CHAPTER II

SECTION I

SYNTHESIS OF PYRANOCCUMESTAN DERIVATIVES
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THEORETICAL

Coumestans are a class of naturally occurring compounds of heterocyclic four-ring system, also known as benzofuro-α-benzopyrone or coumarinobenzofuran. The simple coumestan or 6H-benzofuro(3,2-c)benzopyran-6-one is represented as (I).

\[
\text{I}
\]

Coumesterol (II) is the estrogenic constituent of Ladino clover. Wedelolactone (III), Erosnin (IV), Medicagol (V), Trifolilol (VI), Psoralidin (VII), Sativol (VIII) and Lucernol (IX) are the naturally occurring coumestan derivatives. This class is of particular interest because of the estrogenic properties and has relationship to pathogenic attack of plant."
Few naturally occurring substituted coumestans have been synthesised earlier. Emerson and Bickoff condensed 2,4-dimethoxyphenyl acetonitrile (X) with resorcinol and obtained α-(2,4-dimethoxyphenyl)-2,4-dihydroxyacetophenone (XI), which on treatment with methylchloroformate gave 3-(2,4-dimethoxyphenyl)-4,7-dihydroxycoumarin (XII). This was cyclised by heating with aniline hydrochloride to coumestrol (II) in overall yield of about 17%. Mentzer et al. synthesised coumestan or 6-oxo-6H-benzofuro(3,2-β)benzopyran (I) by thermal condensation of equimolar amounts of o-methoxyphenylmalonate with phenol giving 3-(2-methoxyphenyl)4-hydroxycoumarin (XIII) followed by the cyclisation with pyridine hydrochloride.

Coumestan (I) was also synthesised by Chatterjee and Roy by condensing o-methoxyphenyl acetonitrile (XIV) with ethyl-o-methoxybenzoate (XV) in the presence of sodium ethoxide and treating them intermediate ketonitrile (XVI) with hydrobromic acid.

Jurd synthesised coumestrol and related compounds by hydrogen peroxide oxidation of appropriately substituted 2′-hydroxy-3-methoxyflavylium salts. Yoshiyuki Kawase synthesised the same by different route.

Govindachari and co-workers isolated Wedelolactone (III) from the leaves of Wedelia calendulacea (compositae) and they synthesised substituted wedelolactone.
\[
\text{H}_2\text{O}_2 \text{ in methanol} \\
\text{Acidification}
\]
derivative. Chatterjea and Prasad\textsuperscript{32} reported the synthesis of tri-\text{-}O\text{-}methylwedelolactone (XVII). The ketonitrile (XVIII), obtained by condensation of 2,4,5-trimethoxybenzyl cyanide and ethyl-2,4,6-trimethoxybenzoate in the presence of sodium hydride, was treated with pyridine hydrochloride to yield (XIX), which was readily methylated to trimethoxy-wedelolactone (XVII).
Wanslick and co-workers\textsuperscript{33} prepared wedelolactone (III) by dehydrogenative coupling of catechol with 4,5-di-hydroxy-7-methoxycoumarin (XX) in the presence of potassium ferricyanide or potassium iodate.

\[
\begin{array}{c}
\text{HO} \quad \text{HO} \\
\text{H}_3\text{C} - \quad - \\
\text{O} \quad \text{O} \\
\text{X}
\end{array}
\quad +
\begin{array}{c}
\text{HO} \\
\text{HO}
\end{array}
\xrightarrow{\text{K}_3[\text{FeC(CN)}_6]} 
\begin{array}{c}
\text{HO} \quad \text{HO} \\
\text{H}_3\text{C} - \quad - \\
\text{O} \quad \text{O}
\end{array}
\]

Trifolilol (VI) was isolated from Ladino clover by Jurd and co-workers\textsuperscript{34} and confirmed the structure. They have synthesised it by peroxide oxidation of 5-benzoyloxy-7-hydroxy-3-methoxy-2',4'-dibenzoyloxyflavylium chloride (XXI), followed by methylation and debenzylolation to give 7-benzoyloxy-3-hydroxy-9-methoxycoumestan (XXII) and subsequent alkaline hydrolysis.
\[
\text{(i) } \text{H}_2\text{O}_2 \\
\text{(ii) } (\text{CH}_3)_2\text{SO}_4
\]
Medicagol (V) was isolated as a mixture with pistatin from alfalfa meal and its synthesis is reported by Jurd.

Psoralidine (VII) was first isolated from the pericarp of the seeds of *P. Corylifolia* by Chakravarti and co-workers. Later Sengupta and co-workers isolated the same from the alcoholic extract of the seed kernel of *Psoralea Corylifolia* Linn. and proved that it is the isopentenyl derivative of coumestrol.

As psoralidin is liable to acids, it has not been synthesised but dihydropsoralidine (XXV) is synthesised by different workers by different methods. Nasipuri and Pyne and Bickoff et al. have reported the synthesis of (XXV); 2,4-Dihydroxy-5-isopentenyl-2,4-dimethoxybenzylketone (XXIII), obtained by Hoesch reaction of 2,4-dimethoxybenzyl cyanide and 4-isopentenylresorcinol, was treated with ethyl chloroformate and then subjected with alkali and then with acid to give 4,7-dihydroxy-6-isopentenyl-3-(2',4'-dimethoxy-phenyl)coumarin (XXIV) which on further treatment with aniline hydrochloride gave dihydropsoralidin (XXV).

They have also reported the synthesis of isopsoralidin (XXVIII). Hoesch condensation of 2,4-dimethoxybenzyl cyanide with 7-hydroxy-2,2-dimethylchroman furnished 2,4-dimethoxybenzyl-7-hydroxy-2,2-dimethylchroman-6-yl-ketone (XXVI) which was converted into the 4-hydroxycoumarin derivative (XXVII) by sodium and ethyl carbonate. This, on treating with aniline hydrochloride gave isopsoralidin (XXVIII).
Similarly, they have condensed methyl-2,2-dimethyl-7-methoxycromanbenzoate with 2,4-dimethoxybenzyl cyanide in the presence of sodium hydride followed by the treatment with pyridine hydrochloride to yield isopsoralidin.

