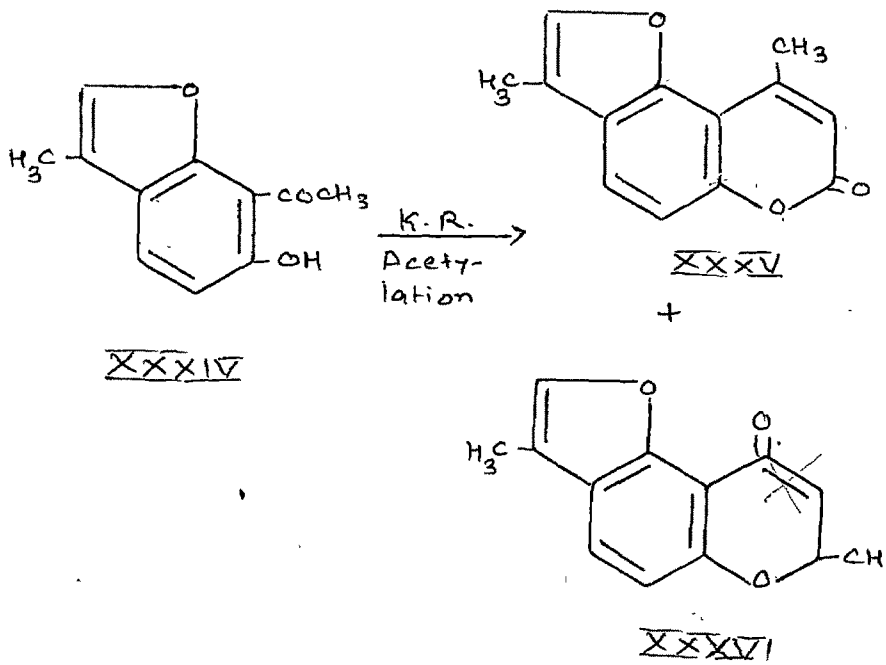
XXXII

XXXI

XXXIII

Furanocoumarins of this type are also a part of this thesis and so they are discussed later on.

Furanocoumarins of type (C) have been synthesised by several workers. Limaye and Sathe[38] subjected 6-hydroxy-7--acetyl-3-methylcoumaron (XXXIV) to Kostanecki-Robinson acetylation and obtained 3,9-dimethyl-7-oxo-7H-furano(2,3-f)-benzopyran (XXXV) in poor yield alongwith 3,7-dimethyl-9--oxo-9H-furano(2,3-f)benzopyran (XXXVI)



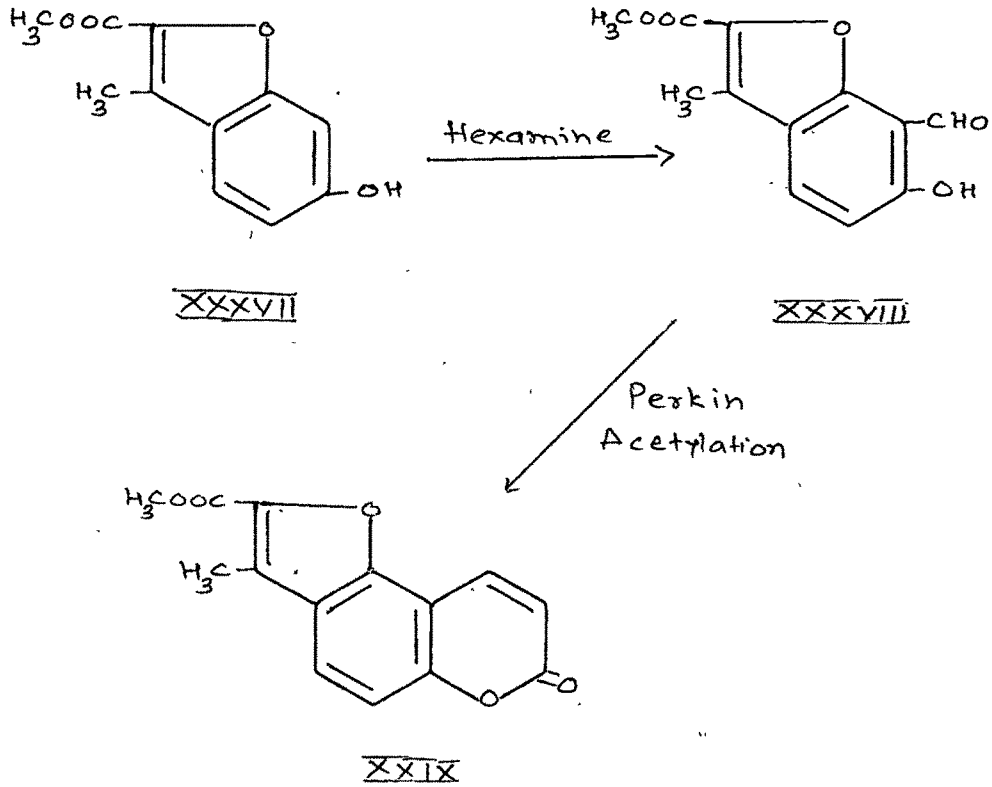
XXXIV

XXXV

+

XXXVI

Shah and Shah[39] and Chudgar and Shah[40] synthesised 3-alkylfuranocoumarins. Salvi and Sethna[41] synthesised this type of furanocoumarins starting from benzofuran derivative. Methyl-6-hydroxy-3-methylcoumarilate (XXXVII) on reaction with hexamine gave the 7-formyl derivative (XXXVIII) which on Perkin acetylation gave 2-carbmethoxy-3-methyl-7-oxo-7H-furano(2,3-f)benzopyran (XXXIX).



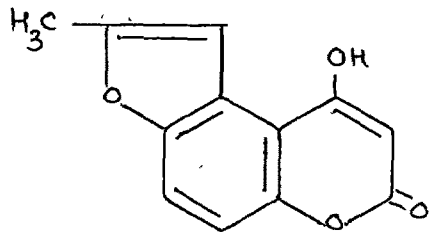
XXXVII XXXVIII XXIX

Trivedi and Sethna[42] made a new approach in synthesising 3-alkylfuranocoumarins of this type.

Kaufmann et al.[43] developed a new synthetic route for the furanocoumarins of type (D). They subjected o-hydroxyallylcoumarin to acetylation followed by bromination and subsequent cyclisation to get this type of furanocoumarins. They also condensed o-hydroxyformyl-coumarins with methylbromoacetate followed by hydrolysis and subsequent cyclisation with partial decarboxylation to get furanocoumarins.

Salvi and Sethna[44] synthesised this type of furanocoumarins by first formylating the hydroxybenzofurans and then subjecting them to Perkin or Knoevenagel reaction.

Dholakia and Trivedi[36] have also synthesised 4-hydroxy-2-methyl-6-oxo-6H-furano(3,2-f)benzopyran (XL).

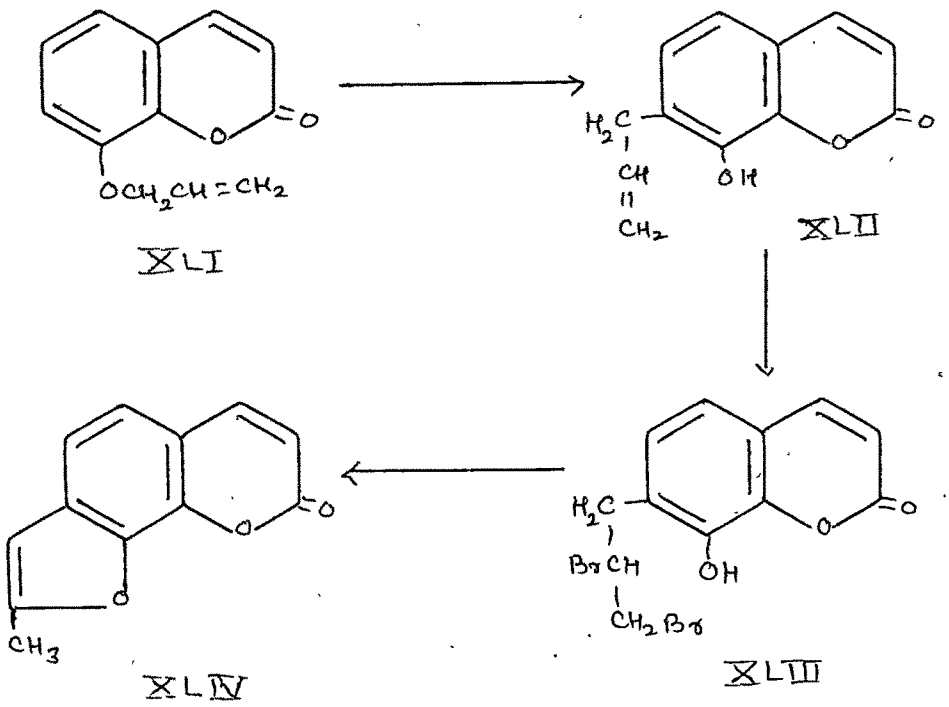


XL

Furanocoumarins of type (E) are also reported by Kaufmann et al.[43].

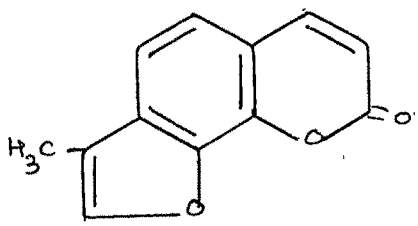
Psoralene or linear furanocoumarins of type (F) and the angular furanocoumarins of type (G) are a subject matter of Chapter II and so it is discussed therein.

Furanocoumarins of type (H) were synthesised by Kaufmann and Russey[45]. They carried out the Claisen rearrangement of 8-allyloxycoumarin (XLI) and obtained 7-allyl-8-hydroxycoumarin (XLII) which on acetylation and subsequent bromination gave a dibromo derivative (XLIII). This dibromo derivative was further treated with sodium ethoxide in absolute ethanol to give 2-methyl-8-oxo-8H-furano(3,2-h)benzopyran(2'-methylfurano-4',5',7,8-coumarin) (XLIV).



XLI XLII XLIII XLIV

Mehta and Sethna[46] also prepared 3-methyl-8--oxo-8H-furano(3,2-h)benzopyran (XLV).



XLV

From the above review, it is revealed that chromenocoumarins and dihydrofuranocoumarins are widely distributed in nature and synthesis of them are achieved

by so many workers in different ways. Such type of chromenocoumarins and dihydrofuranocoumarins of 4-hydroxy-coumarins are not still been obtained from nature or not synthesised. So it was thought of interest to synthesise such type of isoprenoids in order to test their therapeutic properties.

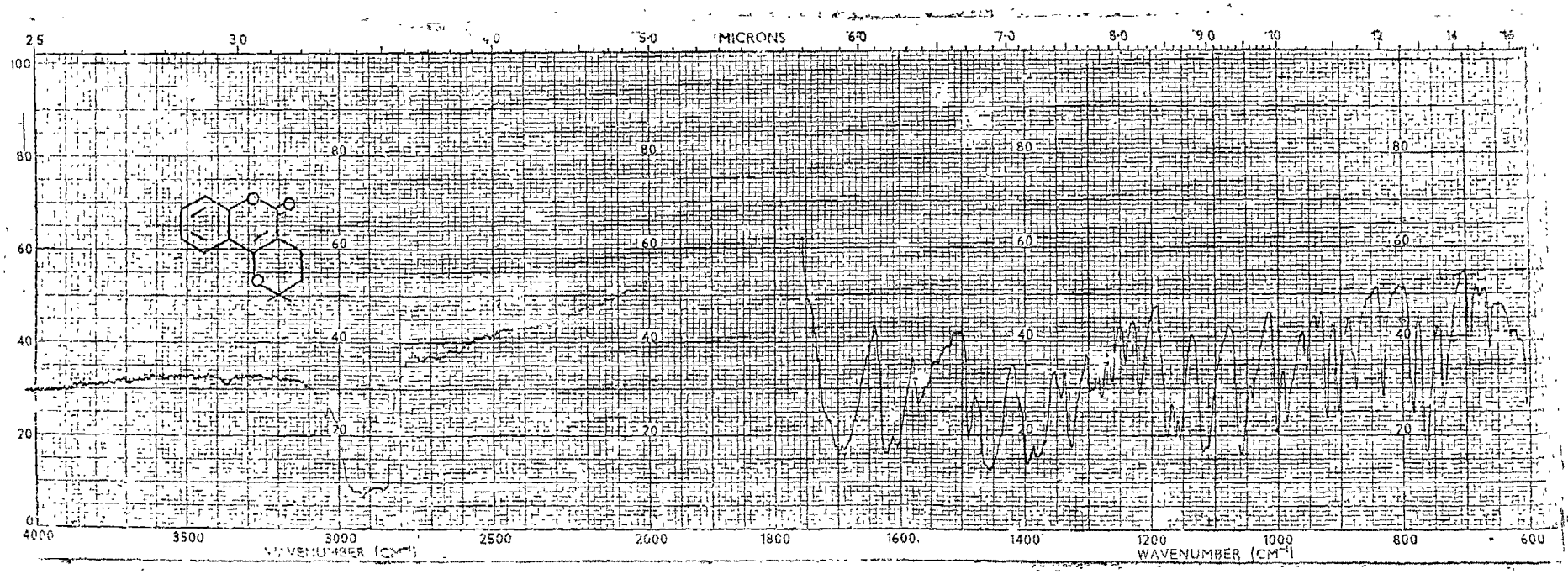
Synthesis of 5-oxo-5H-2,2-dimethylpyrano(3,2-c)benzopyran or 2',2'-dimethylchromeno(3,2-c)coumarin

Direct prenylation of 2,4-dihydroxyacetophenone or polyphenols[47,48] have already been reported earlier. Same method was used in prenylating 4-hydroxycoumarins. 4-Hydroxycoumarin (XLVI) was prenylated by heating it with 2-methyl-but-3-en-2-ol in the presence of BF_3-etherate in dioxan. The reaction mixture was chromatographed over silica gel giving 3,4-dihydro-5-oxo-5H-2,2-dimethylpyrano-(3,2-c)benzopyran (XLVII), the structure of which was confirmed by its IR, UV and NMR spectra.

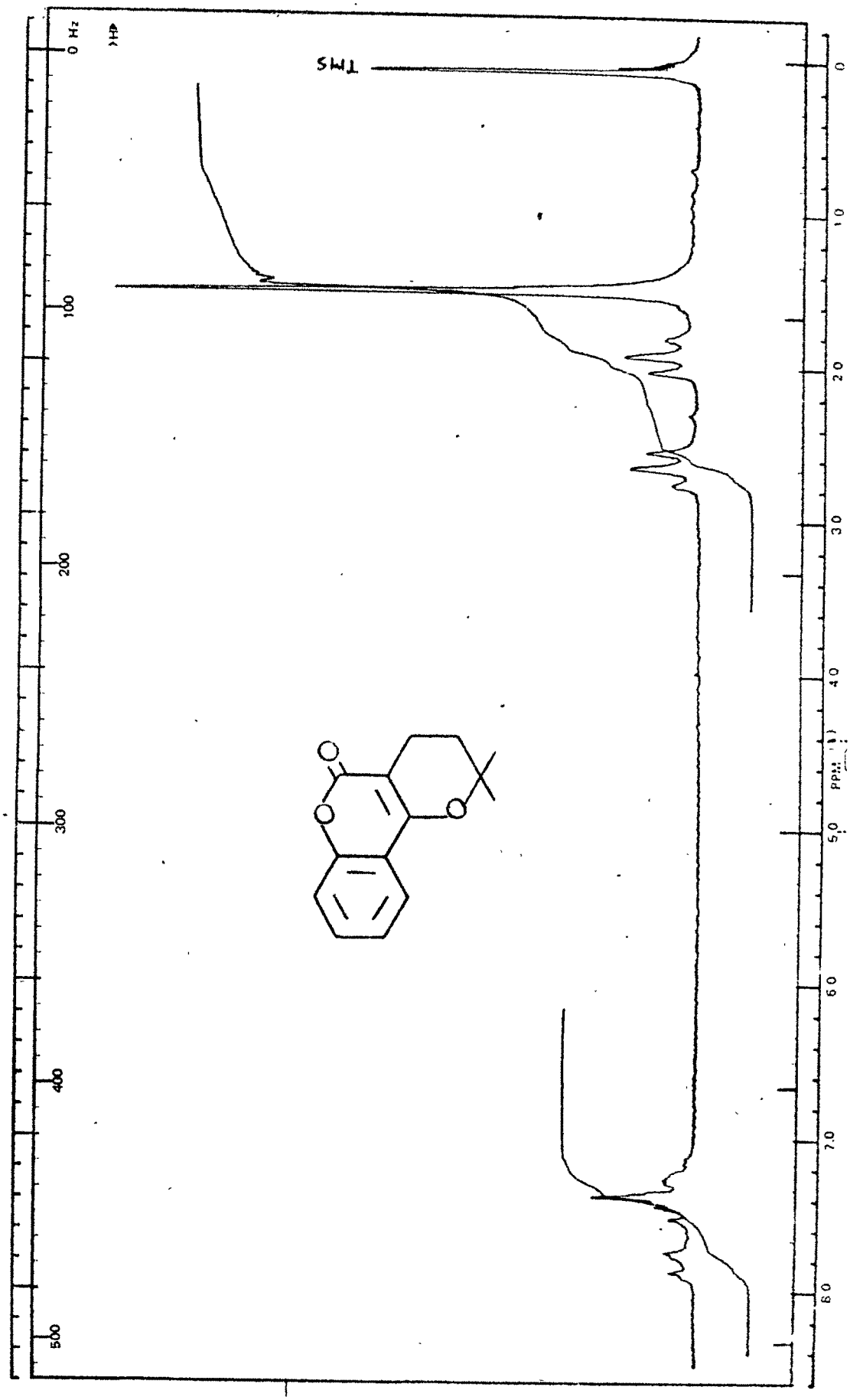
The IR spectrum in nujol showed the bands at 1700 $cm.^{-1}$ (α-pyrone carbonyl stretching frequency) and 1390 $cm.^{-1}$ (geminal dimethyl group stretching frequency). (Fig. 1).

The NMR spectrum in $CDCl_3$ showed the following signals :-

δ 1.5, singlet, geminal dimethyl group at position-2; 1.85 and 2.65, two triplets, J=8Hz, two methylene groups at

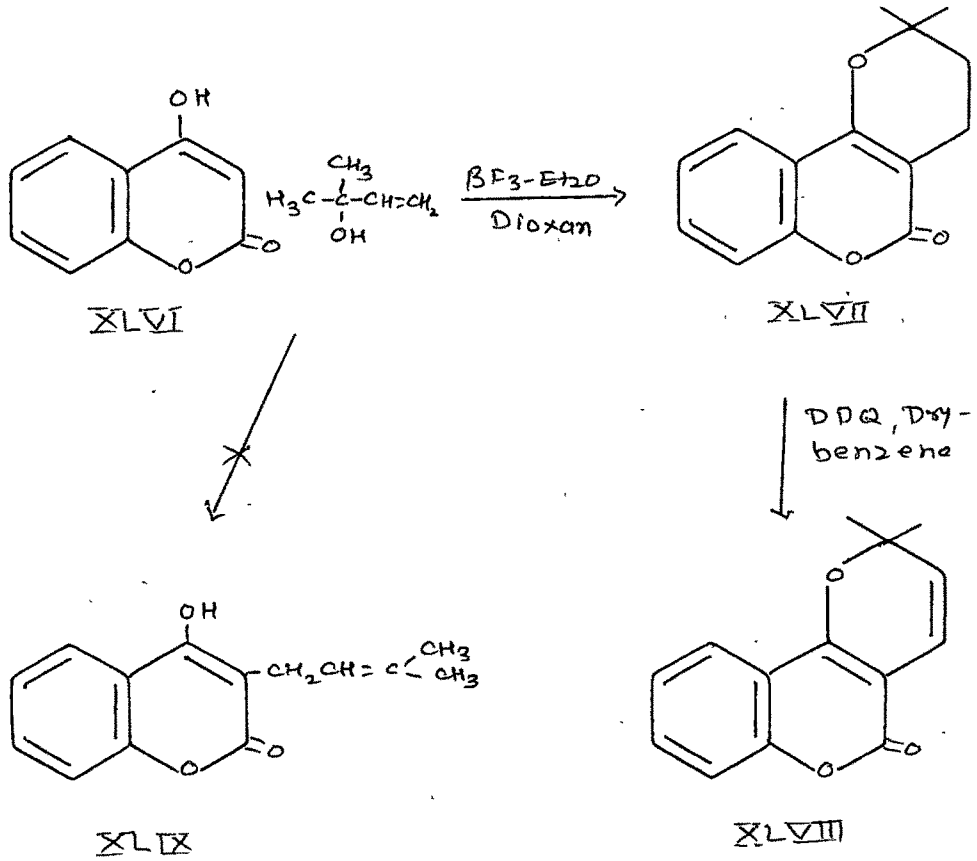


(Fig. 1) : 3,4-Dihydro-5-oxo-5H-2,2-dimethylpyrano(3,2-c)benzopyran



(Fig. 2) : 3,4-Dihydro-5-oxo-5H-2,2-dimethylpyrano(3,2-c)benzopyran

positions-4 and -3 respectively and 7.2 - 7.8, multiplet, four protons aromatic (Fig. 2).



From the spectral data, the possibility of 3-prenyl-4-hydroxycoumarin (XLIX) was ruled out, only 3,4-dihydro-5-oxo-5H-2,2-dimethylpyrano(3,2-c)benzopyran (XLVII) was isolated directly as the cyclised product.