Chatterjea, Banerjee and Prasad have prepared dihydropsoralidin (XXV) and isopsoralidin (XXVIII) using the method of Yoshiyuki Kawase. The condensation of methyl-2,4-dimethoxy-5-isopentenylbenzoate and 2,4-dimethoxybenzyl cyanide in the presence of sodium hydride gave α-(2,4-dimethoxy-5-isopentenylbenzoyl)2,4-dimethoxybenzyl cyanide (XXIX) which when reacted with pyridine hydrochloride gave dihydropsoralidin (XXV).

They have also reported the synthesis of isopsoralidin (XXVIII) by condensing methyl-2,3-dimethyl-7-methoxycromanbenzoate (XXX) with 2,4-dimethoxybenzyl cyanide in the presence of sodium hydride to obtain ketonitrile (XXXI) and subsequent treatment with pyridine hydrochloride.

V.K. Karla and co-workers synthesised sativol (VIII) and lucernol (IX) and their methylether derivatives. Simonova and Shamshurin synthesised 7,11-dihydroxycoumestan by peroxide oxidation of 2′,4′,6′-trihydroxy-3-methoxyflavylium chloride.

Spencer, Knuckles and Bickoff synthesised 7-hydroxy-11,12-dimethoxycoumestan by hydrogen peroxide oxidation of 6,7,2′,4′-tetrahydroxylflavylium salt and selective methylation of 7,11,12-trihydroxycoumestan.
Recently Thomas Kappe and Schmidt reported a new method of synthesis of coumestan derivatives, starting with 4-hydroxy-3-phenylcoumarin derivatives. Cyclodehydrogenation of 4-hydroxy-3-phenylcoumarin derivative (XXXII) occurred when the reaction mixture was refluxed with diphenylether and palladised charcoal (10%) and air being bubbled through the reaction mixture giving corresponding coumestan derivative (XXXIII).

\[ \text{XXXII} \]

\[ \xrightarrow{\text{Pd/C, Ph}_2\text{O, Air}} \]

\[ \text{XXXIII} \]

(a) \( R_1=R_2=H \)  
(b) \( R_1=\text{CH}_3; R_2=H \)  
(c) \( R_1=R_2=\text{CH}_3 \)  
(d) \( R_1=\text{OCH}_3; R_2=H \)
Dholakia and Trivedi synthesised coumestan derivatives by oxidative condensation of catechol with different 4-hydroxycoumarins followed by methylation using the method Wanzlick. They have synthesised 2-methyl-8,9-dimethoxy-6H-benzofuro(3,2-c)benzopyran-6-one (XXXIa), 2,8,9-trimethoxy-6H-benzofuro(3,2-c)benzopyran-6-one (XXXIb), 4-methyl-3,8,9-trimethoxy-6H-benzofuro(3,2-c)benzopyran-6-one (XXXIc), 1,8,9-trimethoxy-6H-benzofuro(3,2-c)benzopyran-6-one (XXXId) and 3,4,8,9-tetramethoxy-6H-benzofuro-(3,2-c)benzopyran-6-one (XXXIe).

![Chemical Structure](attachment:image.png)

- (a) $R=R_2=R_3=H, R_1=CH_3$
- (b) $R=R_2=R_3=H, R_1=OCH_3$
- (c) $R=R_1=H, R_2=OCH_3, R_3=CH_3$
- (d) $R=OCH_3; R_1=R_2=R_3=H$
- (e) $R=R_1=H, R_2=R_3=OCH_3$
Shaikh and Trivedi synthesized 1,3,4,8,9-pentamethoxy-6H-benzofuro(3,2-c)benzopyran-6-one (XXXV) by oxidative coupling of 5,7,8-trimethoxy-4-hydroxycoumarin with catechol in the presence of potassium iodate and sodium acetate followed by methylation with dimethyl sulphate.
Subba Rao et al. have also reported similar type of coumestan derivatives, synthesised using the method of Wanzlick.

K. Fukui and N. Nakayama synthesised erosnin (XXXVI) by dehydrogenative coupling of 4-hydroxypsoralene and catachol in the presence of potassium ferricyanide according to the method of Wanzlick.

Shah and Trivedi have reported the synthesis of 5'-methyl-8,9-dimethoxyfuro(2,3-h)coumestan, 4,5'-dimethyl-8,9-dimethoxyfuro(3,2-g)coumestan and 5'-methyl-8,9-dimethoxyfuro(2,3-f)coumestan. They synthesised the furocoumestan derivatives by the following route.

7-Allyloxy-4-hydroxycoumarin (XXXVII) on dehydrogenative coupling with catachol, according to the method of Wanzlick, yielded a coumestan derivative. This on Claisen rearrangement followed by cyclisation and dehydrogenation with palladised charcoal (10 %) gave furocoumestan derivative (XXXVIII).
In continuation of the work on coumestan derivatives carried out in this laboratory by Dholakia, Shaikh, Shah and Trivedi, it was thought of interest to synthesise few more coumestan derivatives having pyran ring, to have psoralidin type coumestan derivatives. This type of coumestans are reported earlier.
Synthesis of 8,9-dimethoxy-2,2-dimethylpyrano-(2,3-h)coumestan

Seshadri et al. prenylated resacetophenone to get C-prenylated resacetophenone which were further cyclised to corresponding chromeno derivatives.

3,4-Dihydro-6-acetyl-5-hydroxy-2,2-dimethylchromene (XXXIX), prepared according to Seshadri et al., was treated with diethyl carbonate in the presence of pulversied sodium, according to the method of Boyd and Robertson, to give corresponding 2,2-dimethyl-3,4-dihydro-8-hydroxy-6-oxo-6H-pyrano(2,3-h)benzopyran (XL). This on dehydrogenative coupling with catechol in the presence of potassium iodate and sodium acetate gave 8,9-dihydroxy-2,2-dimethyl-3,4-dihydropyrano-(2,3-h)coumestan (XLI).

The above coumestan derivative was then methylated with dimethyl sulphate and anhydrous potassium carbonate in acetone to give 8,9-dimethoxy-2,2-dimethyl-3,4-dihydropyrano-(2,3-h)coumestan (XLII). This on dehydrogenation with DDQ in dry benzene or any other solvent like dioxan or chlorobenzene failed to give corresponding dehydrogenated pyranocoumestan derivative (XLIII).
As above compound could not be converted to the title compound by different methods of dehydrogenation, the synthesis of the title compound was finally achieved by the following route.

2,2-Dimethyl-8-hydroxy-6-oxo-6H-pyrano(2,3-h)-benzopyran (XLIV) was prepared from 2,2-dimethyl-6-acetyl-5-hydroxychromene (XLV) by treating it with sodium and diethyl carbonate. 2,2-Dimethyl-8-hydroxy-6-oxo-6H-pyrano-(2,3-h)benzopyran (XLIV) was oxidatively coupled with catechol in the presence of potassium iodate and sodium acetate to give 8,9-dihydroxy-2,2-dimethylpyrano(2,3-h)-coumestan (XLVI), which was methylated to 8,9-dimethoxy-2,2-dimethylpyrano(2,3-h)coumestan (XLIII).

IR (nujol) (XLIII): 1700 cm.¹ (α-pyrone carbonyl stretching frequency), 1365 cm.¹ (geminal dimethyl group stretching frequency) and 1280 cm.¹ (aromatic ether linkage). A band at 3400 cm.¹ is also observed for water.

The NMR spectrum of the compound (XLIII) in CDCl₃ is as under:

δ 1.50, singlet, geminal dimethyl group at position-2; 4.00 and 4.02, two singlets, two methoxy groups at positions-8 and -9; 5.80 and 6.85, two doublets, J=9Hz, two protons at positions-3 and -4 and 7.00-7.85, multiplet, four protons aromatic at positions-7, -10, -12 and -13. (Fig. 1)
8,9-Dimethoxy-2,2-dimethylpyranoc[2,3-h]coumaran
Synthesis of 8,9-dimethoxy-2,2-dimethylpyrano-(3,2-g)coumestan

3,4-Dihydro-6-acetyl-7-hydroxy-2,2-dimethylchromene (XLVII), prepared according to Seshadri et al. 47, was condensed with diethyl carbonate in the presence pulverised sodium to give 2,2-dimethyl-3,4-dihydro-6-hydroxy-8-oxo-8H-pyrano(3,2-g)-benzopyran (XLVIII). This was coupled oxidatively with catechol in the presence of potassium iodate and sodium acetate to give 8,9-dihydroxy-2,2-dimethyl-3,4-dihydropyrano(3,2-g)coumestan (XLIX). This was then directly methylated to 8,9-dimethoxy-2,2-dimethyl-3,4-dihydropyrano(3,2-g)coumestan (L). The IR spectrum showed a strong band at 1730 cm. for α-pyrone carbonyl group and a band at 1370 cm. for a geminal dimethyl group.

This failed to give its dehydrogenated derivative, 8,9-dimethoxy-2,2-dimethylpyrano(3,2-g)coumestan (LI), by different methods of dehydrogenation. To synthesise this, the following alternative route was adopted: -

2,2-Dimethyl-6-hydroxy-8-oxo-8H-pyrano(3,2-g)-benzopyran (LIII) was prepared from 2,2-dimethyl-6-acetyl-7-hydroxychromene (LII) by treating it with sodium and diethylcarbonate. (LIII) was coupled oxidatively with catechol in the presence of potassium iodate and sodium acetate to give 8,9-dihydroxy-2,2-dimethylpyrano(3,2-g)coumestan (LIV). This was then methylated with dimethyl sulphate to 8,9-dimethoxy-
\[ \text{XLVII} \quad \text{Na} \quad \text{EtOH carbonate} \quad \text{XLVIII} \]

\[ \text{XLIX} \]

\[ \text{L} \quad (\text{CH}_3)_2\text{SO}_4 \]

\[ \text{LI} \quad \text{DDE} \quad \text{Pd/C} \]
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-2,2-dimethylpyrano(3,2-g)coumestan. (LI). The IR spectrum showed bands at 3400 cm\(^{-1}\) for water, 1740 cm\(^{-1}\) for \(\alpha\)-pyrone carbonyl group and 1355 cm\(^{-1}\) for geminal dimethyl group.

\[\text{LII} \xrightarrow{\text{Na, EtOH, NaNAc}} \text{LIII}\]

\[\text{LIV} \xrightarrow{\text{KIO\textsubscript{3}, NaOAc}} \]

\[\text{LVI} \xrightarrow{\text{CCl\textsubscript{3}SO\textsubscript{3}H}} \]

Synthesis of 8,9-dimethoxy-2,2,13-trimethyl-
-pyrano(3,2-g)coumestan

2,4-Dihydroxy-3-methylacetophenone (LV) when
condensed with 2-methyl-but-3-en-2-ol in the presence of
BF₃-etherate gave 2,4-dihydroxy-3-methyl-5-prenylacetophenone
(LVI). The IR spectrum showed a broad band at 3280 cm⁻¹ for
hydroxyl groups, a band at 1630 cm⁻¹ for a carbonyl group and
a band at 1350 cm⁻¹ for a geminal dimethyl group. This, (LVI),
was converted to 3,4-dihydro-6-acetyl-7-hydroxy-2,2,8-tri-
methylchromene (LVII) by heating it with formic acid on a
steam bath. This was further reacted with diethylcarbonate
in the presence of pulverised sodium to give 3,4-dihydro-6-
hydroxy-8-oxo-8H-2,2,10-trimethylpyrano(3,2-g)benzopyran
(LVIII). This on oxidative coupling with catechol in the
presence of potassium iodate and sodium acetate gave 8,9-di-
hydroxy-3,4-dihydro-2,2,13-trimethylpyrano(3,2-g)coumestan
(LIX), which was methylated with dimethyl sulphate to 8,9-
dimethoxy-3,4-dihydro-2,2,13-trimethylpyrano(3,2-g)coumestan
(LX). The IR spectrum showed the following bands :-
1740 cm⁻¹ (a-pyrone carbonyl group), 1360 cm⁻¹ (geminal
dimethyl group) and 1280 cm⁻¹ (aromatic ether linkage).