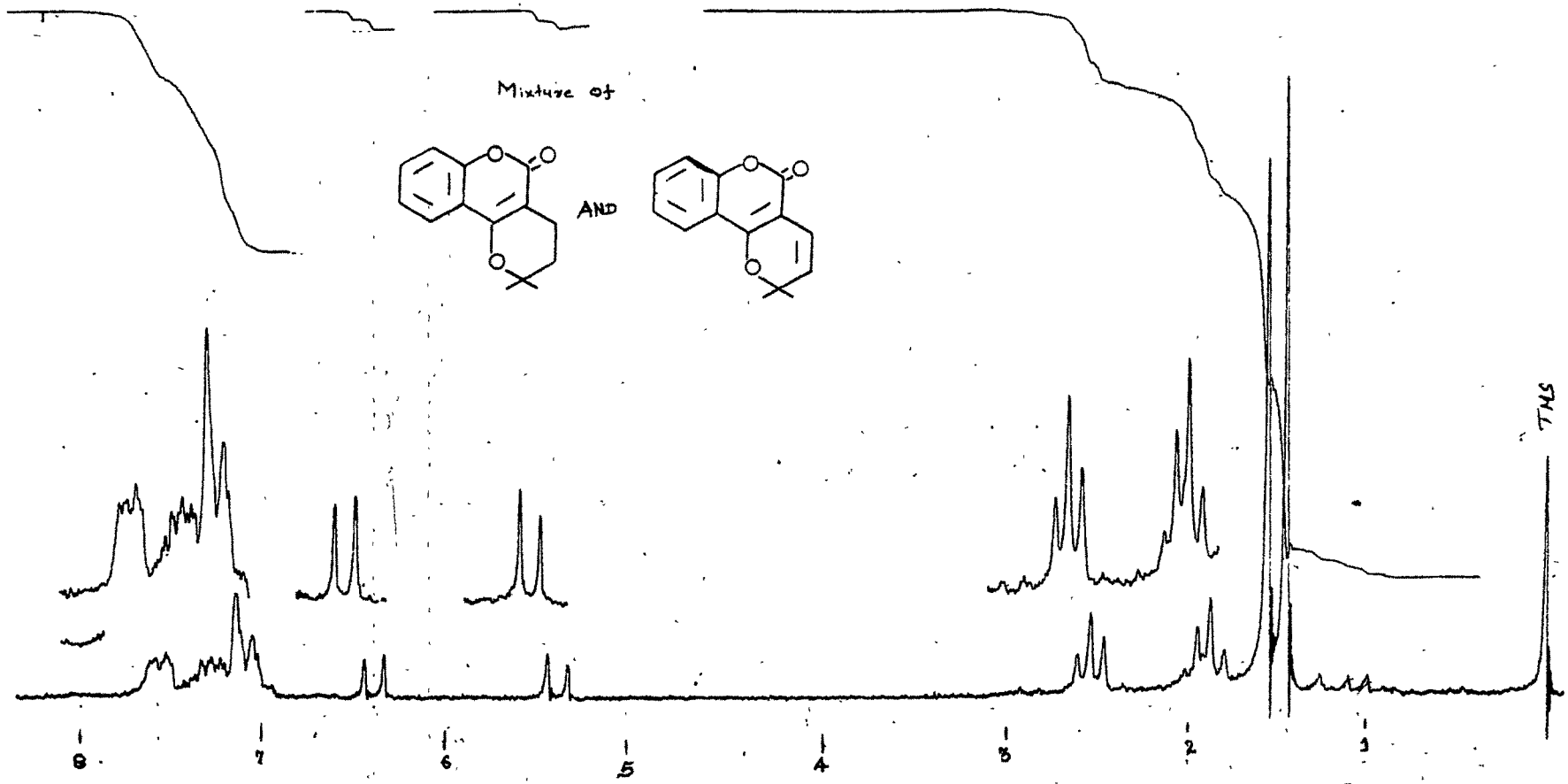
Dehydrogenation of (XLVII) was carried out by DDQ in boiling benzene but it did not give 100 % conversion of (XLVII) to chromenocoumarin (XLVIII). Other solvents were also tried for the successful maximum conversion but failed. Separation of these two products was also found

difficult and the NMR spectrum of the mixture was recorded which indicates 30 % (approximately) conversion of dihydrochromenocoumarin to 5-oxo-5H-2,2-dimethylpyrano(3,2-c)benzopyran (XLVIII). Separation of the mixture by column chromatography or preparative TLC technique, even with impregnated 10 % silver nitrate solution failed. The NMR spectrum of this mixture in $CDCl_3$ is given below :-
δ 1.45 and 1.55, two singlets, geminal dimethyl group at position-2; 1.80 and 2.40, two triplets, two methylene groups at positions-3 and -4 in compound (XLVII); 5.40 and 6.40, two doublets, J=9Hz, two protons at positions-3 and -4 in compound (XLVIII) and 7.20-7.60, multiplet, four protons aromatic (Fig. 3).

Dehydrogenation of (XLVII) with palladised chargoal (10 %) in diphenylether failed to give (XLVIII). Also, the dehydrogenation of the same compound using triphenyl methanol in boiling trifluoroacetic acid[49] failed to give (XLVIII).

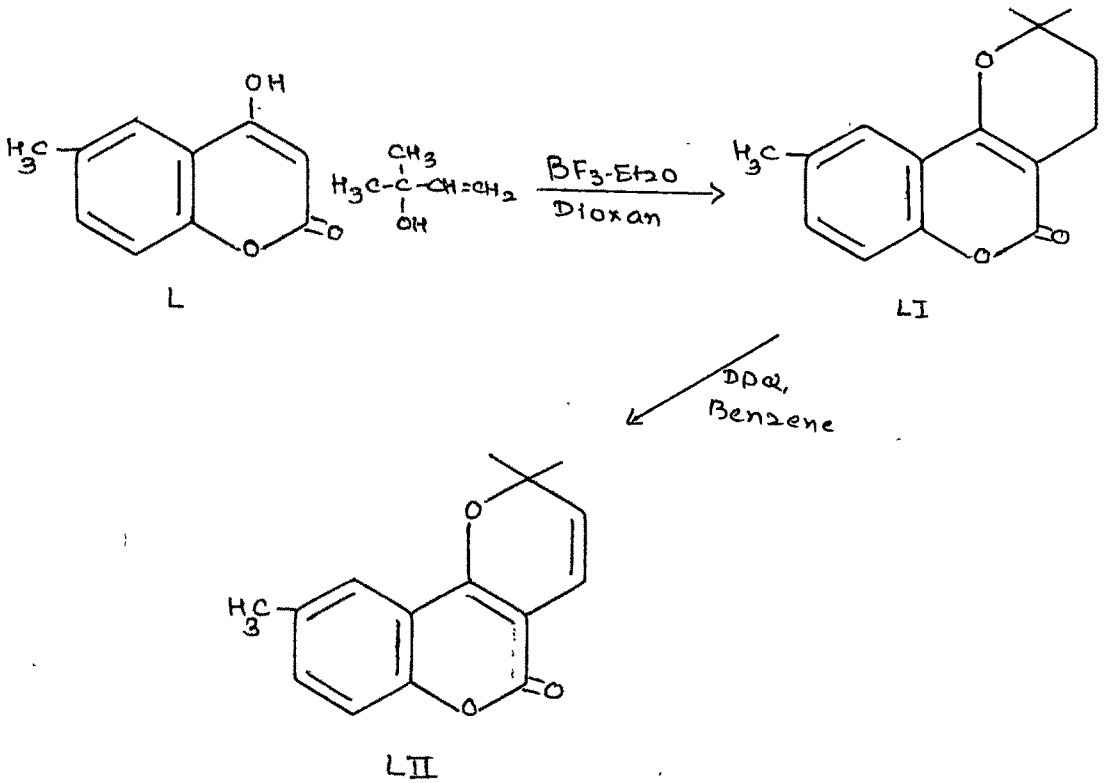
Synthesis of 5-oxo-5H-2,2,9-trimethylpyrano(3,2-c)-benzopyran or 2',2',6-trimethyl(3,2-c)coumarin

4-Hydroxy-6-methylcoumarin (L) was directly prenylated with 2-methyl-but-3-en-2-ol in the presence of BF_3-etherate in dioxan. The reaction mixture was extracted with ether. The residue after evaporation of ether was chromatographed over silica gel. The second elution with benzene-petroleum ether (80:20) gave a solid as 3,4-dihydro-



(Fig. 3) : The NMR spectrum of a mixture of 3,4-dihydro-5-oxo-5H-2,2-dimethylpyrano-(3,2-c)benzopyran and 5-oxo-5H-2,2-dimethylpyrano(3,2-c)benzopyran.

-5-oxo-5H-2,2,9-trimethylpyrano(3,2-c)benzopyran (LI). The NMR spectrum of (LI) in $CDCl_3$ is as given below :- δ 1.50, singlet, geminal dimethyl group at position-2; 2.40, singlet, methyl group at position-9; 1.90 and 2.50, two triplets, J=9Hz, two methylene groups at positions-3 and -4 and 7.20-7.60, multiplet, three protons aromatic. IR (nujol) : 1720 $cm.^{-1}$ (α-pyrone carbonyl stretching frequency) and 1355 $cm.^{-1}$ (geminal dimethyl group stretching frequency).



L LI LII

(LI), on dehydrogenation with DDQ in benzene gave only one product, 5-oxo-5H-2,2,9-trimethylpyrano(3,2-c)-benzopyran (LII), the structure of which is confirmed by its

IR and NMR spectra as given below :-

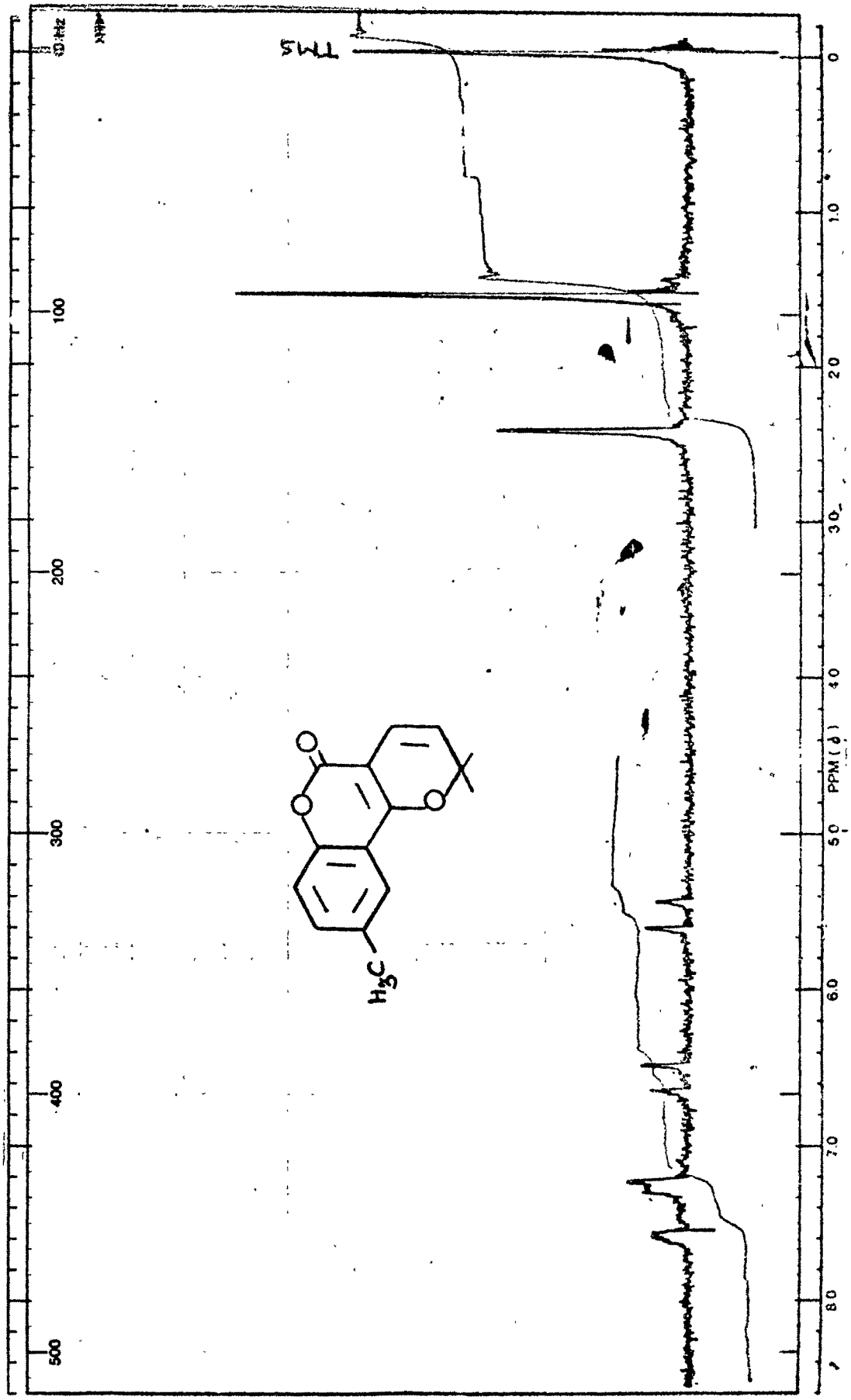
IR (nujol) : 1720 $cm.^{-1}$ (α-pyrone carbonyl stretching frequency) and 1355 $cm.^{-1}$ (geminal dimethyl group stretching frequency).

NMR ($CDCl_3$) : δ 1.52, singlet, geminal dimethyl group at position-2; 2.42, singlet, methyl group at position-9; 5.50 and 6.55, two doublets, J=9Hz, two protons at positions--3 and -4 and 7.20-7.60, multiplet, three protons aromatic (Fig. 4).

Synthesis of 5-oxo-5H-2,2,7-trimethylpyrano-(3,2-c)benzopyran

4-Hydroxy-8-methylcoumarin (LIII), 2-methyl-but--3-en-2-ol and dioxan were heated on water bath, in the presence of BF_3-etherate. The reaction mixture after dilution with water was extracted with ether. The residue, after evaporation of ether, was chromatographed on silica gel and elution with benzene-petroleum ether (80:20) gave 3,4-dihydro-5-oxo-5H-2,2,7-trimethylpyrano(3,2-c)benzopyran (LIV). The structure of (LIV) was assigned on the basis of its NMR spectrum.

NMR ($CDCl_3$) : δ 1.50, singlet, geminal dimethyl group at position-2; 2.38, singlet, methyl group at position-7; 1.95 and 2.60, two triplets, J=8Hz, two $-CH_2$ groups at positions -3 and -4 and 7.10-7.60, multiplet, three protons aromatic.

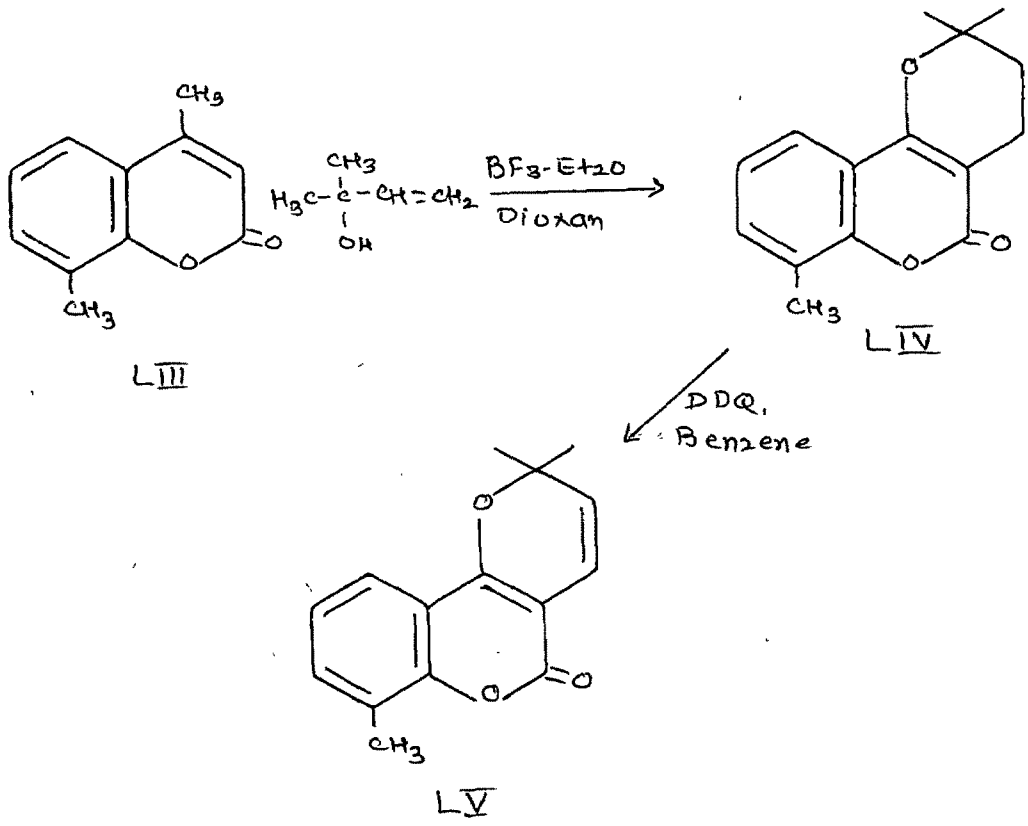


(Fig. 4) : 5-Oxo-5H-2,2,9-trimethylpyrano(3,2-c)benzopyran

(LIV) on boiling with DDQ in dry benzene gave a mixture of 3,4-dihydro-5-oxo-5H-2,2,7-trimethylpyrano-(3,2-c)benzopyran (LIV) and 5-oxo-5H-2,2,7-trimethylpyrano-(3,2-c)benzopyran (LV), which could not be separated by preparative TLC impregnated by 5 % silver nitrate solution.

The NMR spectrum of the mixture in $CDCl_3$ showed the following signals :-

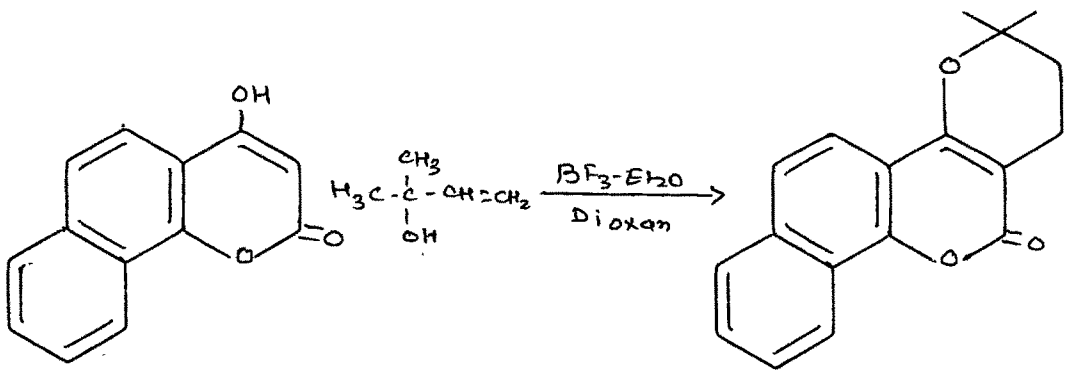
δ 1.52, singlet, geminal dimethyl group at position-2; 2.40, singlet, methyl group at position-7; 1.92 and 2.60, two triplets, two methylene groups at positions-3 and -4 in compound (LIV); 5.60 and 6.50, two doublets, J=9Hz, two protons at positions-3 and -4 in compound (LV) and 7.10-7.60, multiplet, three protons aromatic.



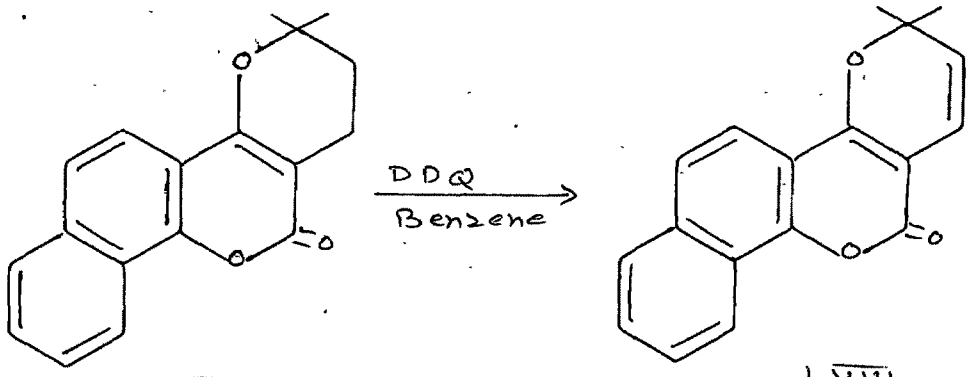
Synthesis of 5-oxo-5H-7,8-benzo-2,2-dimethylpyrano-(3,2-c)benzopyran

4-Hydroxy-7,8-benzocoumarin (LVI) was reacted with 2-methyl-but-3-en-2-ol in dioxan, in the presence of BF_3-etherate on a water bath. The reaction mixture was worked out as before and the residue on chromatography over silica gel gave a product which was given structure as 3,4-dihydro-5-oxo-5H-7,8-benzo-2,2-dimethylpyrano(3,2-c)benzopyran (LVII). This also gave a nonseparable mixture of 3,4-dihydro-5-oxo-5H-7,8-benzo-2,2-dimethylpyrano(3,2-c)-benzopyran and 5-oxo-5H-7,8-benzo-2,2-dimethylpyrano(3,2-c)-benzopyran (LVIII). The structure was assigned on the basis of the NMR spectrum.

NMR ($CDCl_3$) : δ 1.46 and 1.55, two singlets, geminal dimethyl group at position-2; 1.90 and 2.60, two triplets, J=7Hz, two methylene groups at positions-3 and -4 in compound (LVII); 5.46 and 6.55, two doublets, J=10Hz, two protons at positions-3 and -4 in compound (LVIII) and 7.45-7.90 and 8.50, multiplet, six protons aromatic.



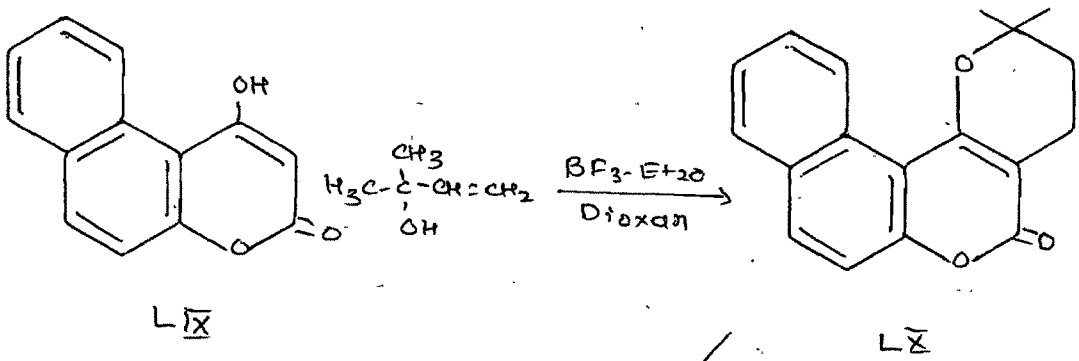
LVI LVII



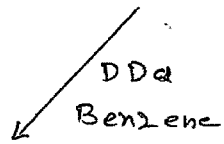
LVII LVIII

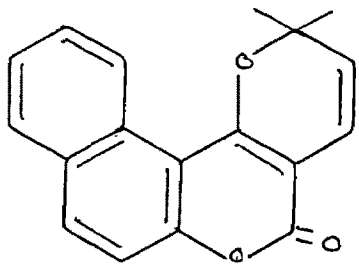
Synthesis of 5-oxo-5H-9,10-benzo-2,2-dimethylpyrano-(3,2-c)benzopyran

4-Hydroxy-5,6-benzocoumarin (LIX) and 2-methyl-but-3-en-2-ol were heated in dioxan in the presence of BF_3-etherate. After working up the reaction mixture as usual



LIX LX



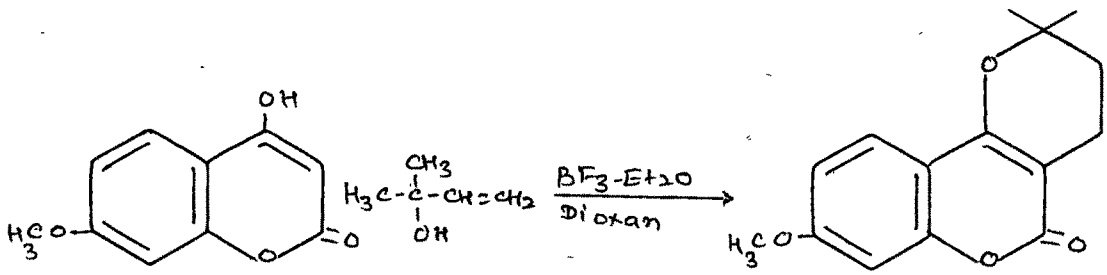


LXI

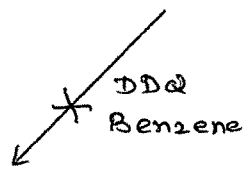
it gave 3,4-dihydro-5-oxo-5H-9,10-benzo-2,2-dimethylpyrano-(3,2-c)benzopyran (LX). This on dehydrogenation with DDQ in dry benzene gave an inseparable mixture of (LX) and 5-oxo-5H-9,10-benzo-2,2-dimethylpyrano(3,2-c)benzopyran (LXI).