The NMR spectrum of (LX) showed the following
signals :-
δ 1.35, singlet, geminal dimethyl group at position-2;
1.85, and 2.87, two triplets, J=7Hz, two methylene groups
at positions -3 and -4; 2.08, singlet, methyl group at position -13; 3.90 and 3.95, two singlets, two methoxy groups at positions -8 and -9; 7.04, singlet, one proton aromatic at position -5 and 7.30 and 7.41, two singlets, two protons aromatic, at positions -7 and -10 (Fig. 2).

![Chemical Structures]

Fig. 2
(Fig. 2) 8,9-Dimethoxy-3,4-dihydro-2,2,13-trimethylpyrano(3,2-g)coumaran
Dehydrogenation of (IX) failed to give 8,9-dimethoxy-2,2,13-trimethylpyran(3,2-g)coumestan (LXI). The following alternative route was then adopted to synthesise (LXI).

2,4-Dihydroxy-3-methyl-5-prenylacetophenone (LVI) on refluxing with DDQ in dry benzene yielded 6-acetyl-7-hydroxy-2,2,8-trimethylchromene (LXII). The structure was confirmed by its IR and NMR spectra:

IR (nujol): 3200 cm\(^{-1}\) (hydroxyl group), 1630 cm\(^{-1}\) (carbonyl group) and 1370 cm\(^{-1}\) (geminal dimethyl group). (Fig. 3)

NMR (CDCl\(_3\)): \(\delta\) 1.42, singlet, geminal dimethyl group at position-2; 2.02, singlet, methyl group of \(-COCH_3\) at position-6; 2.48, singlet, methyl group of at position-8; 5.50 and 6.24, two doublets, \(J=9\) Hz, two protons at positions -3 and -4 and 7.10, singlet, one proton aromatic. (Fig. 4)

(LXII) on treatment with diethyl carbonate in the presence of pulversied sodium gave 6-hydroxy-8-oxo-8H-2,2,10-trimethylpyran(3,2-g)benzopyran (LXIII). This on oxidative coupling with catechol in the presence of potassium iodate and sodium acetate gave 8,9-dihydroxy-2,2,13-trimethylpyran(3,2-g)coumestan (LXIV) which on methylation with dimethyl sulphate gave 8,9-dimethoxy-2,2,13-trimethylpyran(3,2-g)-coumestan (LXI). The structure of (LXI) was confirmed by its IR and NMR spectra.
LVI \rightarrow \text{DDQ} \rightarrow \text{LXII}

Na, Ethyl carbonate

LXII

\[ \text{LXIV} \]

\[ \text{LXI} \]
(Fig. 4) 6-Acetyl-7-hydroxy-2,2,8-trimethylchromene
IR (nujol) : 1735 cm\(^{-1}\) (a-pyrone carbonyl group stretching frequency), 1365 cm\(^{-1}\) (geminal dimethyl group stretching frequency) and 1278 cm\(^{-1}\) (aromatic ether linkage).

NMR (CDCl\(_3\)) : \(\delta 1.50\), singlet, geminal dimethyl group at position-2; 2.35, singlet, methyl group at position -13; 3.92 and 3.98, two singlets, two methoxy groups at positions-8 and -9; 5.70 and 6.40, two doublets, \(J=9\) Hz, two protons at positions-3 and -4 and 7.00-7.80, multiplet, three protons aromatic at positions-5, -7 and -10.
EXPERIMENTAL

8,9-Dimethoxy-2,2-dimethylpyrano(2,3-h)coumestan (XLIII) :
2,2-Dimethyl-3,4-dihydro-8-hydroxy-6-oxo-6H-pyrano(2,3-h)benzopyran (XL) :

3,4-Dihydro-6-acetyl-5-hydroxy-2,2-dimethylchromene was prepared according to Seshadri et al. 47

A mixture of 3,4-dihydro-6-acetyl-5-hydroxy-2,2-dimethylchromene (2.0 g.), diethyl carbonate (10 ml.) and pulverised sodium (2.0 g.) was heated on a water bath for 16 hr. After completion of the reaction, alcohol (10 ml.) was added to decompose the unreacted sodium and then the mixture was added to ice-cold water. The solution was then extracted with ether and the aqueous layer was acidified. The separated product was filtered and again treated with sodium bicarbonate solution. The sodium bicarbonate soluble fraction on acidification gave a solid, 2,2-dimethyl-3,4-dihydro-8-hydroxy-6-oxo-6H-pyrano(2,3-h)benzopyran, crystallised from dilute alcohol, m.p. 172°. Yield 0.8 g.

Analysis : Found : C, 64.21 ; H, 5.72 %
C₁₅H₁₄O₄.H₂O requires : C, 63.63 ; H, 6.06 %.

8,9-Dihydroxy-2,2-dimethyl-3,4-dihydropyrano(2,3-h)-coumestan (XLI) :

Catechol (0.11 g.) was added to a solution of 2,2-dimethyl-3,4-dihydro-8-hydroxy-6-oxo-6H-pyrano(2,3-h)-
-benzopyran (0.23 g.) and sodium acetate (0.25 g.) in aqueous acetone (1:1; 25 ml.). To this solution, aqueous solution of potassium iodate (0.65 g.) and sodium acetate (0.25 g.) was added dropwise with constant stirring. After 15 minutes the separated product was filtered, washed with water several times and dried. The product 8,9-dihydro-2,2-dimethyl-3,4-dihydropyrano(2,3-h)coumestan could not be crystallised, but it gave green colouration with alcoholic ferric chloride solution. M.p. above 300°. It was then directly methylated.

8,9-Dimethoxy-2,2-dimethyl-3,4-dihydropyrano(2,3-h)-
coumestan (XLII):

A mixture of 8,9-dihydroxy-2,2-dimethyl-3,4-dihydropyrano(2,3-h)coumestan (0.3 g.), dimethyl sulphate (0.25 g.), dry acetone (100 ml.) and anhydrous potassium carbonate (1.5 g.) was refluxed on a water bath for 6 hr. On evaporation of acetone the separated product was filtered, washed with dilute sodium hydroxide solution and crystallised from benzene-petroleum ether mixture, m.p. 207-8°. Yield 0.3 g.

C_{22}H_{26}O_6 requires: C, 69.47; H, 5.26.

2,2-Dimethyl-8-hydroxy-6-oxo-6H-pyrano(2,3-h)benzopyran (XLIV):

2,2-Dimethyl-6-acetyl-5-hydroxychromene (1.0 g.), was condensed with diethyl carbonate (6 ml.) and pulverised sodium (1.0 g.) on a water bath for 16 hr. at 60-70°. After completion of the reaction, the alcohol (10 ml.) was added
to decompose the unreacted sodium and then the mixture was added to ice-cold water. The solution was then extracted with ether and the aqueous layer on acidification gave a solid, which was further dissolved in sodium bicarbonate solution. The sodium bicarbonate soluble fraction on acidification gave a solid, 2,2-dimethyl-8-hydroxy-6-oxo-6H-pyrano-(2,3-h)benzopyran, crystallised from dilute alcohol. This was further methylated to its methylether by refluxing with dimethyl sulphate in the presence of anhydrous potassium carbonate in acetone. The solid, 2,2-dimethyl-8-methoxy-6-oxo-6H-pyrano(2,3-h)benzopyran, crystallised from benzene-petroleum ether mixture, m.p. 150°. Yield 0.5 g.

Analysis: Found: C, 69.85; H, 5.26 %

G\textsubscript{15H_{14}O_{4}} requires: C, 69.77; H, 5.42 %.

8,9-Dihydroxy-2,2-dimethylpyrano(2,3-h)coumestan (XLVI):

Catechol (0.11 g.) was added to a solution of 2,2-dimethyl-8-hydroxy-6-oxo-6H-pyrano(2,3-h)benzopyran (0.25 g.) and sodium acetate (0.25 g.) in aqueous acetone (1:1; 25 ml.). To this, a solution of potassium iodate (0.65 g.) and sodium acetate (0.25 g.) was added slowly with constant stirring. The product separated after 15 minutes was filtered, washed with water and dried. The product was directed methylated to its methylether. It gave green colouration with alcoholic ferric chloride solution. M.p. above 300°.
8,9-Dimethoxy-2,2-dimethylpyrano(2,3-h)coumestan (XLIII) :

A mixture of 8,9-dihydroxy-2,2-dimethylpyrano-(2,3-h)coumestan (0.3 g.), dimethyl sulphate (0.25 g.), dry acetone (100 ml.) and anhydrous potassium carbonate (1.5 g.) was refluxed on a water bath for 6 hr. The solid separated after evaporation of acetone was filtered, washed with dilute sodium hydroxide solution and crystallised from benzene-petroleum ether mixture, m.p. 214°. Yield 0.25 g.

Analysis : Found : C, 67.95; H, 4.79 %
C_{22}H_{18}O_{6.1/2}H_{2}O requires : C, 68.24; H, 4.94 %.

8,9-Dimethoxy-2,2-dimethylpyrano(3,2-g)coumestan (LI) :

2,2-Dimethyl-3,4-dihydro-6-hydroxy-8-oxo-8H-pyrano(3,2-g)-benzopyran (XLVIII) :

A mixture of 3,4-dihydro-6-acetyl-7-hydroxy-2,2-dimethylchromene (2.0 g.), diethyl carbonate (10 ml.) and pulverised sodium (2.0 g.) was heated on a water bath for 16 hr. After completion of the reaction it was worked out as before. The solid, 2,2-dimethyl-3,4-dihydro-6-hydroxy-8-oxo-8H-pyrano(3,2-g)benzopyran, obtained after acidification of sodium bicarbonate filtrate, was crystallised from aqueous alcohol, m.p. 138°. Yield 0.6 g.

Analysis : Found : C, 64.55; H, 5.79 %
C_{14}H_{14}O_{4}.H_{2}O requires : C, 63.63; H, 6.06 %.

The methoxy derivative of the above coumarin was prepared by refluxing it (0.2 g.) with dimethyl sulphate (0.2 ml.)
and anhydrous potassium carbonate (1.0 g.) in acetone for 3 hr. Water was added to the solution and the solid, 2,2-dimethyl-3,4-dihydro-6-methoxy-8-oxo-8H-pyrano(3,2-g)benzo-
pyran, separated was filtered and crystallised from benzene-
petroleum ether mixture, m.p. 218-220°. Yield 0.1 g.

Analysis: Found : C, 68.74 ; H, 5.93 %
C13H14O4 requires : C, 69.23 ; H, 6.15 %.

8,9-Dihydroxy-2,2-dimethyl-3,4-dihydropyrano(3,2-g)coumestan
(XLIX) :

Gallocatechol (0.11 g.) was added to a solution of 2,2-
dimethyl-3,4-dihydro-6-hydroxy-8-oxo-8H-pyrano(3,2-g)benzo-
pyran (0.3 g.) and sodium acetate (0.25 g.) in aqueous acetone
(1:1 ; 25 ml.). To this solution, aqueous solution of potassium
iodate (0.65 g.) and sodium acetate (0.25 g.) was added drop-
wise with constant stirring. The stirring was continued for
15 minutes and the product separated was filtered, washed
and dried. It gave green colouration with alcoholic ferric
chloride solution. M.p. above 300°. The product was directly
methylated to its methylether.