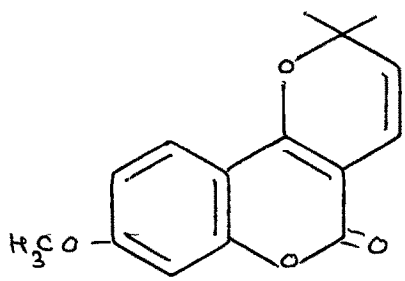
Synthesis of 3,4-dihydro-5-oxo-5H-8-methoxy-2,2-dimethyl--pyrano(3,2-c)benzopyran

4-Hydroxy-7-methoxycoumarin (LXII) was condensed with 2-methyl-but-3-en-2-ol in the presence of BF_3-etherate in dioxan to give 3,4-dihydro-5-oxo-5H-8-methoxy-2,2-dimethylpyrano(3,2-c)benzopyran (LXIII). The product (LXIII), obtained after chromatography over silica gel, failed to



LXII LXIII



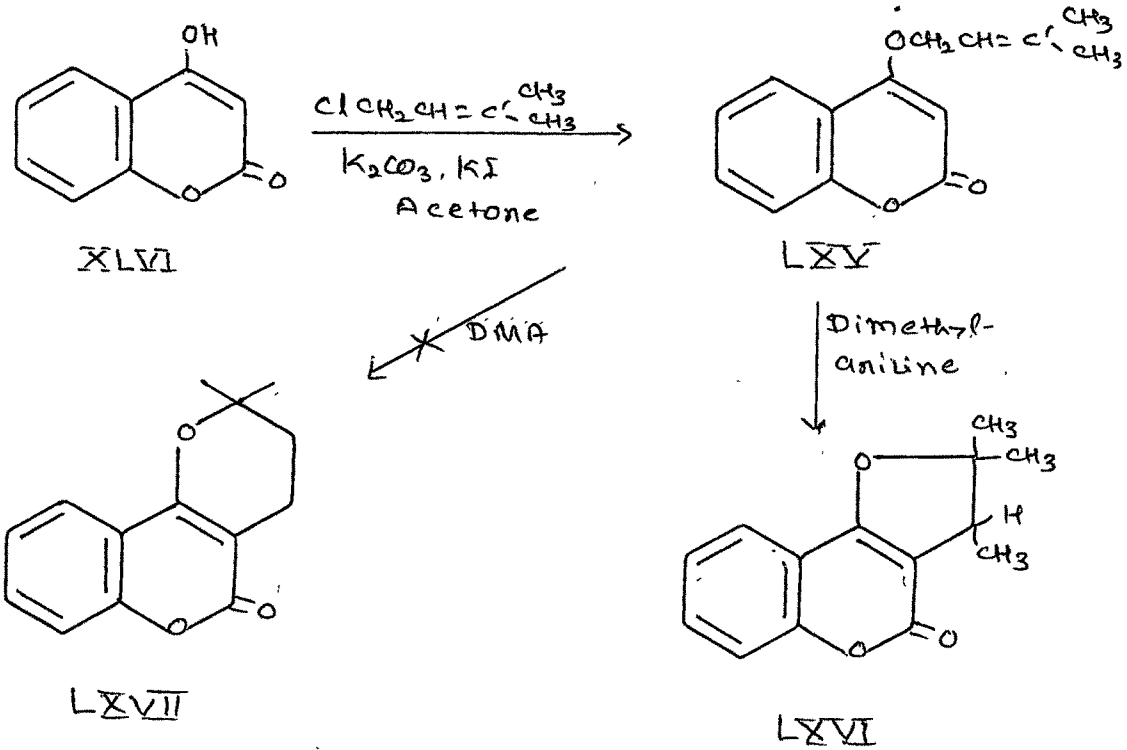


LXIV

undergo dehydrogenation when refluxed with DDQ in dry benzene to give 5-oxo-5H-8-methoxy-2,2-dimethylpyrano-(3,2-c)benzopyran (LXIV).

Synthesis of 2,3-dihydro-4-oxo-4H-2,2,3-trimethyl--furano(3,2-c)benzopyran

In order to prepare the chromenocoumarins obtained by the direct condensation of 2-methyl-but-3-en--2-ol in the presence of BF_3-etherate followed by dehydrogenation, Claisen migration of 4-prenyloxycoumarin (LXV), was first tried. The condensation of 4-hydroxy-coumarin with 1-chloro-3-methyl-but-2-ene in acetone, in the presence of potassium carbonate and potassium iodide was first carried out and the product subjected to Claisen

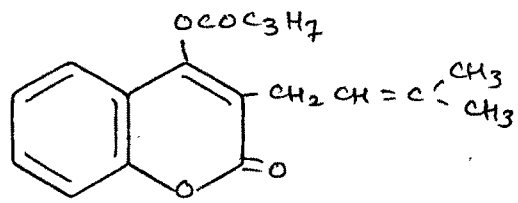


XLVI LXV LXVII LXVI

migration to give chromenocoumarin according to Seshadri et al.[50], but surprisingly an abnormal Claisen migration took place to give the product 2,3-dihydrofuranocoumarin derivative (LXVI) instead of chromenocoumarin (LXVII).

The IR spectrum of 4-prenyloxycoumarin (LXV) in nujol showed the bands at 1720 $cm.^{-1}$ (α-pyrone carbonyl stretching frequency), 1360 $cm.^{-1}$ (geminal dimethyl group stretching frequency) and 925 $cm.^{-1}$ (allylic -C=C- stretching frequency) (Fig. 5).

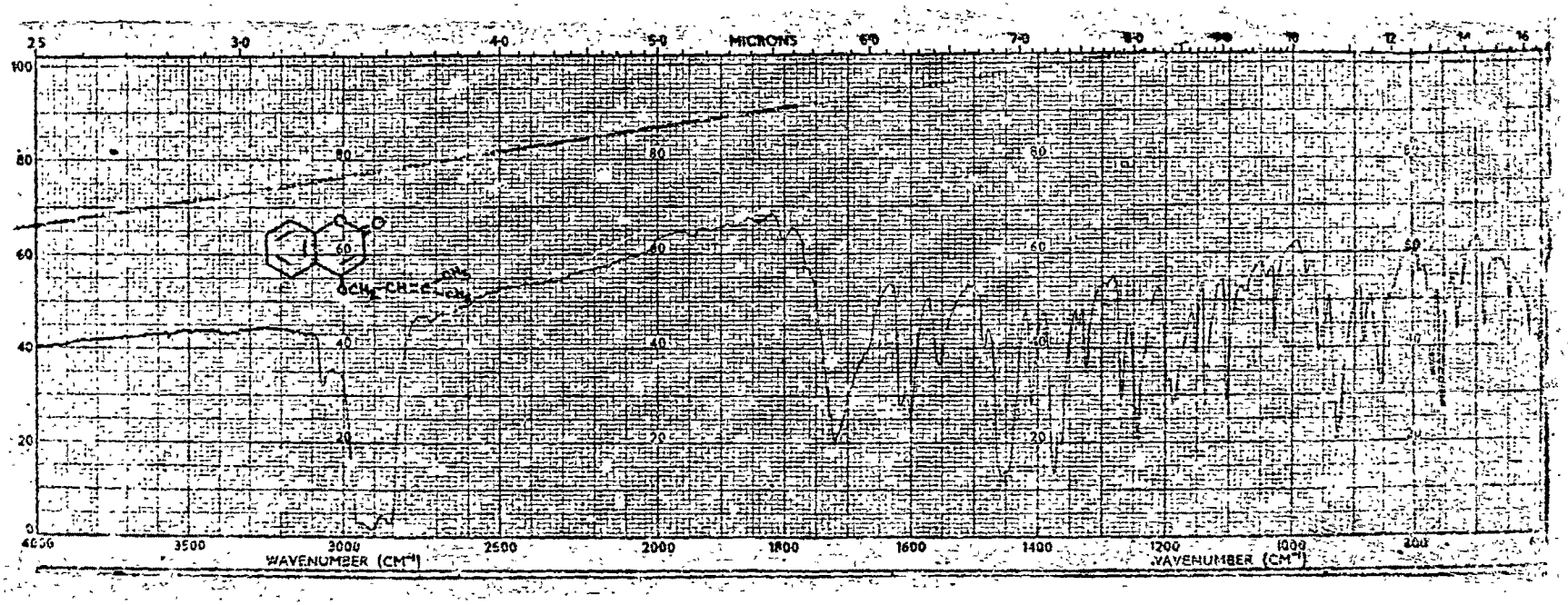
To obtain the intermediate 3-prenyl-4-hydroxycoumarin the trapping reagent butyric anhydride was used during the Claisen migration, but instead of getting 3-prenyl-4-butyroxycoumarin (LXVIII), the same 2,3-dihydro-4-oxo-4H-2,2,3-trimethylfurano(3,2-c)benzopyran (LXVI) was obtained. Thus the trapping of the intermediate failed.



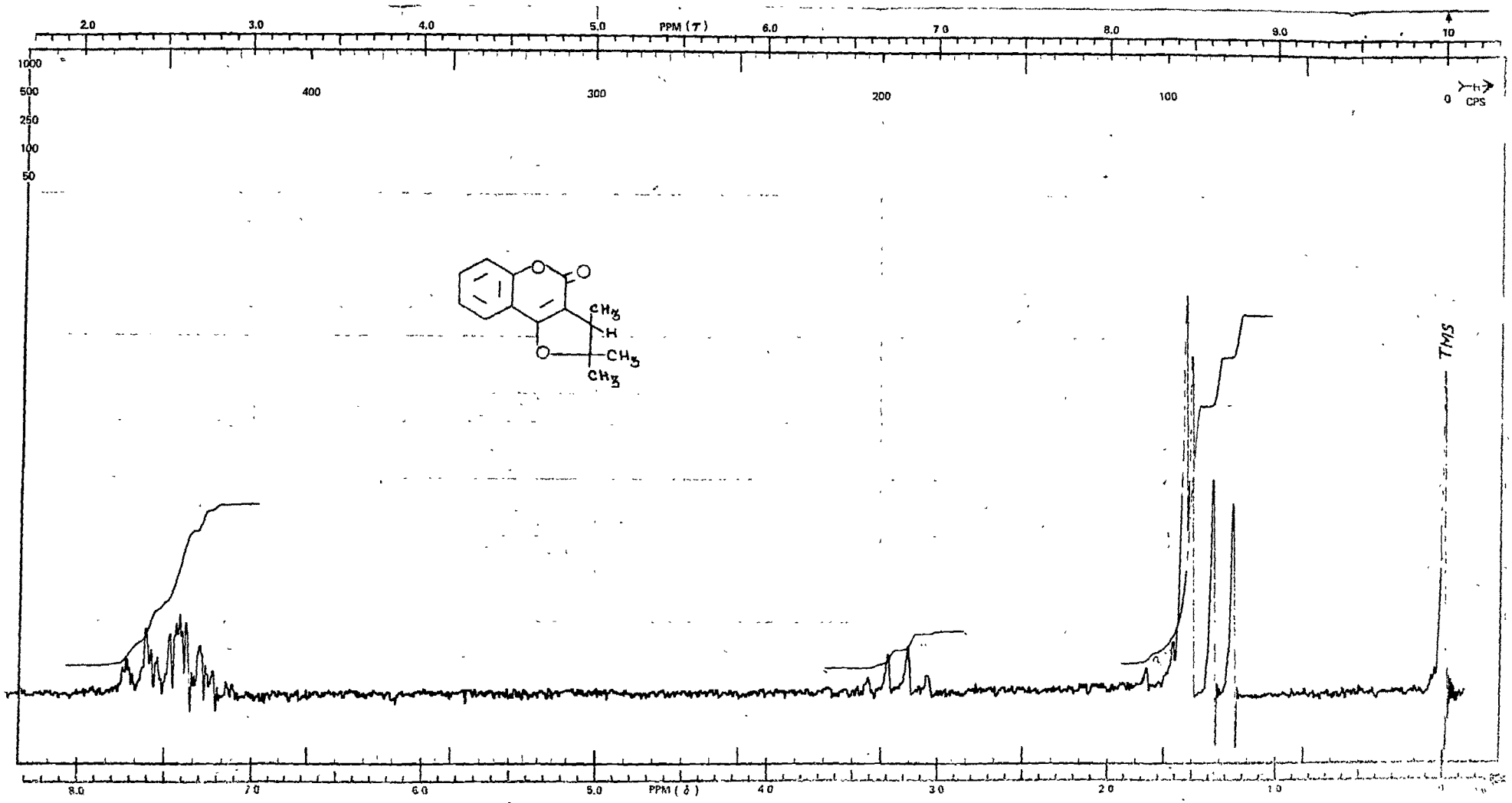
LXVIII

The NMR spectrum of (LXVI) in $CDCl_3$ showed the following signals :-

δ 1.30, doublet, J=8Hz, methyl group at position-3; 1.46 and 1.52, two singlets, geminal dimethyl group at position-2;



(Fig. 5) : 4-Prenyloxycoumarin

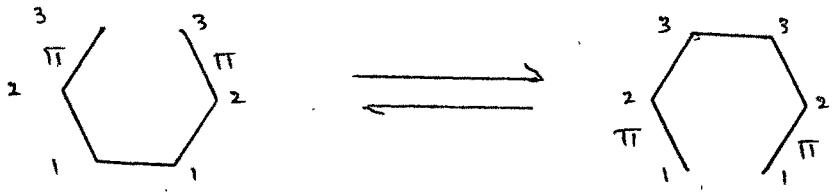


(Fig. 6) : 2,3-Dihydro-4-oxo-4H-2,2,3-trimethylfurano(3,2-c)benzopyran

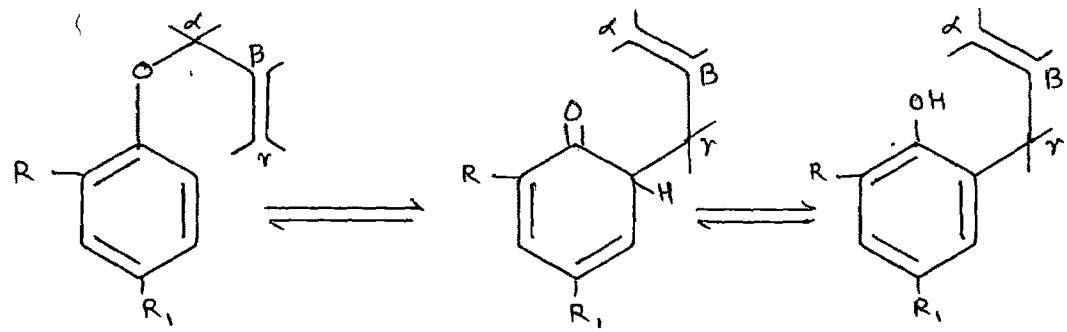
3.25, quartate, one proton at position-3 and 7.20-7.70, multiplet, four protons aromatic (Fig. 6).

A thermally induced rearrangement of a vinyl allylether to the corresponding homoallylic carbonyl compound was observed by Claisen in 1912[51]. Such transformations are known as (3,3) sigmatropic reactions[52,53], viz., the familier ortho and para Claisen rearrangement in aromatic systems.

The overall mechanism of the Claisen rearrangement was specially described by Claisen in 1925[54], as a cyclic process involving simultaneous bond making and bond breaking processes accompanied by relocation of the unsaturated bonds. Theoretical interpretations based on a variety of molecular orbital approaches have been advanced[55-59], since about 1950.



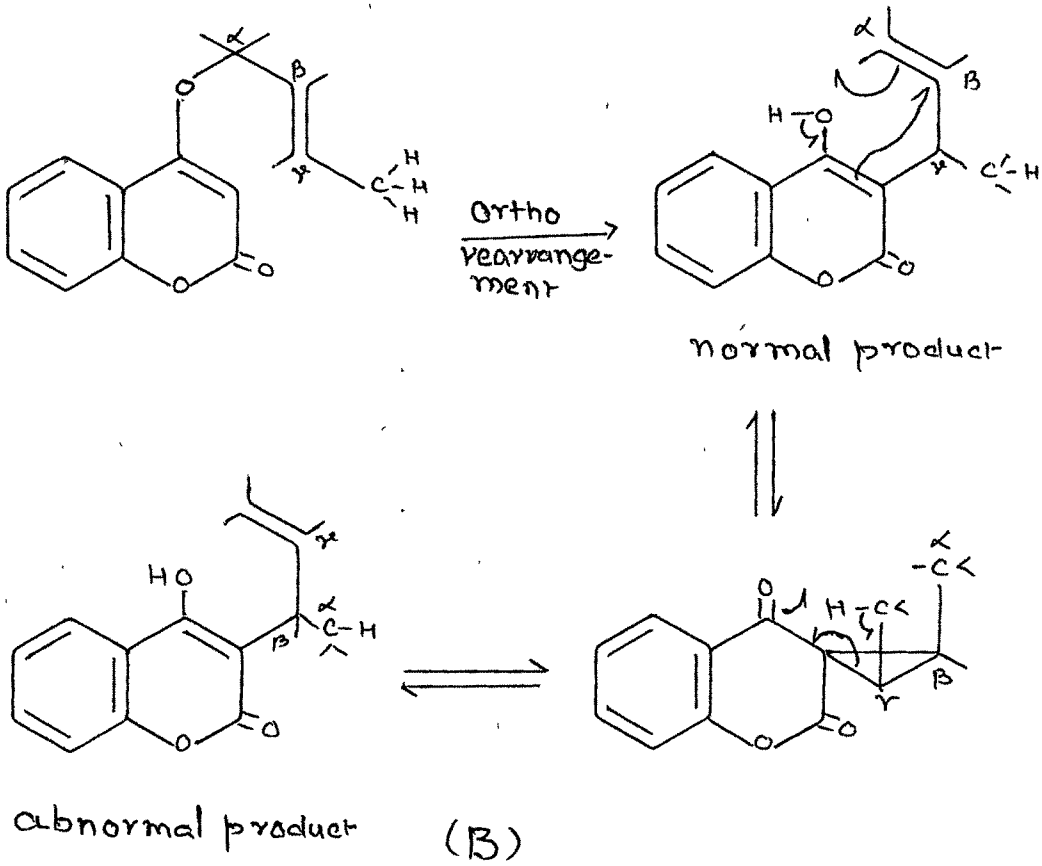
The normal course of Claisen rearrangement can be illustrated as, in an aryl allylether, the first cyclic rearrangement occurs with bonding of the γ-carbon atom of the allylic proton at the ortho-carbon atom of the ring to generate orthodienone A, in which the migrating allyl group has undergone a structural inversion.



(A)

The abnormal rearrangement leading to structural[60-64] and geometric[65-67] isomerisation in the migrating allyl group, is commonly observed to accompany the ortho-rearrangement of ethers bearing γ-alkyl substituents on the allyl group. The abnormal product is produced in a subsequent rearrangement of the normal o-allylphenols[68], and is formed through an intermediate spirocyclopropylcyclohexadienone resulting from hydrogen transfer from the phenolic function to the terminal carbon atom of the allyl group. Reversal of this process, a 1,5-hydrogen shift, but involving a hydrogen from the γ-alkyl group, leads to the abnormal product[64,68,69]. Thus, in an abnormal product, the original β-carbon atom of the side chain is attached to the ring, the original α-carbon atom appears as a saturated β-substituent and the double bond has shifted to a position between the original γ-carbon atom and its hydrogen bearing allyl group. The interconversion of

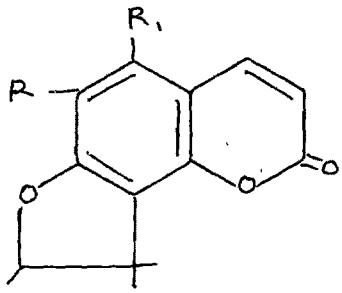
normal and abnormal products through such acylcyclopropyl intermediates is quite common[70] and is recognised as a 'enoline rearrangement[71]'.



(B)

Most abnormal rearrangements are considerably slower than the formation of the normal o-allylphenol.

The 3,3-dimethylallyl group, present as such or as oxygenated form, is a structural feature commonly found in coumarins[72] and other compounds of natural origin[72,73]. Murray and Ballantyne[74,75,76] investigated the Claisen rearrangement of 3,3-dimethylether [7-O(3,3-dimethylallyl)-scopoletin] as a method for synthesising the natural coumarins, nieshoutol (LXIXa) and nieshoutin (LXIXb).

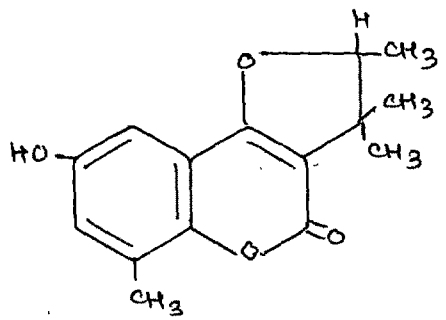


LXIX

(a) R=H; R_1=OMe

(b) R=OMe; R_1=H

Irrie et al.[77] isolated similar type of dihydrocoumarin, i.e. glaupalol from rhizomes of G.Palmatum and established its structure on the basis of the products obtained by chemical degradation and spectral data.



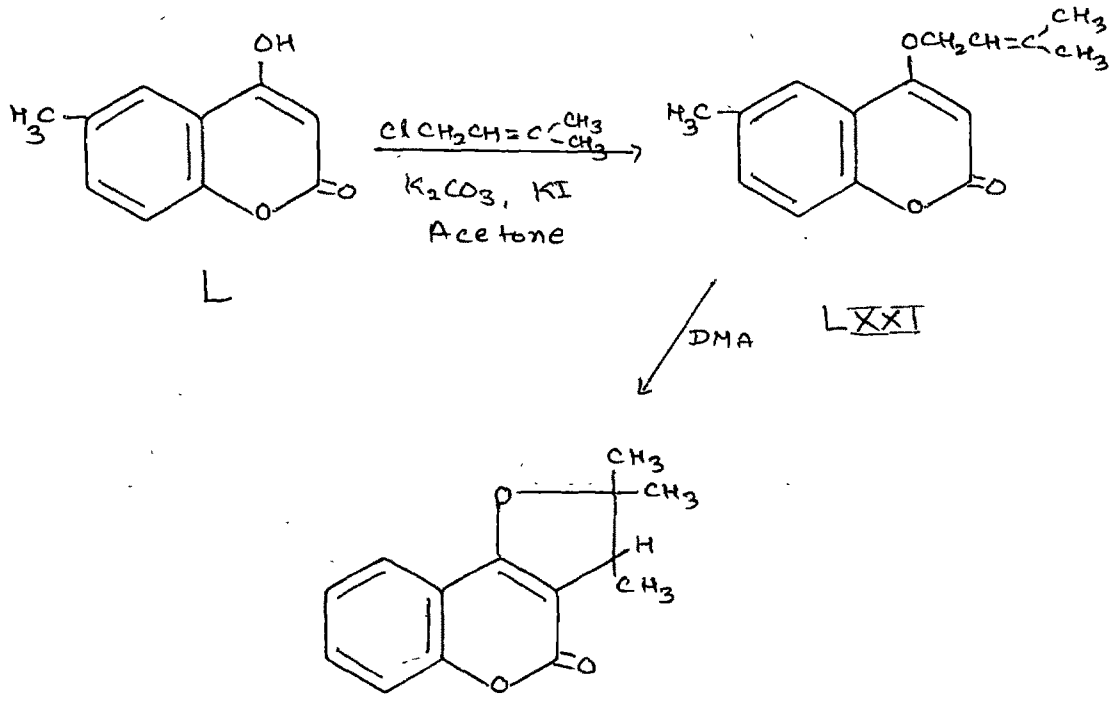
Synthesis of 2,3-dihydro-4-oxo-4H-2,2,3,8-tetramethyl--furano(3,2-c)benzopyran

4-Hydroxy-6-methylcoumarin was refluxed in acetone with 1-chloro-3-methyl-but-2-ene, potassium carbonate and potassium iodide, to give 4-prenyloxy-6-methylcoumarin(LXXI)

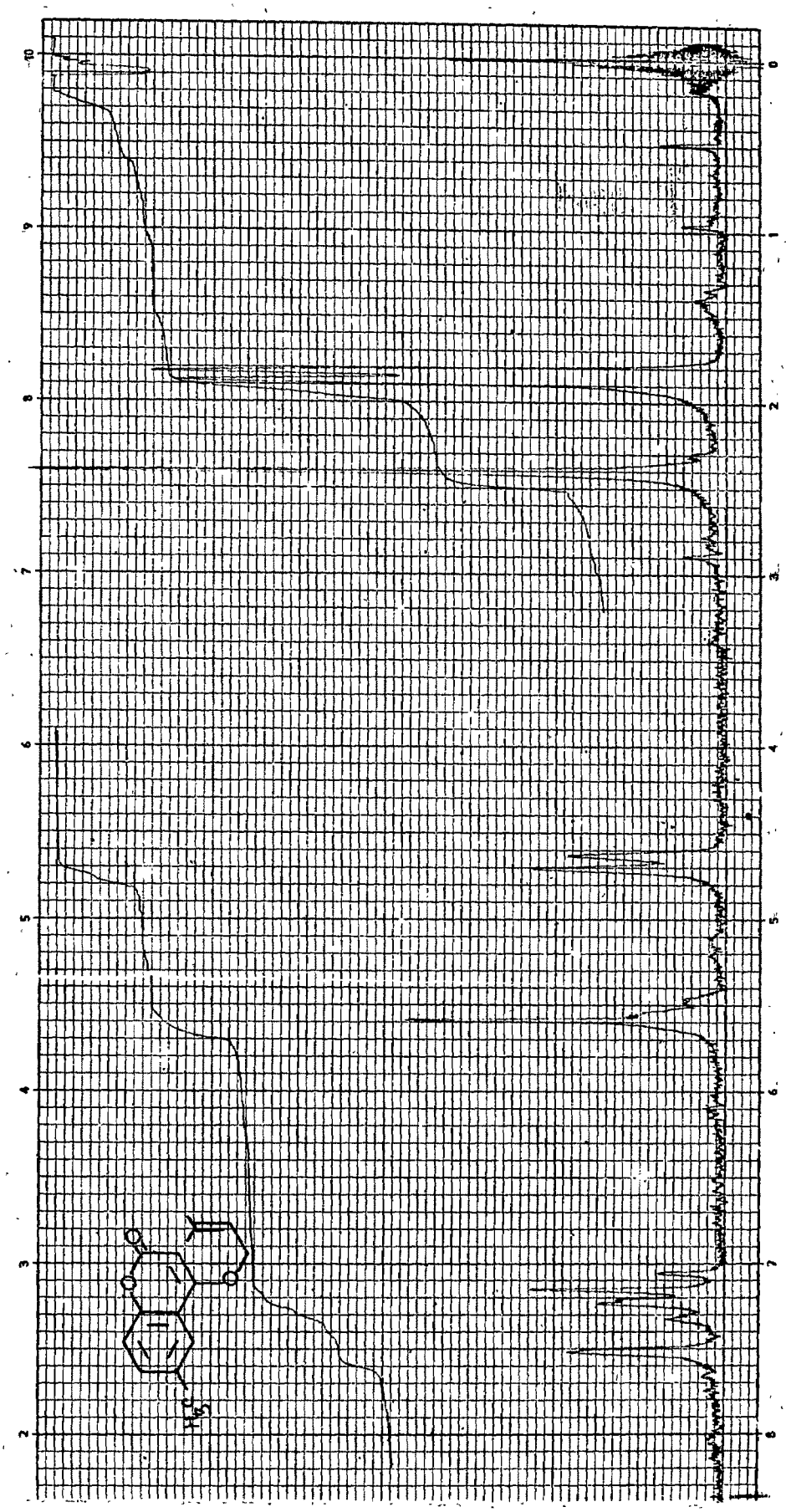
the structure of which was confirmed by its IR and NMR spectra, as given below :-

IR (nujol) : 1720 $cm.^{-1}$ (α-pyrone carbonyl stretching frequency), 1600 $cm.^{-1}$ (aromatic -C=C- stretching frequency), 1360 $cm.^{-1}$ (geminal dimethyl group stretching frequency) and 930 $cm.^{-1}$ (allylic -C=C= stretching frequency).

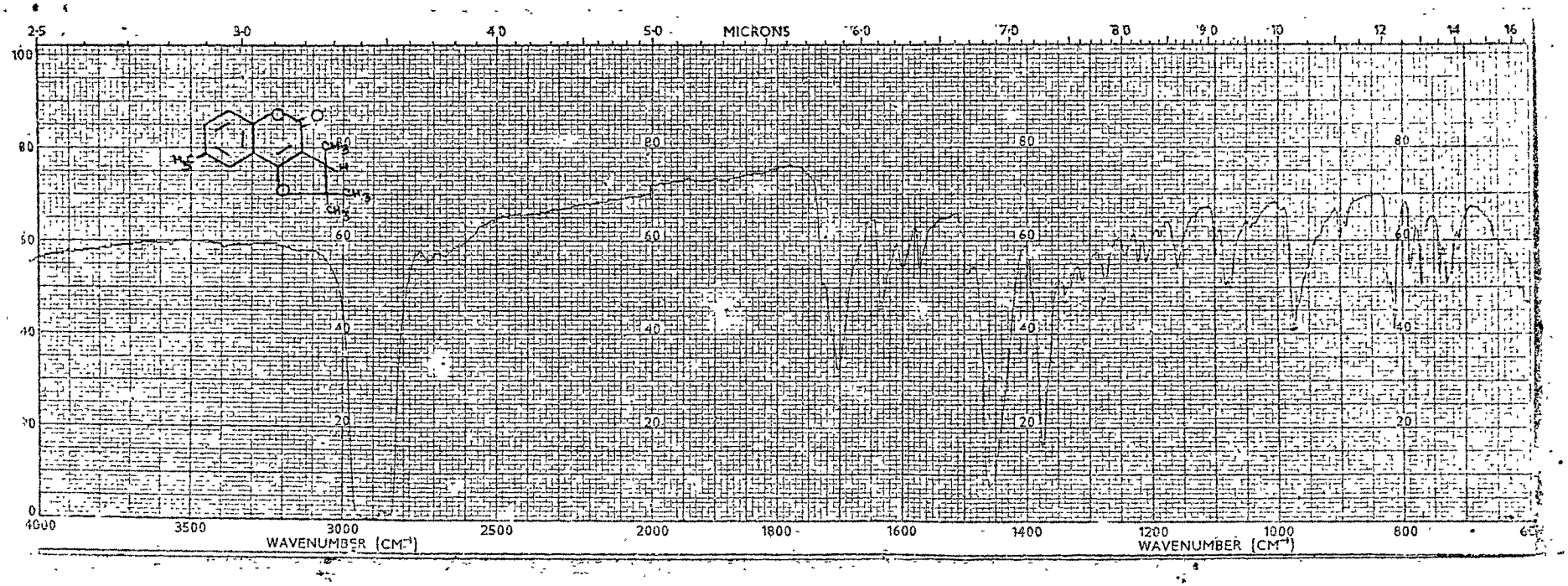
NMR (CCl_4) : δ 1.81 and 1.88, two singlets, geminal dimethyl group; 2.40, singlet, methyl group at position-6; 5.68, doublet, two protons of methylene group attached to ($-OC\underline{H}_2-CH=$); 5.60, triplet, one proton of methine group attached to ($-OCH_2-C\underline{H}=$) and 7.00-7.50, three protons aromatic (Fig. 7).



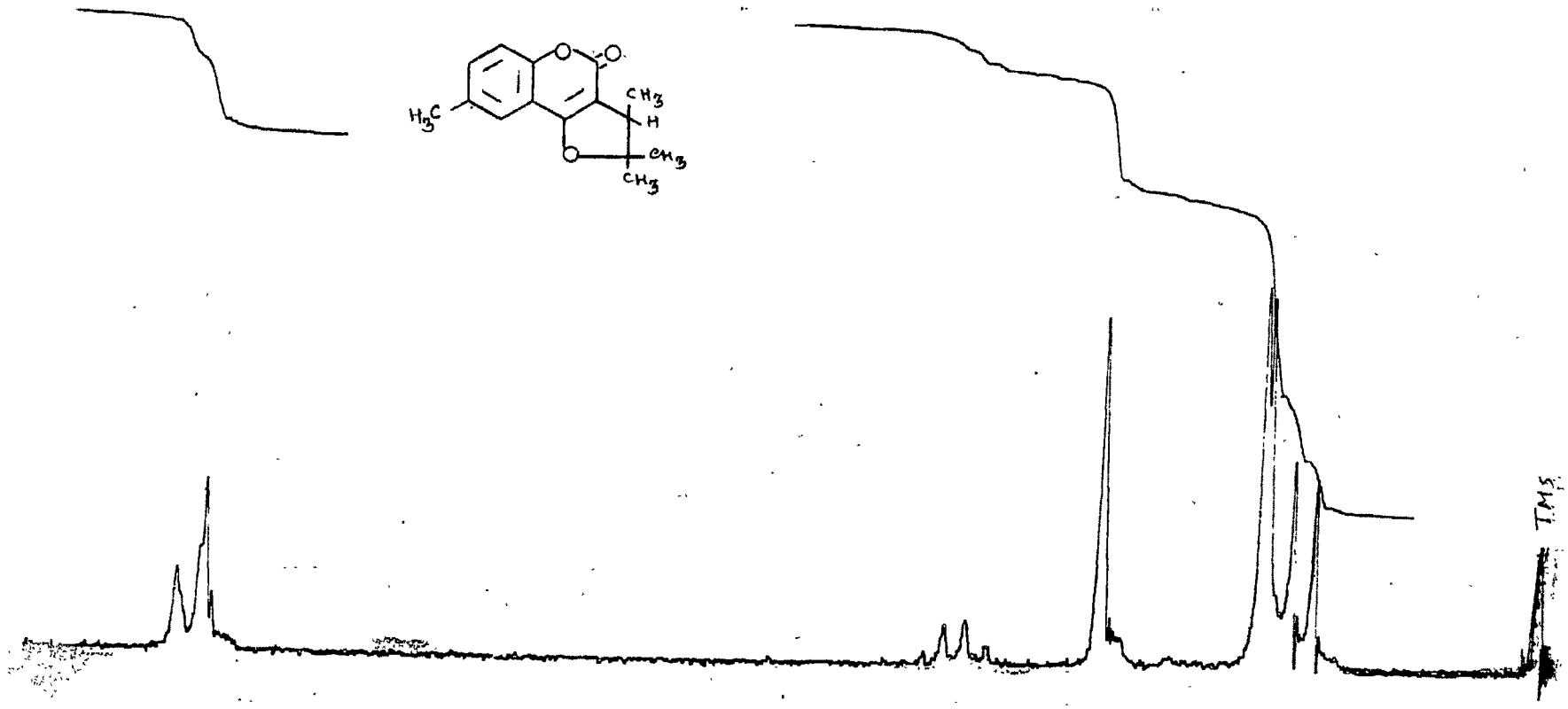
L LXXI LXXII



(Fig. 7) : 4-Prenyloxy-6-methylcoumarin



(Fig. 8) : 2,3-Dihydro-4-oxo-4H-2,2,3,8-tetramethylfurano(3,2-c)benzopyran



(Fig. 9) : 2,3-Dihydro-4-oxo-4H-2,2,3,8-tetramethylfurano(3,2-c)benzopyran

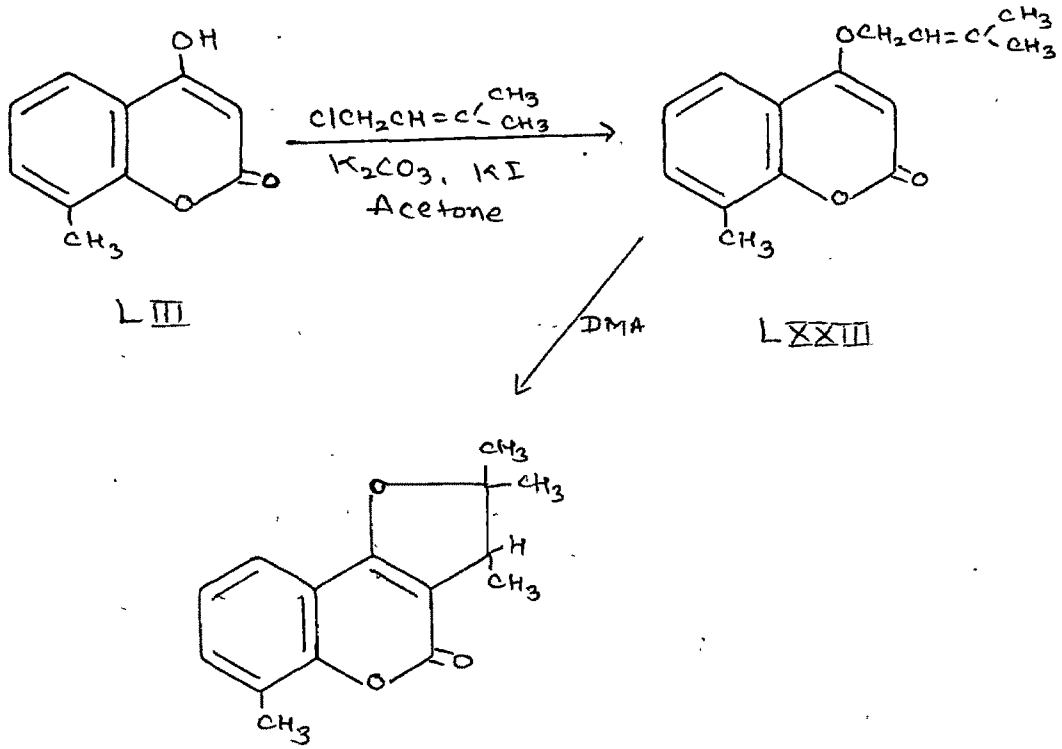
(LXXI) was refluxed with dimethylaniline to undergo abnormal Claisen migration. The structure of 2,3-dihydro--4-oxo-4H-2,2,3,8-tetramethylfurano(3,2-c)benzopyran (LXXII) was confirmed by its IR and NMR spectra.

IR (nujol) : 1705 $cm.^{-1}$ (α-pyrone carbonyl stretching frequency), 1635 $cm.^{-1}$ (aromatic -C=C- stretching frequency), 1390 $cm.^{-1}$ (geminal dimethyl group stretching frequency) and 975 $cm.^{-1}$ (furan).(Fig. 8).

NMR ($CDCl_3$) : δ 1.30, doublet, J=8Hz, methyl group at position-3; 1.50, two singlets, geminal dimethyl group at position-2; 2.40, singlet, methyl group at position-8; 3.20, quartate, J=8Hz, one proton at position-3 and 7.27-7.45, multiplet, three protons aromatic (Fig. 9).

Synthesis of 2,3-dihydro-4-oxo-4H-2,2,3,6-tetramethyl--furano(3,2-c)benzopyran

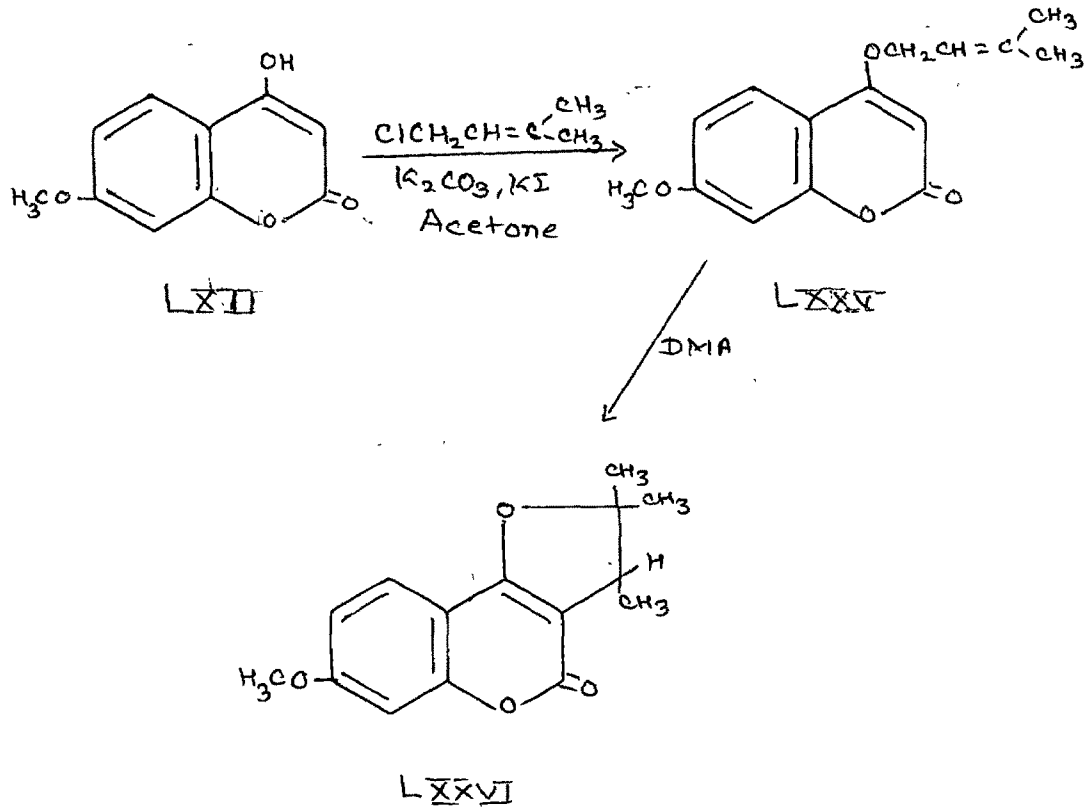
4-Prenyloxy-8-methylcoumarin was obtained by refluxing 4-hydroxy-8-methylcoumarin, 1-chloro-3-methyl-but-2-ene, potassium carbonate and potassium iodide in acetone. (LXXIII) was then refluxed in dimethylaniline to get abnormal Claisen migration product, 2,3-dihydro--4-oxo-4H-2,2,3,6-tetramethylfurano(3,2-c)benzopyran (LXXIV).



LIII LXXIII LXXIV

Synthesis of 2,3-dihydro-4-oxo-4H-7-methoxy--2,2,3-trimethylfurano(3,2-c)benzopyran

4-Prenyloxy-7-methoxycoumarin (LXXV) was obtained by refluxing 4-hydroxy-7-methoxycoumarin, 1-chloro--3-methyl-but-2-ene, potassium carbonate and potassium iodide in acetone. This was then refluxed in dimethylaniline to get abnormal Claisen migration product, 2,3-dihydro-4--oxo-4H-7-methoxy-2,2,3-trimethylfurano(3,2-c)benzopyran (LXXVI).



LXII LXXV

LXXVI

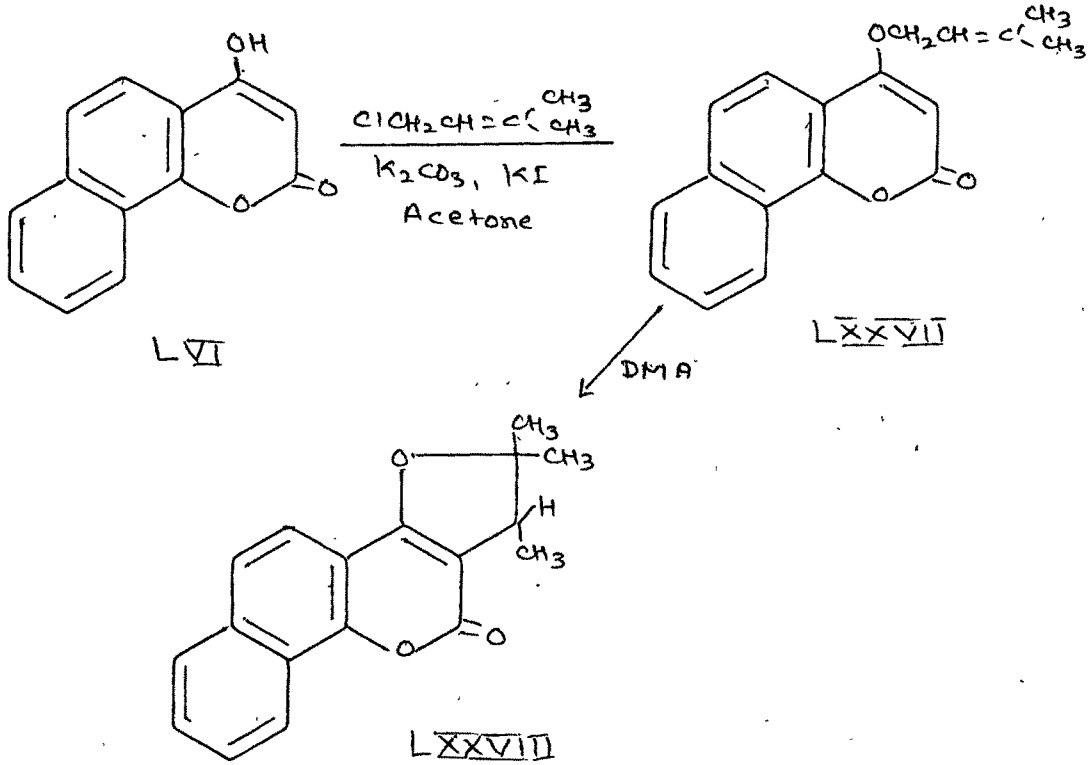
Synthesis of 2,3-dihydro-4-oxo-4H-6,7-benzo--2,2,3-trimethylfurano(3,2-c)benzopyran

4-Prenyloxy-7,8-benzocoumarin (LXXVII)was synthesised by refluxing 4-hydroxy-7,8-benzocoumarin with 1-chloro-3-methyl-but-2-ene, potassium carbonate and potassium iodide in acetone. This,on Claisen migration in dimethylaniline, gave 2,3-dihydro-4-oxo-4H-6,7-benzo-2,2,3-trimethylfurano(3,2-c)benzopyran (LXXVIII) .

The NMR spectrum of (LXXVIII) in $CDCl_3$ showed the following signals :-

δ 1.45, doublet, J=8Hz, methyl group at position-3;

1.55, singlet, geminal dimethyl group at position-2; 3.30, quartate, J=8Hz, one proton at position-2 and 7.40-7.80, multiplet, six protons aromatic.