8,9-Dimethoxy-2,2-dimethyl-3,4-dihydropyrano(3,2-g)coumestan
(L) :

A mixture of 8,9-dihydroxy-2,2-dimethyl-3,4-di-
hydropyrano(3,2-g)coumestan (0.3 g.), dimethyl sulphate
(0.25 g.), dry acetone (100 ml.) and anhydrous potassium
carbonate (1.5 g.) was refluxed on a water bath for 6 hr.
Acetone was evaporated and the solid, 8,9-dimethoxy-2,2-di-
-methyl-3,4-dihydropyrano(3,2-g)coumestan, separated was filtered, washed with dilute sodium hydroxide solution and crystallised from benzene-petroleum ether mixture, m.p. 234-35°. Yield 0.3 g.

Analysis: Found: C, 69.71; H, 5.45%.
C22H20O6 requires: C, 69.47; H, 5.26%.

2,2'-Dimethyl-7-hydroxy-6-acetylchromene (2.0 g.) was heated with diethyl carbonate (10 ml.) in the presence of pulverised sodium (2.0 g.) on a water bath for 6 hr. Alcohol was added to the reaction mixture to destroy the unreacted sodium and diethyl carbonate was removed by ether. The alkaline solution was acidified and the solid obtained was crystallised from alcohol. The product, 2,2-dimethyl-6-hydroxy-8-oxo-8H-pyrano(3,2-g)benzopyran (LIII):

2,2-Dimethyl-6-hydroxy-8-oxo-8H-pyrano(3,2-g)benzopyran was soluble in sodium bicarbonate solution. As the analysis of this compound did not agree with the molecular formula, its methylether was prepared by methylating it (0.2 g.) with dimethyl sulphate (0.2 ml.) in the presence of anhydrous potassium carbonate (1.0 g.) in acetone (20 ml.) and the mixture was refluxed for 3 hr. The product 2,2-dimethyl-6-methoxy-8-oxo-8H-pyrano-(3,2-g)benzopyran, obtained was crystallised from benzene-petroleum ether mixture, m.p. 185°. Yield 0.15 g.

Analysis: Found: C, 69.49; H, 5.88%.
C15H14O4 requires: C, 69.77; H, 5.42%.
2,2-Dimethyl-6-methoxy-8-oxo-8H-pyrano(3,2-g)-benzopyran was also obtained by refluxing 2,2-dimethyl-3,4-dihydro-6-methoxy-8-oxo-8H-pyrano(3,2-g)benzopyran (0.5 g.) with DDQ (0.5 g.) in dry benzene (10 ml.) for 70 hr. on a water bath. The solid separated during the refluxion was filtered hot and the filtrate on concentration followed by column chromatography over silica gel gave 2,2-dimethyl-6-methoxy-8-oxo-8H-pyrano(3,2-g)benzopyran, m.p. 185-86°. Yield 0.3 g.

The mixed m.p. with the product obtained by the above method did not depress.

8,9-Dihydroxy-2,2-dimethylpyrano(3,2-g)coumestan (LIV):

Gallocatechol (0.11 g.) was added to a solution of 2,2-dimethyl-6-hydroxy-8-oxo-8H-pyrano(3,2-g)benzopyran (0.3 g.) and sodium acetate (0.25 g.) in aqueous acetone (1:1; 25 ml.). To this, solution of potassium iodate (0.65 g.) and sodium acetate (0.25 g.) was added slowly with constant stirring. The product separated was filtered, washed with water and dried. M.p. above 300°. It gave green colouration with alcoholic ferric chloride solution.

8,9-Dimethoxy-2,2-dimethylpyrano(3,2-g)coumestan (LI):

A mixture of 8,9-dihydroxy-2,2-dimethylpyrano-(3,2-g)coumestan (0.2 g.), dimethyl sulphate (0.25 ml.), dry acetone (100 ml.) and potassium carbonate (1.5 g.) was refluxed on a water bath for 6 hr. The product, after evaporation of acetone, was filtered, washed with dilute
sodium hydroxide solution and then crystallised from benzene-
petroleum ether mixture to give 8,9-dimethoxy-2,2-dimethyl-
pyrano(3,2-g)coumestan, m.p. 140-42°. Yield 0.2 g.
Analysis : Found : C, 68.64; H, 5.32 %
C_{22}H_{18}O_{6.1/2} H_{2}O requires : C, 68.24; H, 4.94 %

8,9-Dimethoxy-2,2,13-trimethylpyrano(3,2-g)coumestan (LXI) :
2,4-Dihydroxy-3-methyl-5-prenylacetophenone (LVI) :

To a stirred solution of 2,4-dihydroxy-3-methyl-
acetophenone (1.2 g.) in dry dioxan (10 ml.) was added a
solution of 2-methyl-but-3-en-2-ol (0.6 g.) in dioxan (5 ml.)
in the presence of BF_{3}-etherate (0.5 ml.) and the whole
solution was stirred for 1 hr. at room temperature. The
solution was then diluted with ether and the ether layer was
washed with water (3x100 ml.) to discharge the colour. The
solution was then washed with sodium carbonate solution (10 %;
3x100 ml.) which on acidification gave unreacted 2,4-dihydroxy-
3-methylacetophenone (0.5 g.). The ethereal layer on
examination by TLC (chloroform) showed the presence of two
compounds. This was then subjected to the column chromatography
over silica gel and the column successively eluted with (i)
benzene-petroleum ether (80:20) and (ii) benzene-ethyl acetate
(80:20). Fraction (i) gave a solid 2,4-dihydroxy-3-methyl-5-
prenylacetophenone, crystallised from benzene-petroleum ether
mixture, m.p. 117-18°. Yield 0.4 g. Fraction (ii) gave the
original ketone, m.p. 150-51°.
In (nujol) : 3280 cm.\(^{-1}\) (hydroxyl group), 1630 cm.\(^{-1}\) (carbonyl stretching frequency) and 1350 cm.\(^{-1}\) (geminal dimethyl group stretching frequency).

NMR (CCl\(_4\)) : $\delta$ 1.80 and 1.82, two singlets, geminal dimethyl group; 2.10, singlet, methyl group at position 1 of COCH\(_3\); 2.52, singlet, methyl group at position 3; 3.30, doublet, two protons of $-\text{CH}=\text{CH}$; 5.30, triplet, one proton of $-\text{CH}=\text{CH}$; 5.60, singlet, one proton of $-\text{OH}$ group and 7.25, singlet, one proton aromatic at position 6.