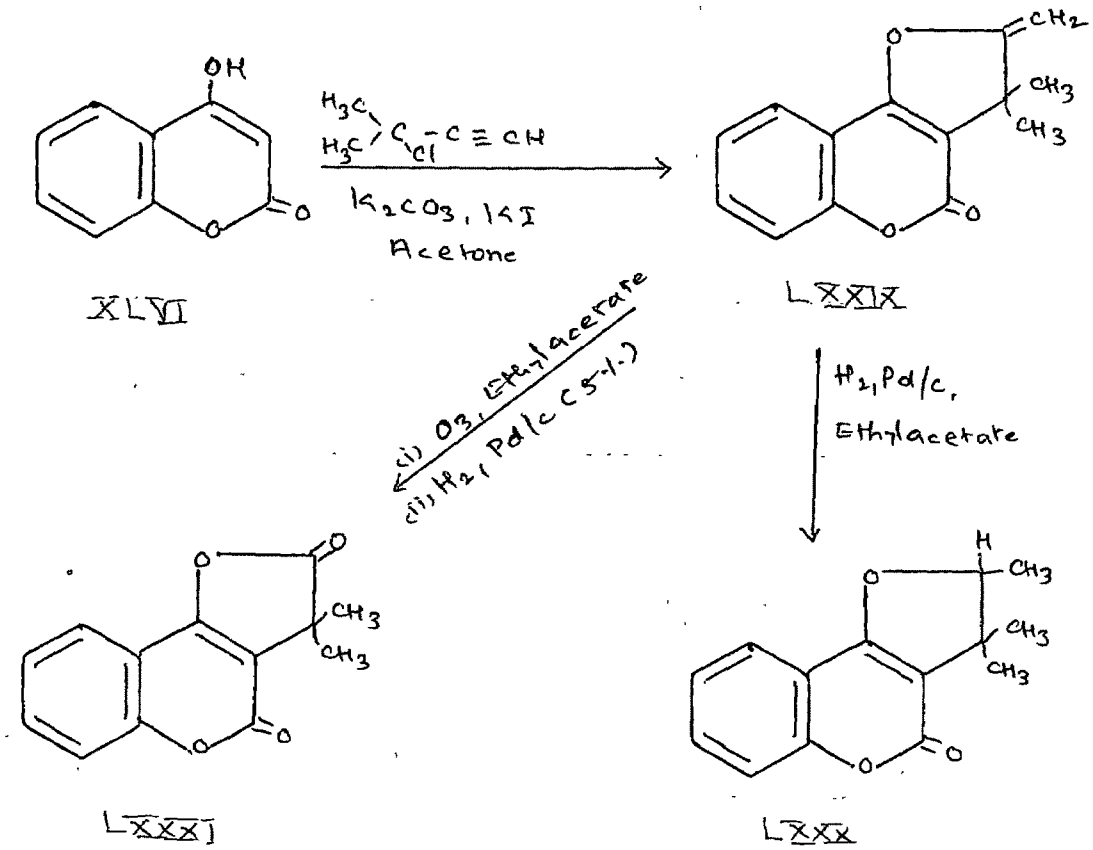


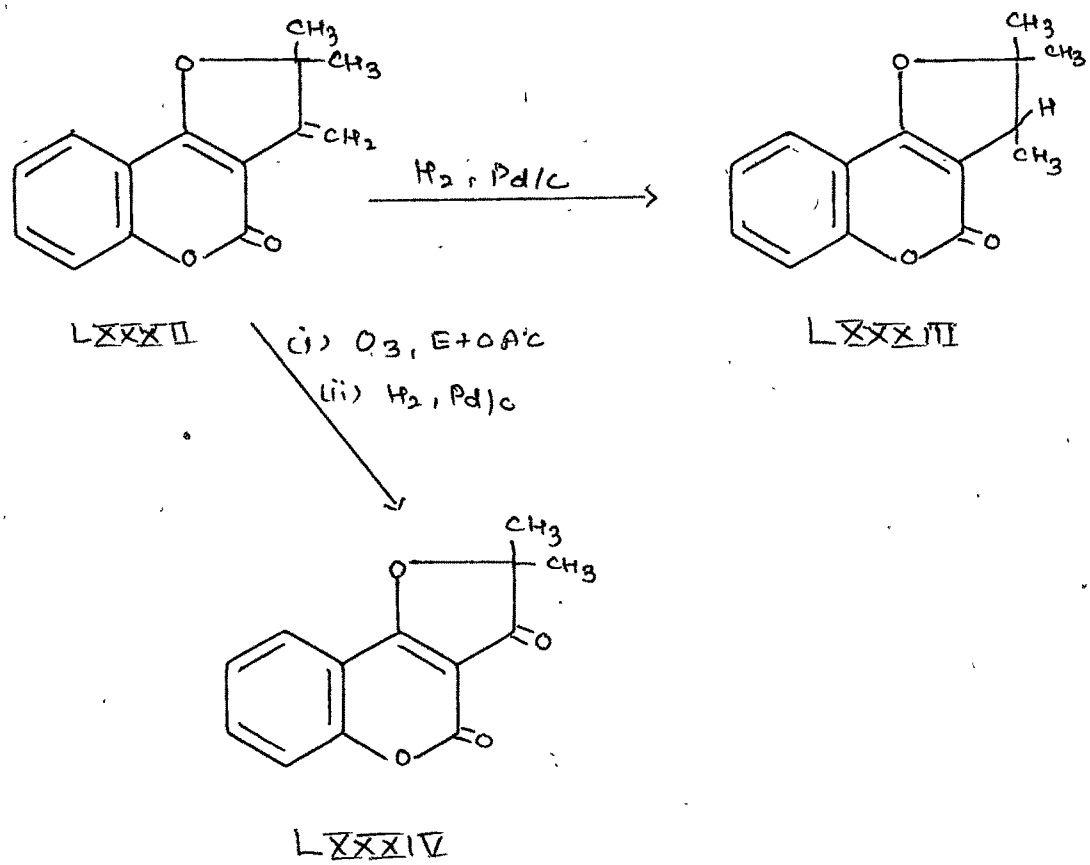
LVI LXXVII LXXVIII

Synthesis of 2,3-dihydro-4-oxo-4H-2,3,3-trimethyl--furano(3,2-c)benzopyran and 2,3-dihydro-2,4-dioxo--4H-3,3-dimethylfurano(3,2-c)benzopyran

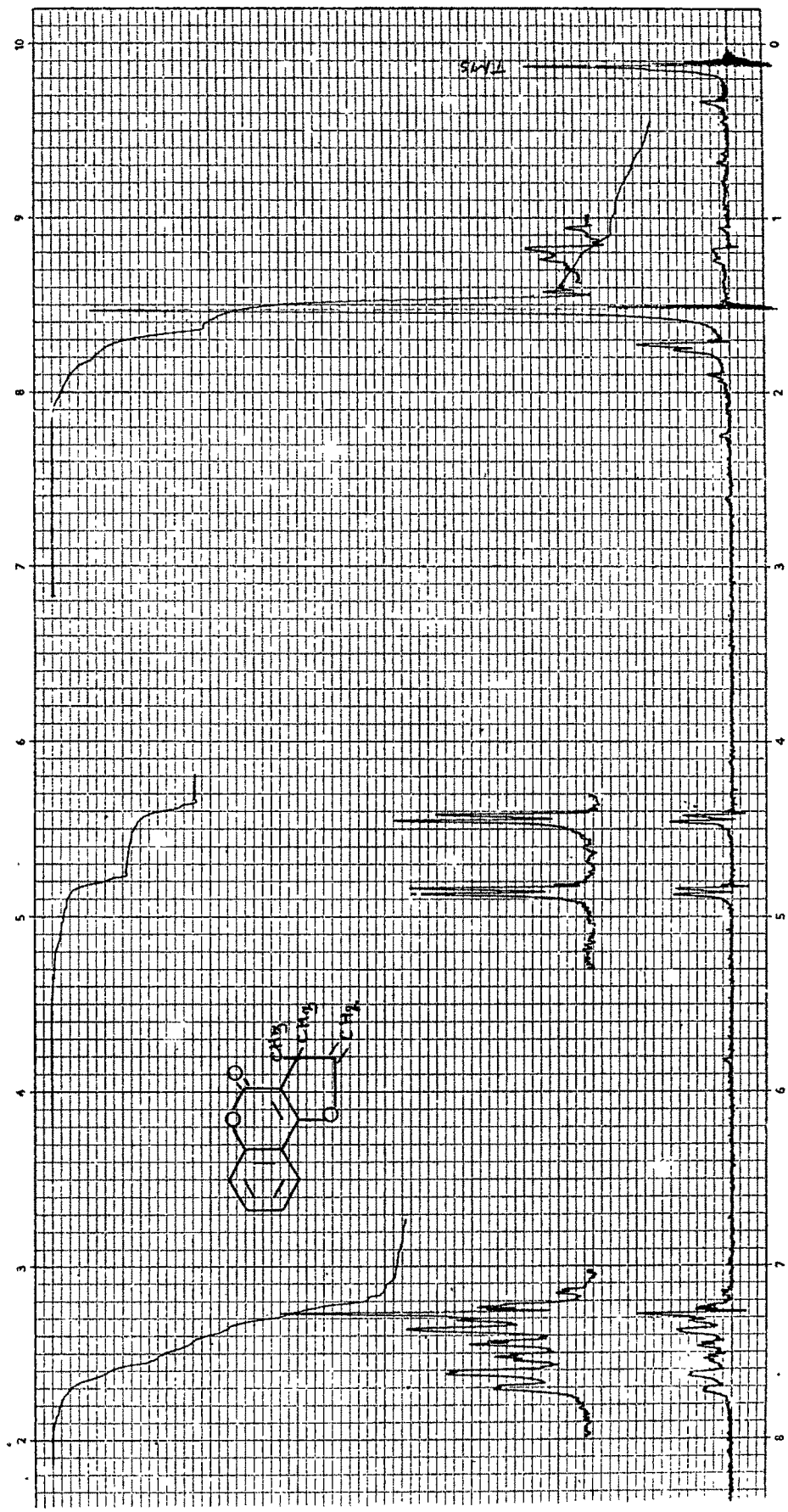
The next method to prepare the chromenocoumarin by condensing 4-hydroxycoumarin with 3-chloro-3-methyl-but--1-yne was tried. Seshadri et al.[14] synthesised chromenocoumarin by the condensation of 4-methylumbelliferon and 4-phenylumbelliferon with 3-chloro-3-methyl-but-1-yne in acetone in the presence of potassium carbonate and potassium

iodide according to the method of Hlubucek et al.[15], followed by Claisen migration. When 4-hydroxycoumarin was condensed with 3-chloro-3-methyl-but-1-yne as above, it did not give the expected 4-propargyloxycoumarin at the first stage of the reaction but, instead, gave 2-methylenefuranocoumarin derivative. This is rather an unusual formation of furanocoumarin derivative. The product was purified by column chromatography over silica gel and was identified as 2,3-dihydro-4-oxo-4H-2-methylene-3,3-dimethylfurano(3,2-c)benzopyran (LXXIX).





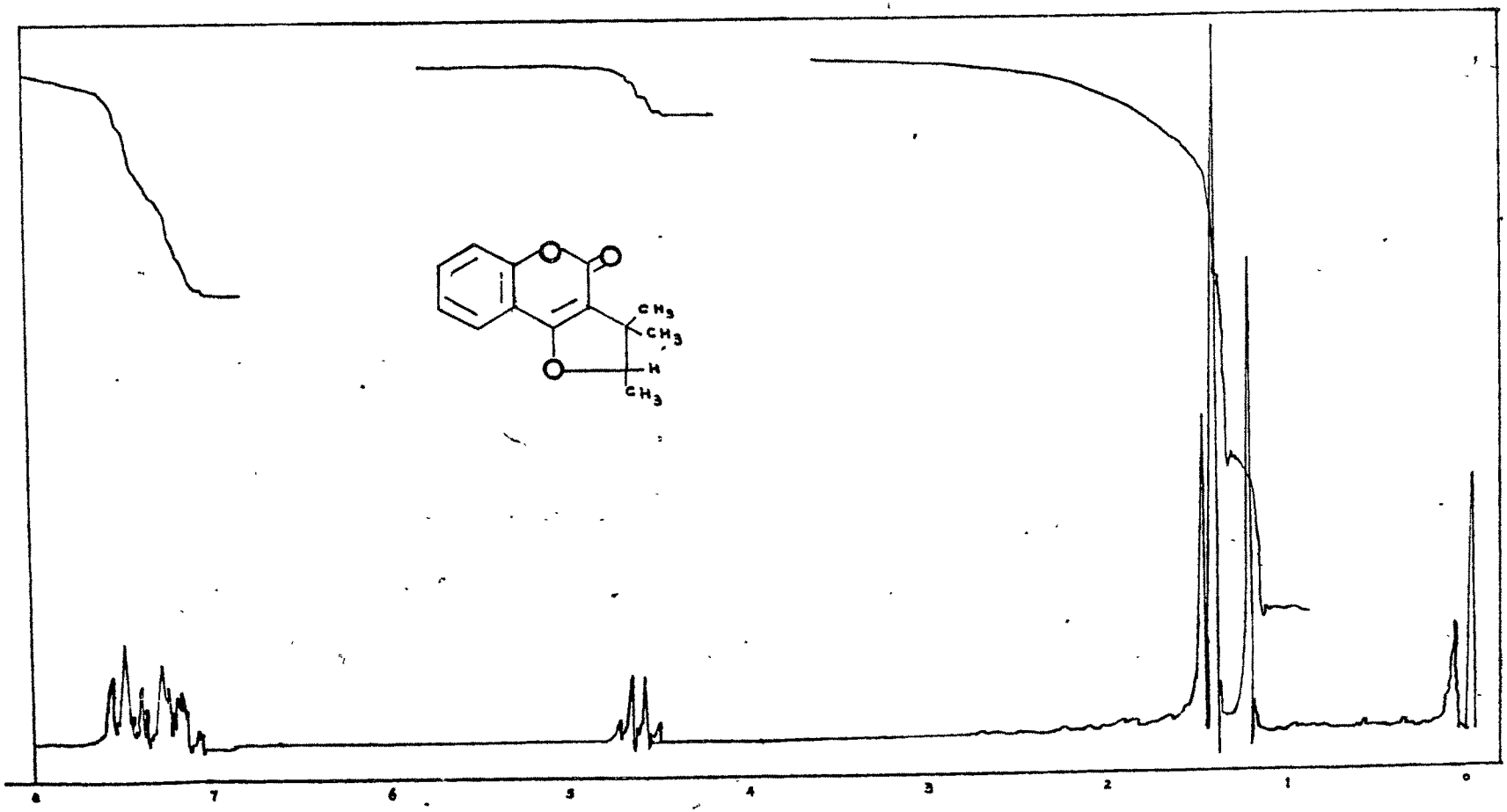
The NMR spectrum of this compound showed two doublets at δ 4.50 and 4.85 having coupling constant J=3Hz for the exocyclic methylene group at position-2 (Fig. 10). This was also supported by its IR spectrum which showed a >C=C< (exocyclic methylene group) stretching frequency at 915 $cm.^{-1}$ and 898 $cm.^{-1}$. The UV spectrum did not show any shift to higher in wavelength so it suggested that the exocyclic methylene group is not in conjugation with the double bond of coumarin ring at 3,4 position. The structure of compound (LXXIX) was further confirmed by its reduction to 2,3-dihydro-4-oxo-4H-2,3,3-trimethylfurano(3,2-c)benzo-



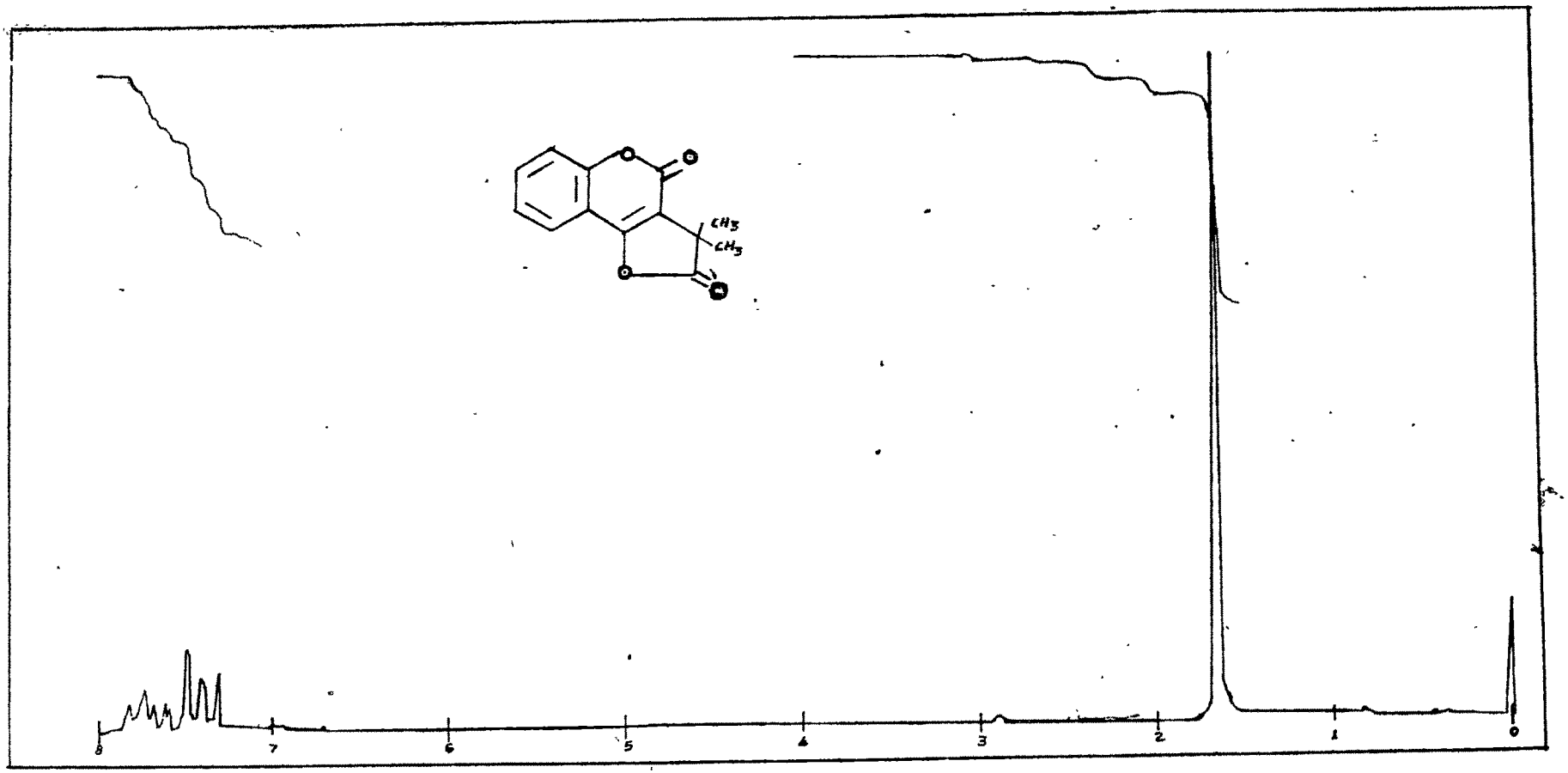
(Fig. 10) : 2,3-Dihydro-4-oxo-4H-2-methylene-3,3-dimethylfurano(3,2-c)benzopyran

-pyran (LXXX) by catalytic hydrogenation over palladised charcoal (10 %). The NMR spectrum of (LXXX) shows a doublet at δ 1.46 for one methyl group at position-2, two singlets at δ 1.22 and 1.42 for geminal dimethyl group at position-3 in the saturated methyl region and a down-field quartate at δ 4.62 for one proton at position-2. This down-field quartate indicates that the methine proton is flanked by methyl group and an oxygen atom, (Fig. 11). If it has structure (LXXXIII), this quartate for one proton would have appeared at δ 3.20 as it is away from the oxygen atom. Moreover, the NMR spectrum of (LXXXIII) would have shown a doublet of methyl group at up-field region and singlets due to geminal methyl group at down-field in saturated methyl region. Secondly, the compound obtained by Claisen rearrangement of 4-prenyloxycoumarin (LXV) would also be identical to (LXXXIII), if the methyl group obtained by the reduction of (LXXXII) is at position-3 in the furan ring.

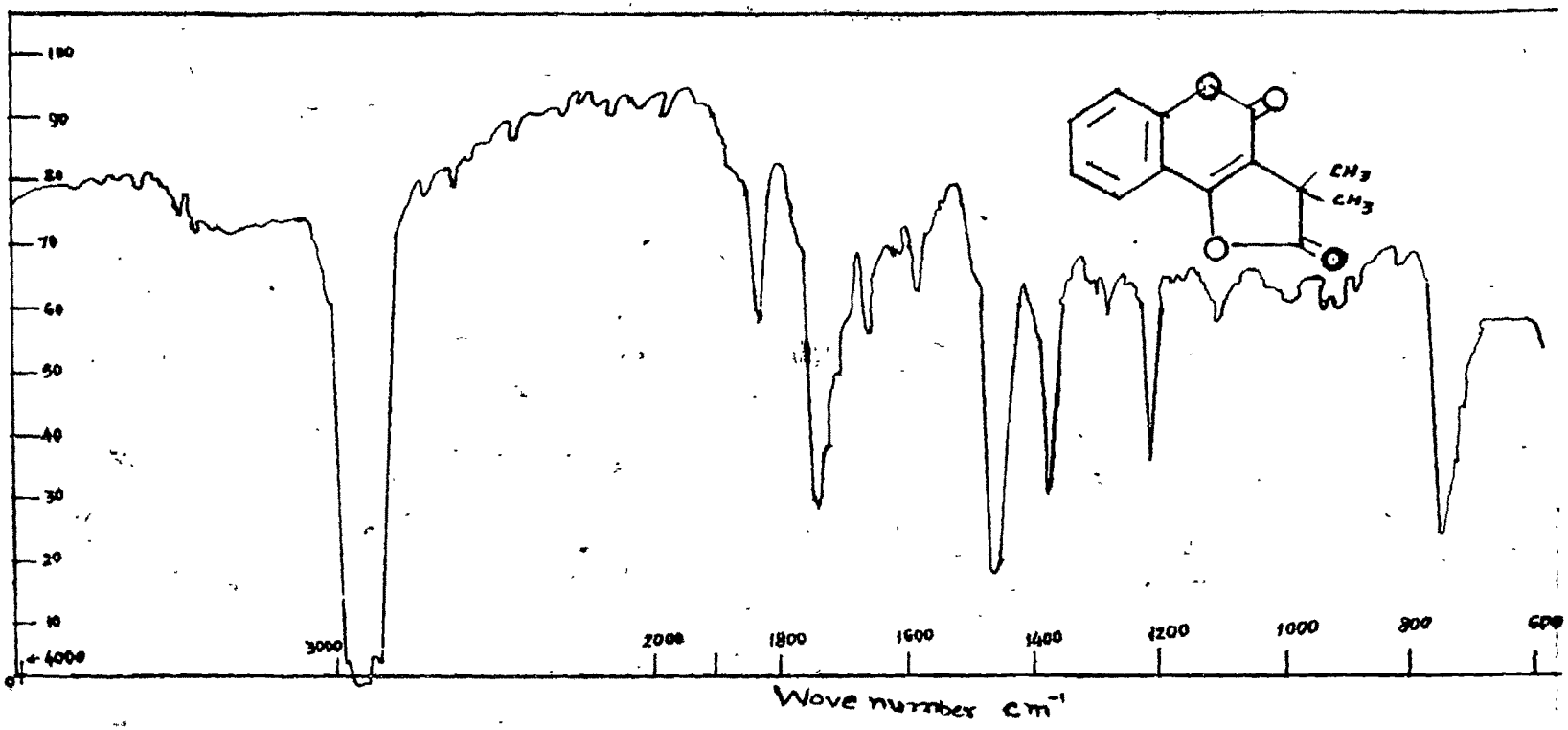
The structure of (LXXIX) was further confirmed by its ozonolysis. 2,3-Dihydro-4-oxo-4H-2-methylene-3,3-dimethylfurano(3,2-c)benzopyran on ozonolysis and subsequent reduction with hydrogen over palladised charcoal (5 %) gave 2,3-dihydro-2,4-dioxo-4H-3,3-dimethylfurano(3,2-c)benzopyran (LXXXI). The NMR spectrum of (LXXXI) in $CDCl_3$ showed the absence of two doublets at δ 4.50 and 4.85 for exocyclic methylene group (Fig. 12), but as expected, the IR spectrum showed the stretching bands at 1830 $cm.^{-1}$ and 1710 $cm.^{-1}$ for



(Fig. 11) : 2,3-Dihydro-4-oxo-4H-2,3,3-trimethylfurano(3,2-c)benzopyran



(Fig. 12) : 2,3-Dihydro-2,4-dioxo-4H-3,3-dimethylfurano(3,2-c)benzopyran



(Fig. 13) : 2,3-Dihydro-2,4-dioxo-4H-3,3-dimethylfurano(3,2-c)benzopyran

five membered lactone and six membered lactone rings (furanone and α-pyrone) respectively (Fig. 13).