Analysis: Found : C, 70.89; H, 7.45%  
C\(_{14}H_{18}O_3\) requires : C, 70.59; H, 7.56%.

3,4-Dihydro-2,2,8-trimethyl-7-hydroxy-6-acetylchromene (LVII):

2,4-Dihydroxy-3-methyl-5-prenylacetophenone (1.0 g.) was heated on a steam bath with formic acid (10 ml.) for 1 1/2 hr. The solution was then poured into the water and the solid was filtered, washed with water and crystallised from petroleum ether to give 3,4-dihydro-2,2,8-trimethyl-7-hydroxy-6-acetylchromene in white plates, m.p. 112°. Yield 0.8 g.

In (nujol) : 3260 cm.\(^{-1}\) (hydroxyl group), 1730 cm.\(^{-1}\) (carbonyl stretching frequency) and 1370 cm.\(^{-1}\) (geminal dimethyl group stretching frequency).

NMR (CCl\(_4\)) : $\delta$ 1.35, singlet, geminal dimethyl group at position 2; 2.00, singlet, methyl group of COCH\(_3\) at position 6; 2.45, singlet, methyl group at position 8; 1.80 and 2.73, two triplets, J=8Hz, two methylene groups at
positions -3 and -4 and 7.20, singlet, one proton aromatic at position -5.

Analysis: Found: C, 70.80; H, 7.64 %

C_{14}H_{18}O_3 requires: C, 70.59; H, 7.56 %.

3,4-Dihydro-6-hydroxy-8-oxo-2,2,10-trimethylpyrano(3,2-g)-
-benzopyran (LVIII):

A mixture of 3,4-dihydro-7-hydroxy-2,2,8-trimethyl-
-6-acetylchromene (2.0 g.), diethyl carbonate (10 ml.) and
pulverised sodium (2.0 g.) was heated on a water bath for 16
hr. Alcohol was added to the reaction mixture to destroy the
the unreacted sodium and diethyl carbonate was removed by
ether. The alkaline solution on acidification, gave a solid,
3,4-dihydro-6-hydroxy-8-oxo-2,2,10-trimethylpyrano(3,2-g)-
benzopyran, crystallised from aqueous alcohol, m.p. 191-93°.
Yield 01.0 g.

This coumarin (0.2 g.) was refluxed with dimethyl
sulphate (0.2 g.) and anhydrous potassium carbonate (1.0 g.)
in dry acetone (10 ml.) for 3 hr. on a water bath. The
solvent was removed and water was added to the residue. The
solid separated was filtered, and crystallised from benzene-
petroleum ether mixture to give 3,4-dihydro-6-methoxy-8-oxo-
-8H-2,2,10-trimethylpyrano(3,2-g)benzopyran, m.p. 178-80°.
Analysis: Found: C, 70.45; H, 6.67 %

C_{16}H_{18}O_4 requires: C, 70.07; H, 6.56 %.
**8,9-Dihydroxy-2,2,13-trimethyl-3,4-dihydropyrano(3,2-g)-coumestan** (LIX):

Catechol (0.11 g.) was added to a solution of 3,4-dihydro-6-hydroxy-8-oxo-8H-2,2,10-trimethylpyrano(3,2-g)-benzopyran (0.3 g.) and sodium acetate (0.25 g.) in aqueous acetone (1:1; 25 ml.). To this, aqueous solution of potassium iodate (0.65 g.) and sodium acetate (0.25 g.) was added drop-wise with constant stirring. After 15 minutes the solid, 8,9-dihydroxy-2,2,13-trimethyl-3,4-dihydropyrano(3,2-g)-coumestan, separated was filtered, washed with water and dried. It gave green colouration with alcoholic ferric chloride solution and it could not be crystallised from any organic solvent, so was directly methylated to its methyl-ether.

**8,9-Dimethoxy-2,2,13-trimethyl-3,4-dihydropyrano(3,2-g)-coumestan** (LX):

A mixture of 8,9-dihydroxy-2,2,13-trimethyl-3,4-dihydropyrano(3,2-g)coumestan (0.2 g.), dimethyl sulphate (0.25 g.), dry acetone (100 ml.) and anhydrous potassium carbonate (1.5 g.) was refluxed on a water bath for 6 hr. After evaporation of the solvent, the solid separated was filtered, washed with dilute solution of sodium hydroxide and crystallised from benzene-petroleum ether mixture, to give 8,9-dimethoxy-2,2,13-trimethyl-3,4-dihydropyrano(3,2-g)-coumestan, m.p. 232-33°. Yield 0.15 g.
Analysis: Found: C, 69.72; H, 5.97 %
C_{23}H_{20}O requires: C, 70.07; H, 5.58 %.

2,2,8-Trimethyl-7-hydroxy-6-acetylchroomene (LXII):

To a solution of 2,4-dihydroxy-3-methyl-5-prenylacetophenone (0.2 g.) in dry benzene (10 ml.) was added DDQ (0.2 g.) and the solution heated on a boiling water bath for 15 minutes, when the solid hydroquinone derivative separated out, it was filtered hot, and the residue washed with benzene. The solvent was distilled off and the residue on chromatography on silica gel gave a solid, 2,2,8-trimethyl-7-hydroxy-6-acetylchromene, crystallised from petroleum ether, m.p. 81°. Yield 0.1 g.

Analysis: Found: C, 72.32; H, 6.68 %
C_{18}H_{16}O requires: C, 72.41; H, 6.89 %.