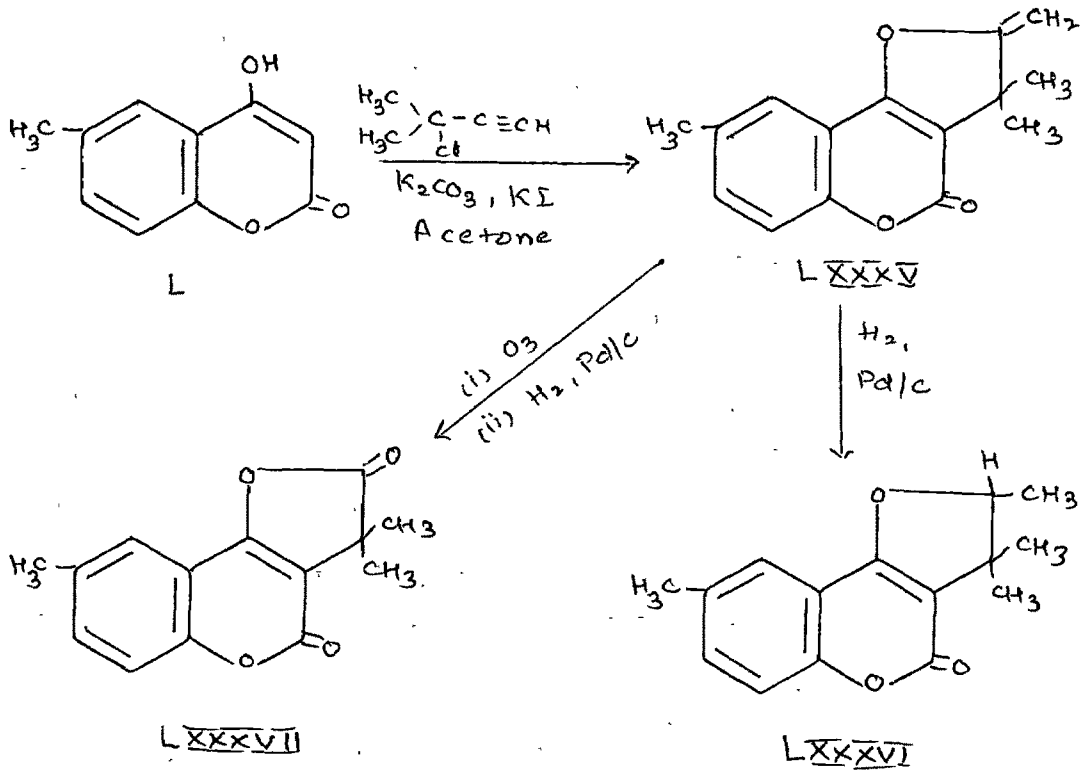
Synthesis of 2,3-dihydro-4-oxo-4H-2,3,3,8-tetramethyl--furano(3,2-c)benzopyran and 2,3-dihydro-2,4-dioxo-4H--3,3,8-trimethylfurano(3,2-c)benzopyran

4-Hydroxy-6-methylcoumarin on refluxing with 3-chloro-3-methyl-but-1-yne, anhydrous potassium carbonate and potassium iodide in acetone, gave 2,3-dihydro-4-oxo-4H-2-methylene-3,3,8-trimethylfurano(3,2-c)benzopyran (LXXXV). The NMR spectrum in CCl_4 showed the signals at δ 1.55, singlets, geminal dimethyl group at position-3; 2.42, singlet, methyl group at position-8; 4.45 and 4.85, two doublets, J=3Hz, two protons of methylene group at position-2 and 7.25-7.45, multiplet, three protons aromatic (Fig. 14). The IR spectrum in nujol showed a band at 1730 $cm.^{-1}$ for α-pyrone carbonyl group stretching and a band at 900 $cm.^{-1}$ for >C=C< (exocyclic methylene group) stretching (Fig. 15).

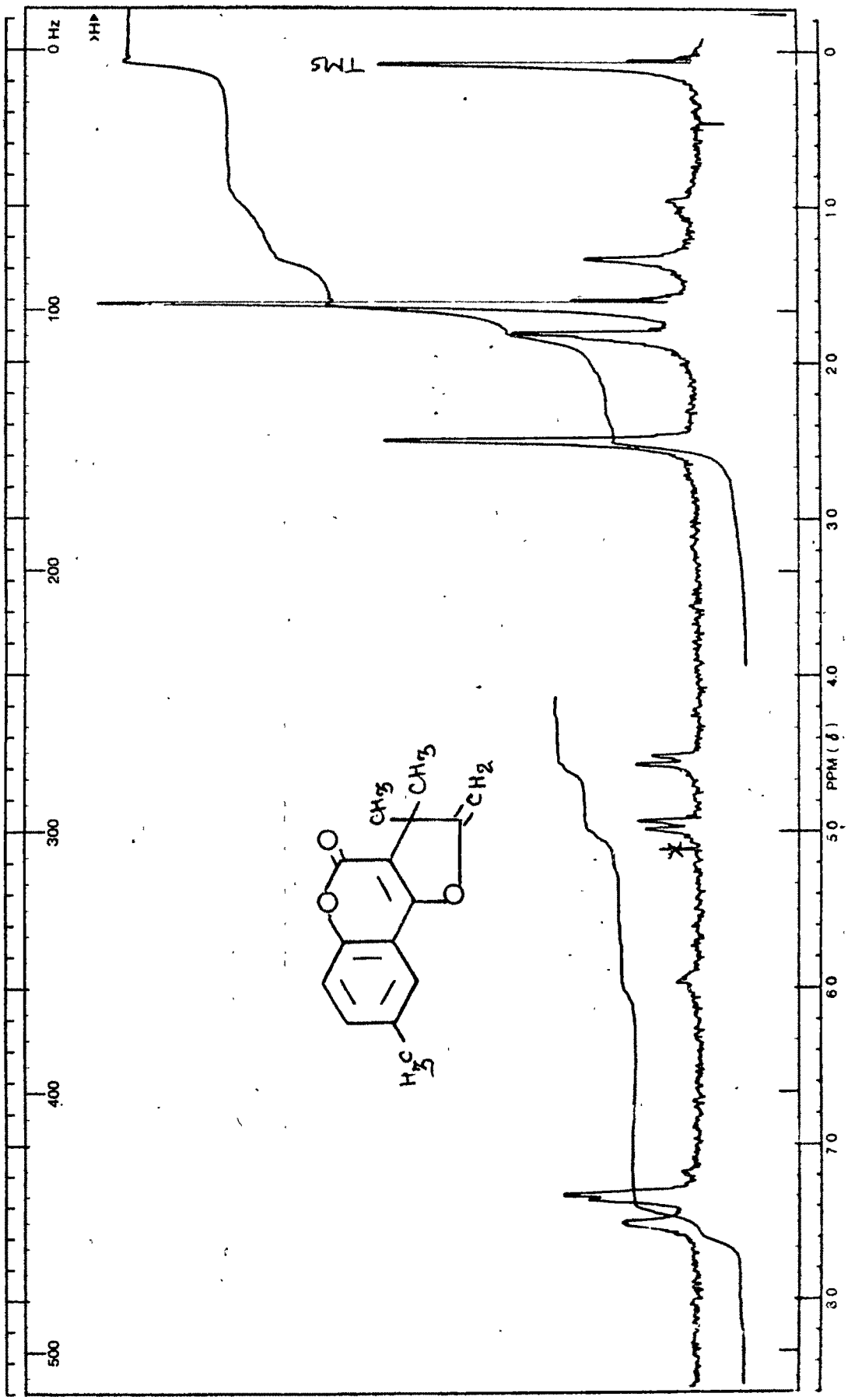
This was reduced with hydrogen in the presence of palladised charcoal (10 %) as a catalyst, to 2,3-dihydro-4-oxo-4H-2,3,3,8-tetramethylfurano(3,2-c)benzopyran (LXXXVI).

The NMR spectrum of (LXXXVI) in CCl_4 showed the following signals :-

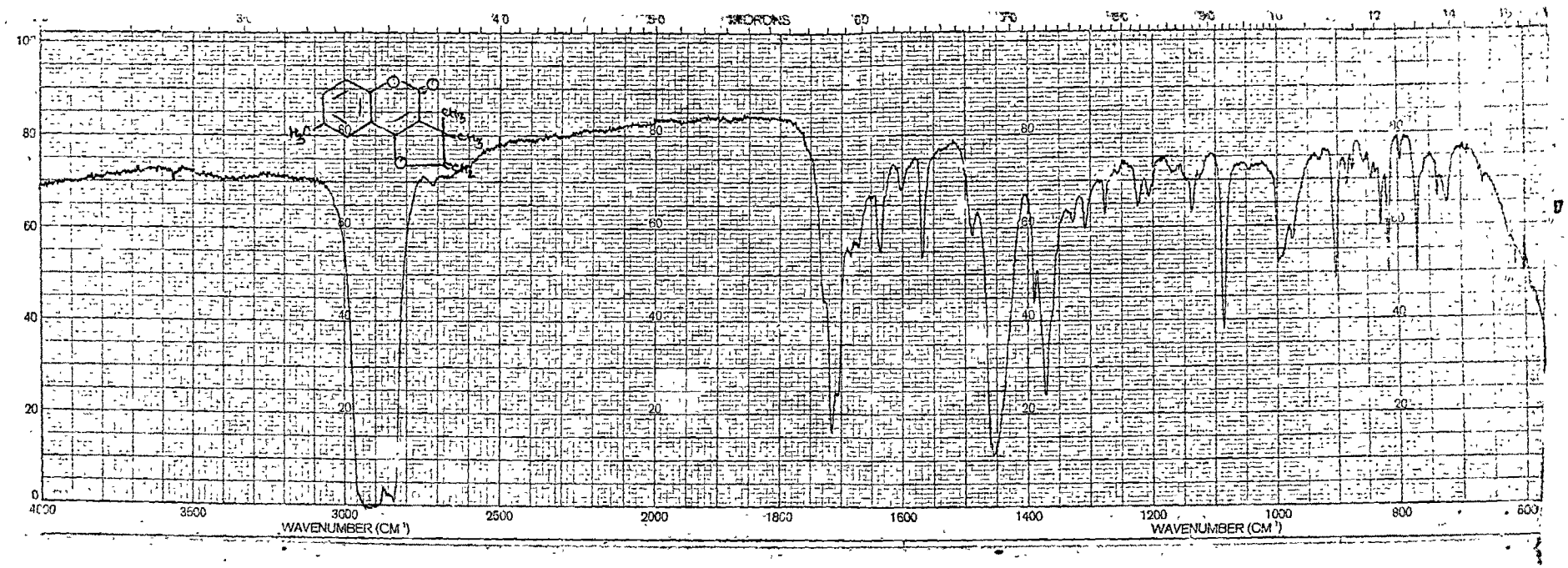
δ 1.25 and 1.28, two singlets, geminal dimethyl group at position-3; 1.45, doublet, J=7Hz, methyl group at position-2; 2.37, singlet, methyl group at position-8; 4.58, quartate, J=7Hz, one proton at position-2 and 7.02-7.52, multiplet, three protons aromatic (Fig. 16).



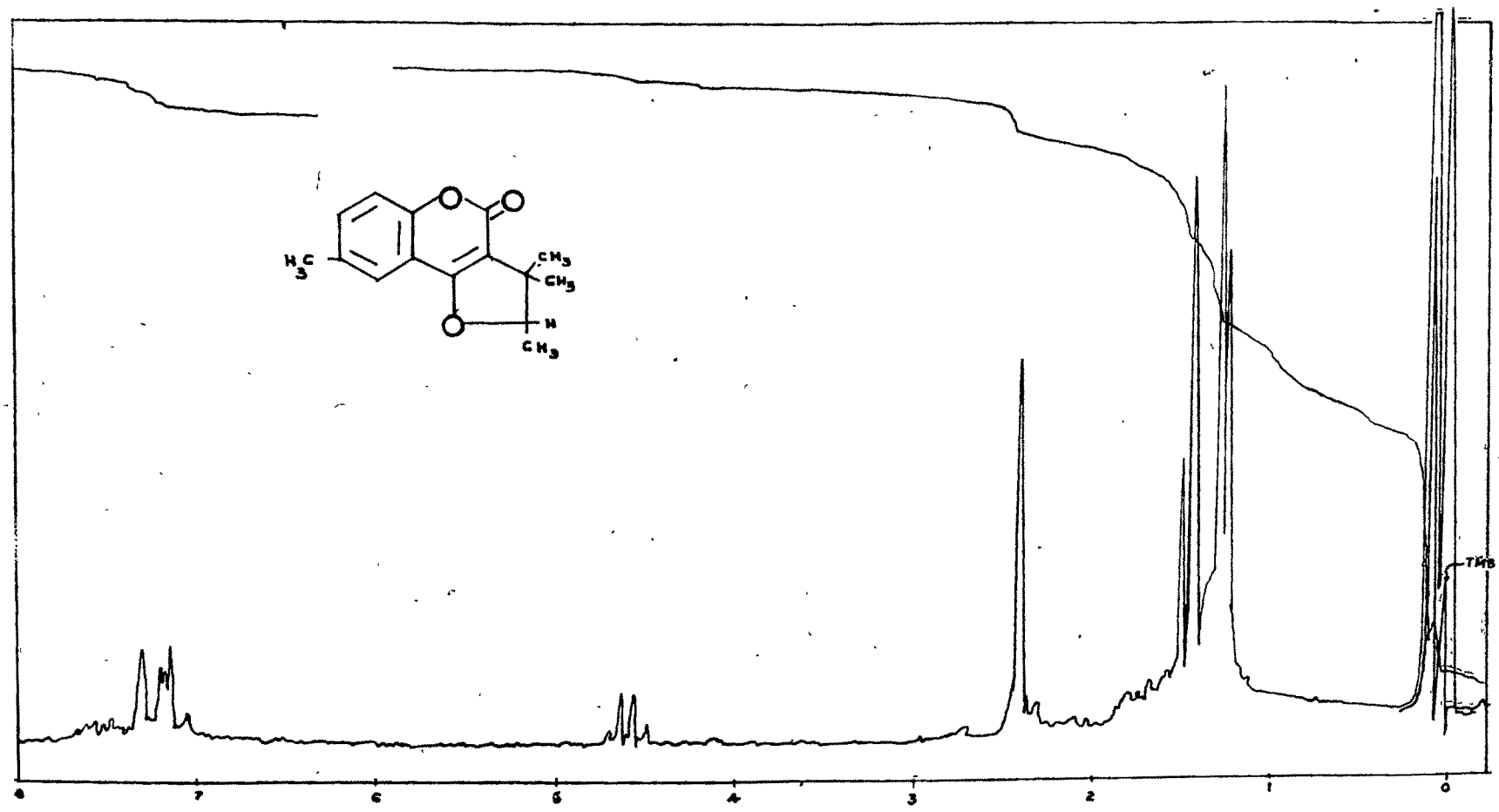
Ozonolysis of (LXXXV) gave a keto-lactonyl derivative, 2,3-dihydro-2,4-dioxo-4H-3,3,8-trimethylfurano-(3,2-c)benzopyran (LXXXVII) and the structure of it was confirmed by its NMR. It showed the absence of two signals at δ 4.35 and 4.85 for two protons of exocyclic methylene group (Fig. 17). The IR spectrum in nujol showed a band at



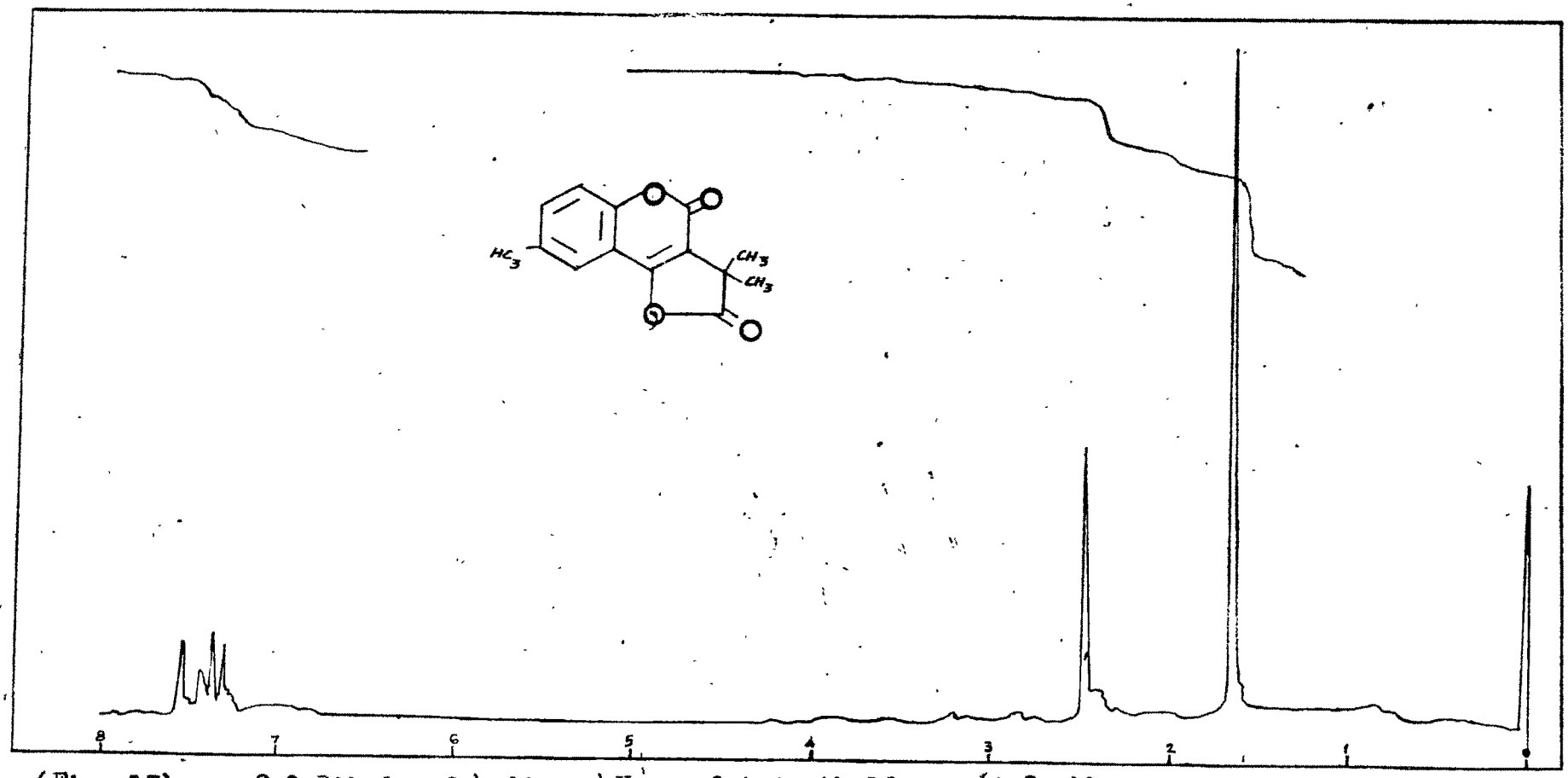
(Fig. 14) : 2,3-Dihydro-4-oxo-4H-2-methylene-3,3,8-trimethylfurano(3,2-c)benzopyran



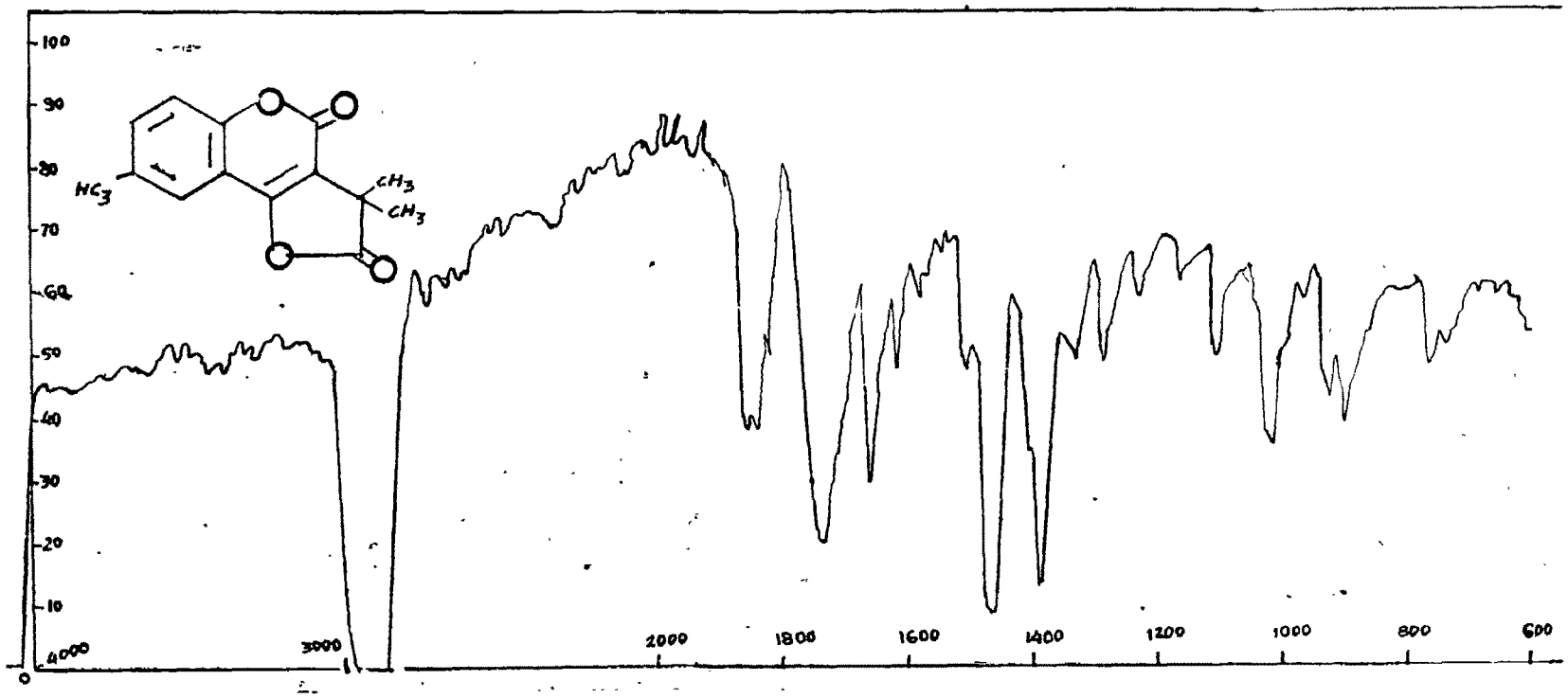
(Fig. 15) : 2,3-Dihydro-4-oxo-4H-2-methylene-3,3,8-trimethylfurano(3,2-c)benzopyran



(Fig. 16) : 2,3-Dihydro-4-oxo-4H-2,3,3,8-tetramethylfurano(3,2-c)benzopyran.



(Fig. 17) : 2,3-Dihydro-2,4-dioxo-4H-3,3,8-trimethylfurano(3,2-c)benzopyran.

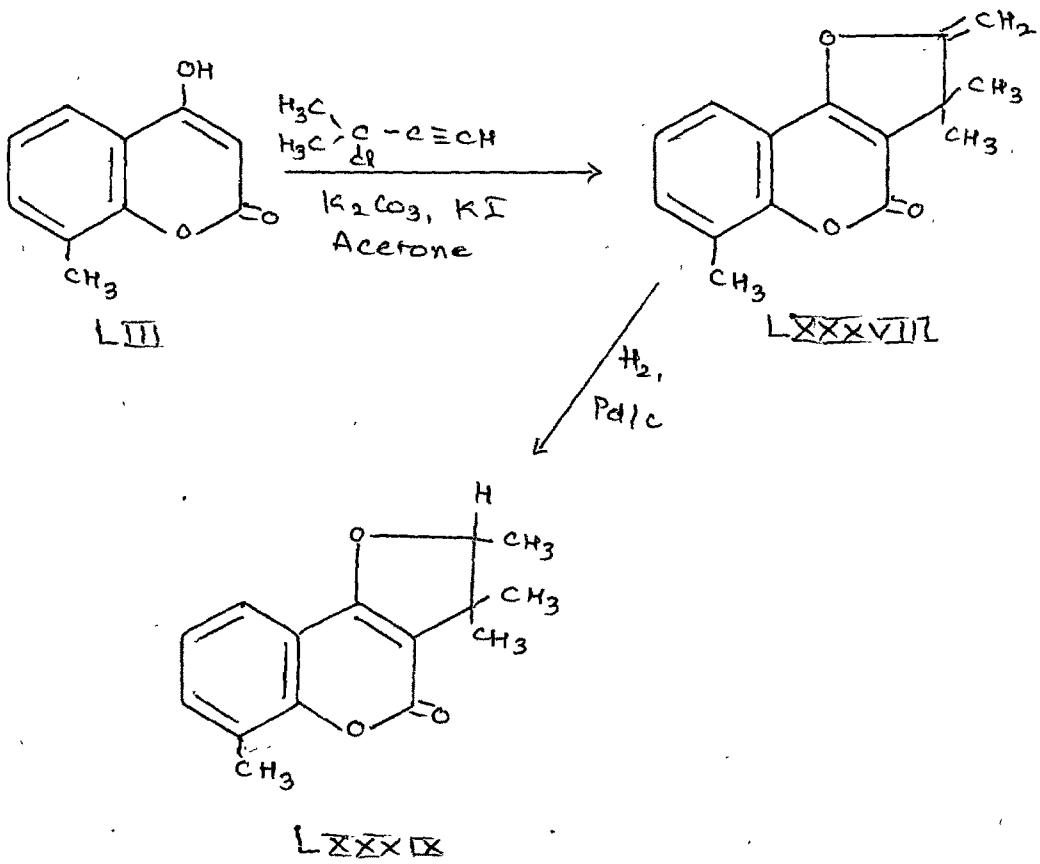


(Fig. 18) : 2,3-Dihydro-2,4-dioxo-4H-3,3,8-trimethylfurano(3,2-c)benzopyran

1835 $cm.^{-1}$ for five membered lactone (Fig. 18).

Synthesis of 2,3-dihydro -4-oxo-4H-2,3,3,6-tetramethyl--furano(3,2-c)benzopyran

4-Hydroxy-8-methylcoumarin was refluxed with 3-chloro-3-methyl-but-1-yne, anhydrous potassium carbonate and potassium iodide in acetone to give 2,3-dihydro-4-oxo--4H-2-methylene-3,3,6-trimethylfurano(3,2-c)benzopyran (LXXXVIII). This was further reduced to 2,3-dihydro-4-oxo--4H-2,3,3,6-tetramethylfurano(3,2-c)benzopyran (LXXXIX) with hydrogen in the presence of palladised charcoal (10 %).



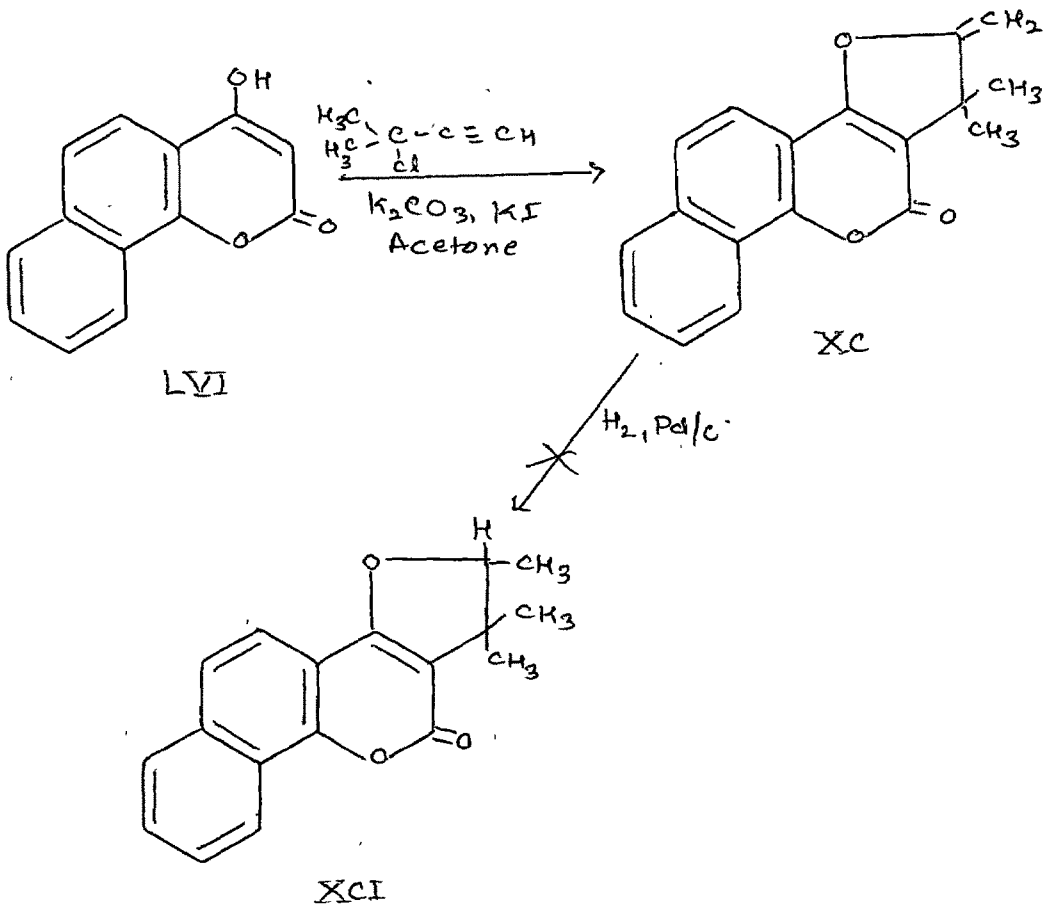
LIII

LXXXVIII

LXXXIX

Synthesis of 2,3-dihydro-4-oxo-4H-2,3,3-trimethyl--6,7-benzofurano(3,2-c)benzopyran

4-Hydroxy-7,8-benzocoumarin was condensed with 3-chloro-3-methyl-but-1-yne in the presence of anhydrous potassium carbonate and potassium iodide in acetone, to give 2,3-dihydro-4-oxo-4H-2-methylene-3,3-dimethyl-6,7--benzofurano(3,2-c)benzopyran (XC). This on reduction with hydrogen in the presence of palladised charcoal (10 %) gave an oil which could not be identified as 2,3-dihydro-4-oxo-4H--2,3,3-trimethyl-6,7-benzofurano(3,2-c)benzopyran (XCI).



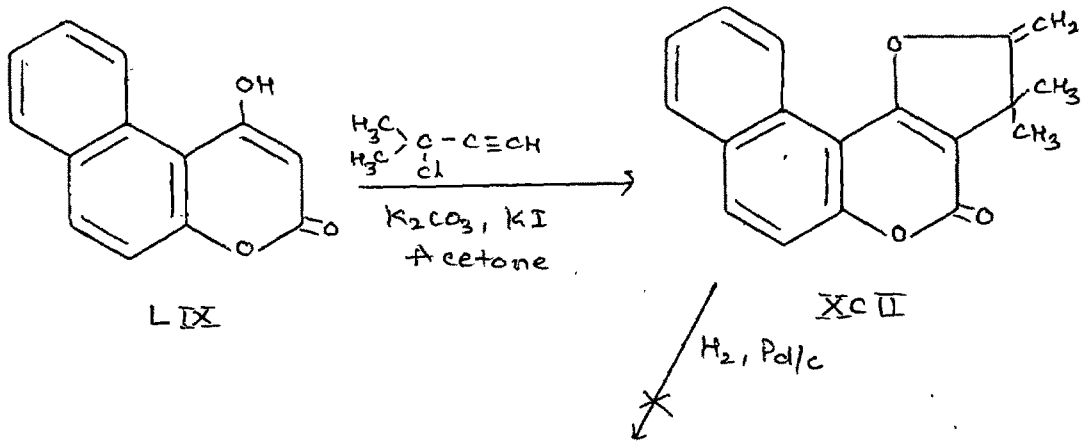
LVI

XC

XCI

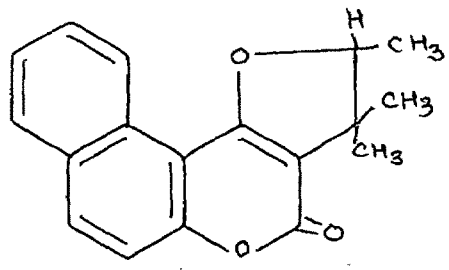
Synthesis of 2,3-dihydro-4-oxo-4H-2,3,3-trimethyl-=8,9-benzofurano(3,2-c)benzopyran

4-Hydroxy-5,6-benzocoumarin was condensed with 3-chloro-3-methyl-but-1-yne in the presence of anhydrous potassium carbonate and potassium iodide in acetone to give 2,3-dihydro-4-oxo-4H-2-methylene-3,3-dimethyl-8,9-benzofurano(3,2-c)benzopyran (XCII). This on reduction with hydrogen in the presence of palladised charcoal (10 %) failed to give 2,3-dihydro-4-oxo-4H-2,3,3-trimethyl-8,9--benzofurano(3,2-c)benzopyran (XCIII), but gave an oil which could not be identified.



LIX

XCII



XCIII

EXPERIMENTAL

5-Oxo-5H-2,2-dimethylpyrano(3,2-c)benzopyran (XLVIII) : 3,4-Dihydro-5-oxo-5H-2,2-dimethylpyrano(3,2-c)benzopyran (XLVII) :

To a solution of 4-hydroxycoumarin (1.1 g.) in dry dioxan (12 ml.) was added gradually BF_3-etherate (0.6 ml.) at room temperature. To this was added a solution of 2-methyl-but-3-en-2-ol (0.6 g.) in anhydrous dioxan (5 ml.) and the whole solution was heated on a water bath for 8 hr. The solution was cooled and diluted with ether (100 ml.). The solution was washed with water (3x50 ml.) to discharge the colour. The solution was then extracted with sodium carbonate solution (15 % ; 3x50 ml.), which on acidification gave unreacted 4-hydroxycoumarin (0.8 g.). The ethereal solution was evaporated and the residue was dissolved in chloroform, which showed the presence of two compounds. Hence, it was subjected to column chromatography over silica gel and the column eluted successively with (i) benzene-light petroleum ether (25:75) and (ii) benzene-light petroleum ether (70:30). Fraction (i) was an oily product, which was not identified. Fraction (ii), on evaporation of the solvent, gave a solid(XLVII), crystallised from petroleum ether, m.p. 124°. Yield 0.2 g.

UV (methanol) : λ max. (log e), 270 (3.98), 282 (4.08), 304 (4.0) and 318 (3.79).

Analysis : Found : C, 73.05 ; H, 5.97 %

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

5-Oxo-5H-2,2-dimethylpyrano(3,2-c)benzopyran (XLVIII) :

DDQ (Dichlorodicyanobenzoquinone) (0.2 g.) was added to a solution of 3,4-dihydro-5-oxo-5H-2,2-dimethylpyrano(3,2-c)benzopyran (0.2 g.) in dry benzene (5 ml.) and was refluxed for 50 hr., when the yellow coloured hydroquinone separated out. It was filtered hot and the residue was washed with hot dry benzene. The solvent was removed by distillation and the residue was chromatographed on silica gel, and elution with benzene-petroleum ether (2:1) gave a product, which according to its NMR spectrum was a mixture of 3,4-dihydro-5-oxo-5H-2,2-dimethylpyrano(3,2-c)-benzopyran and 5-oxo-5H-2,2-dimethylpyrano(3,2-c)benzopyran, which could not be separated even on preparative TLC, impregnated with silver nitrate solution (10 %), crystallised from petroleum ether, m.p. 95-96°.

UV (methanol) : λ max (log e), 270 (3.98), 282 (4.0), 304 (3.99), 318 (3.82), 332 (2.78) and 340 (2.91).

Analysis : Found : C, 73.78 ; H, 5.47 %

$C_{14}H_{12}O_3$ requires : C, 73.67 ; H, 5.30 %.

5-Oxo-5H-2,2,9-trimethylpyrano(3,2-c)benzopyran (LII) :

3,4-Dihydro-5-oxo-5H-2,2,9-trimethylpyrano(3,2-c)benzopyran (LI) :

To a solution of 4-hydroxy-6-methylcoumarin (1.2 g.) in dry dioxan (15 ml.), was added gradually

BF_3-etherate (0.6 ml.) at room temperature. To this was added a solution of 2-methyl-but-3-en-2-ol (0.6 g.) in dry dioxan (5 ml.) and the whole solution was heated on a water bath for 8 hr. The solution was cooled and diluted with ether (100 ml.) . The solution was washed with water (3x50 ml.) and then with sodium carbonate solution (15 % ; 3x50 ml.), which on acidification gave unreacted 4-hydroxy-6-methylcoumarin. The ethereal solution was evaporated and the residue was dissolved in benzene and on examination by TLC showed the presence of two compounds. Hence it was subjected to the column chromatography, and the column eluted successively with (i) benzene-petroleum ether (25:75), to yield an unidentifiable oily product and (ii) benzene-petroleum ether (80:20), yielded a solid, 3,4-dihydro-5-oxo-5H-2,2,9-trimethylpyrano(3,2-c)benzopyran, crystallised from petroleum ether, m.p. 157-58°. Yield 0.25 g.

UV (methanol) : λ max (log e)272 (3.98), 284 (4.00) and 310 (3.86).

Analysis : Found : C, 73.58 ; H, 6.52 %

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

5-Oxo-5H-2,2,9-trimethylpyrano(3,2-c)benzopyran (LII) :

DDQ (0.20 g.) was added to a solution of 3,4-dihydro-5-oxo-5H-2,2,9-trimethylpyrano(3,2-c)benzopyran (0.21 g.) in dry benzene and was refluxed for 48 hr. The solid separated was filtered hot and washed with hot benzene. The filtrate was concentrated by distilling off the solvent

and was chromatographed on silica gel. Elution with benzene-petroleum ether (75:25) gave a solid, 5-oxo-5H-2,2,9-trimethylpyrano(3,2-c)benzopyran, crystallised from petroleum ether, m.p. 136-37°. Yield 0.15 g.

UV (methanol) : λmax (log e), 272 (3.99), 284 (4.02) and 324 (3.92).

Analysis : Found : C, 74.66 ; H, 5.54 %

$C_{15}H_{14}O_6$ requires : C, 74.36 ; H, 5.58 %.

5-Oxo-5H-2,2,7-trimethylpyrano(3,2-c)benzopyran (LV) : 3,4-Dihydro-5-oxo-5H-2,2,7-trimethylpyrano(3,2-c)benzopyran (LIV) :

To a solution of 4-hydroxy-8-methylcoumarin (1.2 g.) in dioxan (15 ml.) was added gradually BF_3-etherate (0.6 ml.) at room temperature. To this was added a solution of 2-methyl-but-3-en-2-ol (0.6 g.) in dry dioxan (5 ml.) and the whole solution heated on a water bath for 8 hr. The reaction mixture was worked up as before. The product, 3,4-dihydro-5-oxo-5H-2,2,7-trimethylpyrano(3,2-c)benzopyran, crystallised from petroleum ether, m.p. 156°. Yield 0.2 g.

IR (nujol) : 1720 $cm.^{-1}$ (α-pyrone carbonyl stretching frequency) and 1370 $cm.^{-1}$ (geminal dimethyl group stretching frequency).

UV (methanol) : λ max (log e), 272 (3.92), 284 (4.02) and 308 (4.00).

Analysis : Found : C, 73.41 ; H, 6.47 %

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

5-Oxo-5H-2,2,7-trimethylpyrano(3,2-c)benzopyran (LV) :

To a solution of 3,4-dihydro-5-oxo-5H-2,2,7-trimethylpyrano(3,2-c)benzopyran (0.2 g.) in dry benzene (10 ml.) was added DDQ (0.2 g.) and the mixture was refluxed for 48 hr. when a solid hydroquinone separated. It was filtered hot and the residue was washed with hot benzene. The filtrate was distilled to remove the solvent and the residue chromatographed on silica gel. Elution with benzene-petroleum ether (75:25) gave a solid which crystallised from petroleum ether. The NMR spectrum of the product indicated it to be a mixture of 3,4-dihydro-5-oxo-5H-2,2,7-trimethylpyrano(3,2-c)-benzopyran and 5-oxo-5H-2,2,7-trimethylpyrano(3,2-c)benzo-pyran which could not be separated by TLC impregnated by silver nitrate solution (5 %) or column chromatographic methods. M.p. 137°. Yield 0.15 g.

UV (methanol) : λ max (log e), 245 (3.98) and 355 (4.00).

The NMR spectrum of the mixture is discussed on page 43 .

Analysis : Found : C, 74.37 ; H, 5.72 %

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

5-Oxo-5H-7,8-benzo-2,2-dimethylpyrano(3,2-c)benzopyran (LVIII) :

3,4-Dihydro-5-oxo-5H-7,8-benzo-2,2-dimethylpyrano(3,2-c)--benzopyran (LVII) :

To a solution of 4-hydroxy-7,8-benzocoumarin (1.6 g.)

in dry dioxan (20 ml.) was added gradually BF_3-etherate (0.6 ml.) at room temperature. To this was added a solution of 2-methyl-but-3-en-2-ol (0.6 g.) in dry dioxan (5 ml.), and the whole solution was heated on a water bath for 8 hr. The reaction mixture was worked up as before. The ethereal solution left a residue on evaporation of the solvent which was found to be a mixture of more than two compounds on TLC. This was subjected to column chromatography on silica gel. Elution with benzene-petroleum ether (25:75) gave an oily product. Second elution with benzene-petroleum ether, (75:25) yielded a solid, 3,4-dihydro-5-oxo-5H-7,8-benzo-2,2-dimethylpyrano(3,2-c)benzopyran, crystallised from petroleum ether, m.p. 134-36°. Yield 0.3 g.

UV (methanol) : λ max (log e), 252 (2.98), 264 (3.90), 274 (3.98), 292 (4.02) and 314 (3.92).

Analysis : Found : C, 77.34 ; H, 5.70 %

$C_{18}H_{16}O_3$ requires : C, 77.14 ; H, 5.71 %.

5-Oxo-5H-7,8-benzo-2,2-dimethylpyrano(3,2-c)benzopyran (LVIII) :

DDQ (0.16 g.) was added to a solution of 3,4-dihydro-5-oxo-5H-7,8-benzo-2,2-dimethylpyrano(3,2-c)benzopyran (0.2 g.) in dry benzene and was refluxed for 48 hr. The solid separated was filtered when hot and the solid was washed with dry benzene. The filtrate was distilled to remove the solvent, and the residue was chromatographed on silica gel. The NMR spectrum of the product indicated it to be a mixture of 3,4-dihydro-5-oxo-5H-7,8-benzo-2,2-di-

-methylpyrano(3,2-c)benzopyran and 5-oxo-5H-7,8-benzo-2,2-dimethylpyrano(3,2-c)benzopyran (page 44), crystallised from petroleum ether. M.p. 159-61°. Yield 0.15 g.

UV (methanol) : λ max (log e), 233 (2.80), 282 (3.98), 294 (4.02), 358 (3.80) and 372 (3.82).

Analysis : Found : C, 77.39 ; H, 5.39 %

$C_{18}H_{14}O_3$ requires : C, 77.68 ; H, 5.07 %.

5-Oxo-5H-9,10-benzo-2,2-dimethylpyrano(3,2-c)benzopyran (LXI) : 3,4-Dihydro-5-oxo-5H-9,10-benzo-2,2-dimethylpyrano(3,2-c)benzopyran (LX) :

To a solution of 4-hydroxy-5,6-benzocoumarin (1.6 g.) in dry dioxan (20 ml.) was added gradually BF_3-etherate (0.6 ml.) at room temperature. To this was added a solution of 2-methyl-but-3-en-2-ol (0.6 g.) in dry dioxan (5 ml.) and the whole solution was heated on a water bath for 8 hr. The reaction was worked up as before and the residue obtained, on examination by TLC showed more than two compounds. It was, hence, subjected to column chromatography on silica gel. First fraction was eluted with petroleum ether-benzene (75:25) which gave an oily substance. The second fraction, on elution with benzene-petroleum ether (80:20) gave a solid, 3,4-dihydro-5-oxo-5H-9,10-benzo-2,2-dimethylpyrano(3,2-c)benzopyran, crystallised from petroleum ether, m.p. 133-34°. Yield 0.2 g.

UV (methanol) : λ max (log e), 242 (3.99), 268 (4.00) and 306 (3.82).

Analysis : Found : C, 77.14 ; H, 5.62 %

$C_{18}H_{16}O_3$ requires : C, 77.14 ; H, 5.71 %.

5-Oxo-5H-9,10-benzo-2,2-dimethylpyrano(3,2-c)benzopyran (LXI) :

To a solution of 3,4-dihydro-5-oxo-5H-9,10--benzo-2,2-dimethylpyrano(3,2-c)benzopyran (0.2 g.) in dry benzene, was added DDQ (0.15 g.) and was refluxed for 60 hr. The solid separated was filtered and the residue was washed with hot benzene. The filtrate was distilled to remove the solvent and the residue was chromatographed on silica gel. The product appeared to be a mixture of 3,4-dihydro-5-oxo-5H-9,10-benzo-2,2-dimethylpyrano(3,2-c)-benzopyran and 5-oxo-5H-9,10-benzo-2,2-dimethylpyrano-(3,2-c)benzopyran, crystallised from petroleum ether, m.p. 129°. Yield 0.1 g.

UV (methanol) : λ max (log e), 232 (3.80), 242 (3.90), 306 (4.02) and 340 (3.98).

Analysis : Found : C, 77.61 ; H, 5.47 %

$C_{18}H_{14}O_3$ requires : C, 77.68 ; H, 5.07 %.

3,4-Dihydro-5-oxo-5H-8-methoxy-2,2-dimethylpyrano(3,2-c)-benzopyran (LXIII) :

To a solution of 4-hydroxy-7-methoxycoumarin (1.2 g.) in dry dioxan (12 ml.) was added gradually BF_3-etherate (0.6 ml.) at room temperature. To this was added a solution of 2-methyl-but-3-en-2-ol (0.6 g.) in dioxan (5 ml.).

The whole solution was heated on water bath for 8 hr. The reaction was worked up as before and the residue obtained was subjected to column chromatography on silica gel and the column eluted successively with benzene-petroleum ether (25:75) and benzene-petroleum ether (70:30). The second fraction gave a solid, 3,4-dihydro-5-oxo-5H-8-methoxy-2,2-dimethylpyrano(3,2-c)benzopyran, crystallised from petroleum ether, m.p. 90-92°. Yield 0.2 g.

Analysis : Found : C, 69.13 ; H, 6.58 %

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

2,3-Dihydro-4-oxo-4H-2,2,3-trimethylfurano(3,2-c)benzopyran (LXVI) : 4-Prenyloxycoumarin (LXV) :

A solution of 4-hydroxycoumarin (1.58 g.), anhydrous potassium carbonate (3.0 g.), potassium iodide (1.0 g.) and 1-chloro-3-methyl-but-2-ene (1.0 g.) in acetone (100 ml.) was refluxed on a water for 10 hr. Acetone was distilled off and water was added to the residue to dissolve potassium carbonate and potassium iodide. The residue was extracted with ether and ethereal solution was evaporated. The residue was then chromatographed on alumina and eluted with benzene. The solid, 4-prenyloxycoumarin, crystallised from petroleum ether, m.p. 98°. Yield 0.2 g.

Analysis : Found : C, 73.26 ; H, 5.96 %

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

Claisen migration of 4-prenyloxycoumarin : 2,3-Dihydro-4--oxo-4H-2,2,3-trimethylfurano(3,2-c)benzopyran (LXVI) :

4-Prenyloxycoumarin (0.5 g.) was refluxed with dimethylaniline (3 ml.) for 6 hr. The solution was cooled and added to ice-cold hydrochloric acid solution. The solution was extracted with ether and the ethereal solution was evaporated to give a solid, after washing with sodium hydroxide solution (1 %). The solid was then crystallised from petroleum ether, m.p. 85-86°. Yield 0.3 g.

Analysis : Found : C, 73.02 ; H, 6.17 %

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

2,3-Dihydro-4-oxo-4H-2,2,3,8-tetramethylfurano(3,2-c)benzopyran (LXXII) : 6-Methyl-4-prenyloxycoumarin (LXXI) :

A solution of 6-methyl-4-hydroxycoumarin (1.7 g.), anhydrous potassium carbonate (3.0 g.), potassium iodide (1.0 g.) and 1-chloro-3-methyl-but-2-ene (1.0 g.) in acetone (100 ml.) was refluxed on a water bath for 8 hr. Acetone was distilled off and the residue was diluted with water and extracted with ether. The ethereal layer was evaporated and the residue was chromatographed on alumina. Elution with benzene gave a solid, 6-methyl-4-prenyloxycoumarin, crystallised from petroleum ether, m.p. 140°. Yield 0.3 g.

Analysis : Found : C, 74.04 ; H, 6.22 %

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

Claisen migration of 6-methyl-4-prenyloxycoumarin : 2,3-Dihydro-4-oxo-4H-2,2,3,8-tetramethylfurano(3,2-c)benzopyran (LXXII) :

6-Methyl-4-prenyloxycoumarin (0.5 g.) was refluxed in dimethylaniline (5 ml.) on a wire gauze for 6 hr. The solution was cooled and added to ice-cold dilute hydrochloric acid solution. The solution was extracted with ether and the ethereal solution on evaporation gave a solid, 2,3-dihydro-4-oxo-4H-2,2,3,8-tetramethylfurano(3,2-c)benzopyran, crystallised from petroleum ether, m.p. 115°. Yield 0.35 g.

Analysis : Found : C, 73.26 ; H, 6.56 %

$C_{15}H_{16}O_3$ requires : C, 73.75 ; H, 6.56 %.

2,3-Dihydro-4-oxo-4H-2,2,3,6-tetramethylfurano(3,2-c)benzopyran (LXXIV) : 8-Methyl-4-prenyloxycoumarin (LXXIII) :

A solution of 4-hydroxy-8-methylcoumarin (1.7 g.), anhydrous potassium carbonate (3.0 g.), potassium iodide (1.0 g.) and 1-chloro-3-methyl-but-2-ene (1.0 g.) in acetone (100 ml.) was refluxed on a water bath for 8 hr. Acetone was distilled off and the residue was diluted with water and extracted with ether. The ethereal layer was evaporated and the residue was chromatographed on alumina. Elution with benzene gave a solid, 8-methyl-4-prenyloxycoumarin, crystallised from petroleum ether, m.p. 92°. Yield 0.4 g.

Analysis : Found : C, 73.91 ; H, 6.80 %

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

Claisen migration of 8-methyl-4-prenyloxycoumarin : 2,3-Dihydro-4-oxo-4H-2,2,3,6-tetramethylfurano(3,2-c)-benzopyran (LXXIV) :

8-Methyl-4-prenyloxycoumarin (0.5 g.) was refluxed in dimethylaniline (5 ml.) on a wire gauze for 6 hr. The solution was cooled and added to ice-cold dilute hydrochloric acid solution. The solution was extracted with ether and the ethereal solution on evaporation gave a solid, 2,3-dihydro-4-oxo-4H-2,2,3,6-tetramethylfurano(3,2-c)benzopyran, crystallised from petroleum ether, m.p. 105-6°. Yield 0.25 g.

Analysis : Found : C, 73.69 ; H, 6.47 %

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

2,3-Dihydro-4-oxo-4H-7-methoxy-2,2,3-trimethylfurano(3,2-c)--benzopyran (LXXVI) : 7-Methoxy-4-prenyloxycoumarin (LXXV) :

A solution of 4-hydroxy-7-methoxycoumarin (1.75 g.), anhydrous potassium carbonate (3.5 g.), potassium iodide (1.0 g.) and 1-chloro-3-methyl-but-2-ene (1.0 g.) in acetone (100 ml.) was refluxed on a water bath for 8 hr. The solvent was removed by evaporation and the residue was diluted with water. The solution was then extracted with ether and the ethereal layer was evaporated. The residue was passed through alumina column and eluted with benzene. The solid, 7-methoxy-4-prenyloxycoumarin, obtained after evaporation of the solvent, crystallised from petroleum ether, m.p. 76-8°.

Yield 0.3 g.

Analysis : Found : C, 68.77 ; H, 5.94 %

$C_{15}H_{16}O_4$ requires : C, 69.24 ; H, 6.15 %.

Claisen migration of 7-methoxy-4-prenyloxycoumarin : 2,3-Dihydro-4-oxo-4H-7-methoxy-2,2,3-trimethylfurano--(3,2-c)benzopyran (LXXVI) :

7-Methoxy-4-prenyloxycoumarin (0.5 g.) was refluxed in dimethylaniline (5 ml.) for 6 hr. The reaction mixture was poured into ice-cold dilute hydrochloric acid solution and extracted with ether. The ethereal solution was evaporated and the solid, 2,3-dihydro-4-oxo-4H-7--methoxy-2,2,3,trimethylfurano(3,2-c)benzopyran, crystallised from petroleum ether, m.p. 96-7°. Yield 0.3 g.

Analysis : Found : C, 69.31 ; H, 6.05 %.

$C_{15}H_{16}O_4$ requires : C, 69.24 ; H, 6.15 %.

2,3-Dihydro-4-oxo-4H-6,7-benzo-2,2,3-trimethylfurano--(3,2-c)benzopyran (LXXVIII) : 4-Prenyloxy-7,8-benzocoumarin (LXXVII) :

A mixture of 4-hydroxy-7,8-benzocoumarin (1.8 g.), anhydrous potassium carbonate (3.0 g.), potassium iodide (1.0 g.), 1-chloro-3-methyl-but-2-ene (1.0 g.) and acetone (100 ml.) was refluxed on a water bath for 8 hr. The solvent was evaporated and the residue was diluted with water. It was then extracted with ether and the ethereal solution was evaporated. The residue obtained was passed over alumina. Elution with benzene gave a solid,

4-prenyloxy-7,8-benzocoumarin, crystallised from petroleum ether, m.p. 147°. Yield 0.5 g.

Analysis : Found : C, 77.20 ; H, 5.29 %

$C_{18}H_{16}O_3$ requires : C, 77.14 ; H, 5.71 %.

Claisen migration of 4-prenyloxy-7,8-benzocoumarin : 2,3-Dihydro-4-oxo-4H-6,7-benzo-2,2,3-trimethylfurano-(3,2-c)benzopyran (LXXVIII) :

4-Prenyloxy-7,8-benzocoumarin (0.5 g.) was refluxed in dimethylaniline (5 ml.) for 6 hr. The solution was poured into the ice-cold hydrochloric acid solution and was extracted with ether. The ethereal solution was evaporated and the solid, 2,3-dihydro-4-oxo-4H-6,7-benzo-2,2,3-trimethylfurano(3,2-c)benzopyran, crystallised from petroleum ether, m.p. 108°. Yield 0.4 g.

Analysis : Found : C, 77.49 ; H, 5.52 %

$C_{18}H_{16}O_3$ requires : C, 77.14 ; H, 5.71 %.

2,3-Dihydro-4-oxo-4H-2,2,3-trimethylfurano(3,2-c)benzo-pyran (LXXX) : 2,3-Dihydro-4-oxo-4H-2-methylene-3,3-dimethylfurano-(3,2-c)benzopyran (LXXIX) :

A mixture of 4-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.) was refluxed in acetone (50 ml.) on a water bath for 24 hr. 3-Chloro-3-methyl-but-1-yne (3 ml.) was added to the above mixture again and refluxed for 30 hr. Acetone, then was

distilled off and water was added to the residue and it was then extracted with ether. The ethereal solution was evaporated and the residue on examination by TLC (chloroform) showed a number of compounds. Hence, it was subjected to the column chromatography on silica gel and was eluted successively with (i) benzene-petroleum ether (25:75) and (ii) benzene-petroleum ether (40:60). Fraction (i) gave an oil which could not be identified. Fraction (ii) gave a solid, 2,3-dihydro-4-oxo-4H-2-methylene-3,3-dimethylfurano(3,2-c)benzopyran, crystallised from petroleum ether, m.p. 80-2°. Yield 0.1 g.

IR (nujol) : 1720 $cm.^{-1}$ (α-pyrone carbonyl stretching frequency), 1630 $cm.^{-1}$, 1600 $cm.^{-1}$ (aromatic -C=C- stretching frequency) and 915 $cm.^{-1}$ (exocyclic >C=C stretching frequency).

NMR (CCl_4) : δ 1.50, singlet, geminal dimethyl group at position-3; 4.45 and 4.85, two doublets, J=3Hz, two protons of methylene group at position-2 and 7.20-7.70, multiplet, four protons aromatic.

Analysis : Found : C, 73.38 ; H, 5.10 %

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

2,3-Dihydro-4-oxo-4H-2,3,3-trimethylfurano(3,2-c)benzopyran (LXXX) :

2,3-Dihydro-4-oxo-4H-2-methylene-3,3-dimethyl--furano(3,2-c)benzopyran (0.1 g.) was dissolved in ethyl acetate (10 ml.). This was added to prehydrogenated

palladised charcoal (10 % ; 0.05 g.) in ethyl acetate (20 ml.). The mixture was stirred for 3 hr. in an atmosphere of hydrogen for catalytic hydrogenation. The catalyst was filtered off and the solvent was removed by distillation. The solid, 2,3-dihydro-4-oxo-4H-2,3,3-trimethylfurano(3,2-c)-benzopyran, crystallised from petroleum ether, m.p. 62-3°. Yield 0.05 g.

NMR (CCl_4) : δ 1.22 and 1.42, two singlets, geminal dimethyl group at position-3; 1.46, doublet, J=7Hz, methyl group at position-2; 4.62, quartate, J=7Hz, one proton at position-2 and 7.20-7.50, multiplet, four protons aromatic.

Analysis : Found : C, 73.11 ; H, 5.96 %

$C_{14}H_{14}O_3$ requires : C, 73.04 ; H, 6.08 %.

2,3-Dihydro-2,4-dioxo-4H-3,3-dimethylfurano(3,2-c)benzo-pyran (LXXXI) :

Ozonolysis of 2,3-dihydro-4-oxo-4H-2-methylene--3,3-dimethylfurano(3,2-c)benzopyran (0.2 g.) in ethyl acetate (100 ml.) was carried out by passing ozone gas for 30 minutes. The reaction mixture was worked out by reducing it with hydrogen in the presence palladised charcoal (5 % ; 0.05 g.) for 2 hr. The catalyst was filtered off and the solid obtained after evaporating the solvent, 2,3-dihydro-2,4-dioxo-4H-3,3-dimethylfurano(3,2-c)benzopyran, crystallised from benzene-petroleum ether, m.p. 154-5°. Yield 0.15 g.

IR (nujol) : 1830 $cm.^{-1}$ (furanone), 1725 $cm.^{-1}$ (α-pyrone carbonyl stretching frequency), 1640 $cm.^{-1}$ (aromatic -C=C- stretching frequency) and 1370 $cm.^{-1}$ (geminal dimethyl group stretching frequency).

NMR ($CDCl_3$) : δ 1.65, singlet, geminal dimethyl group at position-3 and 7.30-7.80, multiplet, four protons aromatic.

Analysis : Found : C, 67.47 ; H, 3.87 %

$C_{13}H_{10}O_4$ requires : C, 67.82 ; H, 4.35 %.

2,3-Dihydro-4-oxo-4H-2,3,3,8-tetramethylfurano(3,2-c)benzopyran (LXXXVI) : 2,3-Dihydro-4-oxo-4H-2-methylene-3,3,8-trimethylfurano(3,2-c)benzopyran (LXXXV) :

A mixture of 4-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.) was refluxed in acetone on a water bath for 24 hr. 3-Chloro-3-methyl-but-1-yne (3 ml.) was added again and refluxed for 24 hr. The reaction was worked out as before. The product on examination by TLC (chloroform) showed a number of products. It was subjected to column chromatography on silica gel and the column was eluted successively with (i) benzene-petroleum ether (1:2) and (ii) benzene-petroleum ether (2:3). Fraction (i) gave an oil which could not be identified and fraction (ii) gave a solid, 2,3-dihydro-4-oxo-4H-2-methylene-3,3,8-trimethylfurano(3,2-c)benzopyran, crystallised from petroleum ether, m.p. 136-38°. Yield 0.2 g.

Analysis : Found : C, 74.66 ; H, 6.26 %

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

2,3-Dihydro-4-oxo-4H-2,3,3,8-tetramethylfurano(3,2-c)benzopyran (LXXXVI) :

2,3-Dihydro-4-oxo-4H-2-methylene-3,3,8-trimethylfurano(3,2-c)benzopyran (0.1 g.) was dissolved in ethyl acetate (10 ml.) and was added to prehydrogenated palladised charcoal (10 % ; 0.05 g.) in ethyl acetate (20 ml.) for catalytic hydrogenation. The mixture was stirred for 3 hr. in the atmosphere of hydrogen. The reaction was worked out as before and the solid, 2,3-dihydro-4-oxo-4H-2,3,3,8-tetramethylfurano(3,2-c)benzopyran, crystallised from petroleum ether, m.p. 120°. Yield 0.05 g.

Analysis : Found : C, 74.20 ; H, 6.30 %

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

2,3-Dihydro-2,4-dioxo-4H-3,3,8-trimethylfurano(3,2-c)-benzopyran (LXXXVII) :

Ozonolysis of 2,3-dihydro-4-oxo-4H-2-methylene--3,3,8-trimethylfurano(3,2-c)benzopyran (0.2 g.) in ethyl acetate (100 ml.) was carried out by passing ozone gas for 30 minutes and the reaction was worked as before. The solid, 2,3-dihydro-2,4-dioxo-4H-3,3,8-trimethylfurano(3,2-c)benzo--pyran, crystallised from benzene-petroleum ether, m.p. 146-47°. Yield 0.15 g.

IR (nujol) : 1835 $cm.^{-1}$ (furanone), 1740 $cm.^{-1}$ (α-pyrone carbonyl stretching frequency), 1650 $cm.^{-1}$ (aromatic -C=C- stretching frequency) and 1370 $cm.^{-1}$ (geminal dimethyl group stretching frequency).

NMR ($CDCl_3$) : δ 1.65, singlet, geminal dimethyl group at position-3; 2.48, singlet, methyl group at position-8; and 7.30-7.55, multiplet, three protons aromatic.

Analysis : Found : C, 68.35 ; H, 4.72 %

$C_{14}H_{12}O_4$ requires : C, 68.81 ; H, 4.91 %.

2,3-Dihydro-4-oxo-4H-2,3,3,6-tetramethylfurano(3,2-c)benzopyran (LXXXIX) : 2,3-Dihydro-4-oxo-4H-2-methylene-3,3,6-trimethylfurano(3,2-c)benzopyran (LXXXVIII) :

A mixture of 4-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.) in acetone was refluxed for 24 hr. The refluxion was further continued for 24 hr. after the addition of 3-chloro-3-methyl-but-1-yne (3 ml.). The reaction was worked out as before. The residue was subjected to column chromatography on silica gel. Elution with benzene-petroleum ether (1:1) gave a solid, 2,3-dihydro-4-oxo-4H-2-methylene-3,3,6-trimethylfurano(3,2-c)benzopyran, crystallised from petroleum ether, m.p. 152-54°. Yield 0.15 g.

NMR ($CDCl_3$) : δ 1.55, singlet, geminal dimethyl group at position-3; 2.45, singlet, methyl group at position-6; 4.5 and 4.95, two doublets, J=3Hz, two protons of methylene

group at position-2; 7.20-7.55, multiplet, three protons aromatic.

Analysis : Found : C, 74.82 ; H, 6.26 %

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

2,3-Dihydro-4-oxo-4H-2,3,3,6-tetramethylfurano(3,2-c)benzopyran (LXXXIX) :

2,3-Dihydro-4-oxo-4H-2-methylene-3,3,6-trimethylfurano(3,2-c)benzopyran (0.1 g.) was dissolved in ethyl acetate (10 ml.) and added to prehydrogenated palladised charcoal (10 % ; 0.05 g.) in ethyl acetate for catalytic hydrogenation. The mixture was stirred for 3 hr. in the hydrogen atmosphere. The reaction was worked out as before and the solid, 2,3-dihydro-4-oxo-4H-2,3,3,6-tetramethylfurano(3,2-c)benzopyran, crystallised from petroleum ether, m.p. 135°. Yield 0.05 g.

Analysis : Found : C, 74.27 ; H, 6.61 %

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

2,3-Dihydro-4-oxo-4H-6,7-benzo-2,3,3-trimethylfurano(3,2-c)--benzopyran (XCI) : 2,3-Dihydro-4-oxo-4H-6,7-benzo-2-methylene-3,3-dimethylfurano(3,2-c)benzopyran (XC) :

A mixture of 4-hydroxy-7,8-benzocoumarin (1.25 g.), anhydrous potassium carbonate (3.0 g.), potassium iodide (1.0 g.) and 3-chloro-3-methyl-but-1-yne (3 ml.) was refluxed in acetone for 24 hr. Excess of 3-chloro-3-methyl-but-1-yne (3 ml.) was added and continued the refluxion for further 24 hr. The reaction was worked out as before. The residue on

chromatography over silica gel and subsequent elution with benzene-petroleum ether (2:1) gave a solid, 2,3-dihydro--4-oxo-4H-6,7-benzo-2-methylene-3,3-dimethylfurano(3,2-c)-benzopyran, crystallised from petroleum ether, m.p. 191-93°. Yield 0.1 g.

Analysis : Found : C, 77.25 ; H, 4.87 %

$C_{18}H_{14}O_3$ requires : C, 77.68 ; H, 5.07 %.

2,3-Dihydro-4-oxo-4H-6,7-benzo-2,3,3-trimethylfurano(3,2-c)--benzopyran (XCI) :

2,3-Dihydro-4-oxo-4H-6,7-benzo-2-methylene-3,3-dimethylfurano(3,2-c)benzopyran (0.1 g.), was dissolved in ethyl acetate (10 ml.) and was added to prehydrogenated palladised charcoal (10 % ; 0.05 g.) in ethyl acetate for catalytic hydrogenation. The mixture was stirred for 3 hr. in the hydrogen atmosphere. The reaction was worked out as before. It gave an oil which could not be identified as 2,3-dihydro-4-oxo-4H-6,7-benzo-2,3,3-trimethylfurano(3,2-c)--benzopyran.

2,3-Dihydro-4-oxo-4H-8,9-benzo-2,3,3-trimethylfurano(3,2-c)--benzopyran (XCIII) : 2,3-Dihydro-4-oxo-4H-8,9-benzo--2-methylene-3,3-dimethylfurano(3,2-c)benzopyran (XCII) :

A mixture of 4-hydroxy-5,6-benzocoumarin (1.25 g.), anhydrous potassium carbonate (3.0 g.), potassium iodide (1.0 g.) and 3-chloro-3-methyl-but-1-yne (3 ml.) was refluxed in acetone for 24 hr. 3-Chloro-3-methyl-but-1-yne (3 ml.) was added again and the reaction was further continued for

24 hr. The reaction was worked out as before and the residue was subjected to column chromatography over silica gel. Elution with benzene gave a solid, 2,3-dihydro-4-oxo-4H--8,9-benzo-2-methylene-2,3-dimethylfurano(3,2-c)benzopyran, crystallised from petroleum ether, m.p. 95-7°. Yield 0.08 g.

Analysis : Found : C, 77.20 ; H, 5.52 %

$C_{18}H_{14}O_3$ requires : C, 77.68 ; H, 5.07 %.

2,3-Dihydro-4-oxo-4H-8,9-benzo-2,3,3-trimethylfurano(3,2-c)--benzopyran (XCIII) :

2,3-Dihydro-4-oxo-4H-8,9-benzo-2-methylene-3,3-dimethylfurano(3,2-c)benzopyran (0.1 g.) dissolved in ethyl acetate and added to prehydrogenated palladised charcoal (10 % ; 0.05 g.) in ethyl acetate for catalytic hydrogenation. The mixture was stirred for 3 hr.in the hydrogen atmosphere. The reaction was worked out as before and the oily product obtained could not be identified as 2,3-dihydro-4-oxo-4H-8,9-benzo-2,3,3-trimethylfurano(3,2-c)benzopyran.

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