6-Hydroxy-8-oxo-8H-2,2,10-trimethylpyrano(3,2-g)benzopyran (LXIII):

2,2,8-Trimethyl-7-hydroxy-6-acetylchromene (2.0 g.) was condensed with diethyl carbonate (10 ml.) in the presence of pulverised sodium (2.0 g.) on heating in a water bath for 12 hr. Alcohol was added to the reaction mixture to destroy the unreacted sodium and diethyl carbonate was removed by ether. The alkaline solution, on acidification, gave 6-hydroxy-8-oxo-8H-2,2,10-trimethylpyrano(3,2-g)benzopyran, crystallised from aqueous alcohol, m.p. 210-12°. Yield 0.6 g.
This was directly refluxed with dimethyl sulphate (0.5 ml.) in the presence of anhydrous potassium carbonate (2.0 g.) in acetone (20 ml.). The solid obtained after working up the reaction, crystallised from benzene-petroleum ether mixture, to give 6-methoxy-8-oxo-8H-2,2,10-trimethylpyrano(3,2-g)benzopyran, m.p. 174-76°. Yield 0.5 g.

Analysis: Found: C, 71.04; H, 5.69 %
C_{16}H_{16}O_{4} requires: C, 70.58; H, 5.88 %.

6-Methoxy-8-oxo-8H-2,2,10-trimethylpyrano(3,2-g)benzopyran was also obtained by refluxing 3,4-dihydro-6-methoxy-8-oxo-8H-2,2,10-trimethylpyrano(3,2-g)benzopyran (0.5 g.) in dry benzene (20 ml.) with DDQ (0.5 g.) for 70 hr. and working up the reaction was carried out by filtering it hot and concentrating the filtrate. The solid obtained after chromatography over silica gel, crystallised from benzene-petroleum ether mixture, m.p. 175°. Yield 0.2 g.

The mixed m.p. of this compound did not depress with the compound prepared by the above method.

8,9-Dihydroxy-2,2,13-trimethylpyrano(3,2-g)coumestan (LXIV):

Catechol (0.11 g.) was added to a solution of 6-hydroxy-8-oxo-8H-2,2,10-trimethylpyrano(3,2-g)benzopyran (0.2 g.) and sodium acetate (0.25 g.) in aqueous acetone (1:1; 25 ml.). To this, a solution of potassium iodate (0.65 g.) and sodium acetate (0.25 g.) was added dropwise with constant stirring. The solid separated after 15 minutes, was filtered,
washed with water and dried. 8,9-Dihydroxy-2,2,13-trimethyl-
-pyrano(3,2-g)coumestan, gave green colouration with
alcoholic ferric chloride solution, m.p. above 300°. It was
directly methylated to its methylether.

8,9-Dimethoxy-2,2,13-trimethylpyrano(3,2-g)coumestan (LXI) :

A mixture of 8,9-dihydroxy-2,2,13-trimethylpyrano-
-(3,2-g)coumestan (0.2 g.), dimethyl sulphate (0.25 g.), dry
acetone (100 ml.) and anhydrous potassium carbonate (1.5 g.)
was refluxed on a water bath for 6 hr. The residue after
evaporation of solvent was diluted with water, filtered,
washed with dilute sodium hydroxide solution and crystallised
from benzene-petroleum ether mixture to give 8,9-dimethoxy-
-2,2,13-trimethylpyrano(3,2-g)coumestan, m.p. 220-222°.
Yield 0.2 g.)

Analysis : Found : C, 68.66 ; H, 5.07 %
C23H20O6,1/2 H2O requires : C, 68.82 ; H, 5.27 %.
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CHAPTER II

SECTION II

SYNTHESIS OF FURANOUCUMARINS
The review of the introductory furanocoumarins of other types, except types (F) and (G), being the matter of Chapter I is described therein. The methods for the synthesis of furanocoumarins of types (F) and (G) are as given below:

Psoralene or linear furanocoumarin of type (F), also known as ficusin, occurs in *Ficus Carica* Linn. and *Psoralea Corylifolia* Linn. has been synthesised by Spath from 6-hydroxybenzofuran (I) which was hydrogenated to

\[
\begin{align*}
\text{I} & \xrightarrow{\text{H}_2} \text{II} \\
\text{I} & \xrightarrow{\text{Malic acid, H}_2\text{SO}_4} \text{IV} \\
\text{IV} & \xleftarrow{\text{Pd/C, H}_2} \text{III}
\end{align*}
\]
coumaran (II) followed by condensation with malic acid in the presence of sulphuric acid according to the von Pechmann procedure, giving 4',5'-dihydrpsoralene (III), which on dehydrogenation gave psoralene (IV).

Later, Horning and Reisner prepared different 5-substituted psoralenes. Bergaptol (V) is of this type and was synthesised by Spath.

Xanthotoxin (VI) or 8-methoxypsoralene occurs in the seeds of Fagara xanthoxyloids Lam., which was synthesised by Spath and later by Rodighiero and Antonello by first preparing 7-hydroxy-8-methoxy-6-formylcoumarin (VII) and then treating it with ethylbromoacetate followed by hydrolysis, cyclisation and decarboxylation.
Ray, Silooja and Vaid\textsuperscript{11} synthesised 3-methylpsoralene from umbelliferon. Limaye and Gangal\textsuperscript{12} and Foster et al.\textsuperscript{13} also synthesised some psoralene derivatives.

Kaufmann\textsuperscript{14} prepared 4,5',8-trimethylpsoralene (Xa) and 5',8-dimethylpsoralene (Xb) by first carrying out Claisen migration of 7-allyloxy-4,8-dimethyl- (VIIIa) and 7-allyloxy-
-8-methylcoumarin (VIIIb) to 7-hydroxy-6-allyl-4,8-dimethyl-
(IXa) and 7-hydroxy-6-allyl-8-methylcoumarin (IXb),
respectively. These were then acetylated, brominated and
cyclised to obtain psoralene derivatives (Xa and Xb).

Using similar method Kaufmann synthesised 4',5'-di-
methylpsoralene. Kaufmann and coworkers synthesized
psoralene derivatives having different substituents in
8-position using 8-aminopsoralene as an intermediate product.

Seshadri and coworkers have obtained psoralene
by ozonolysis of 6-dimethylallyl-7-hydroxycoumarin, followed
by cyclisation of the aldehyde with o-phosphoric acid. Using
the same method they have also synthesised xanthotoxin (VI).

Goudou and Blanchecotte have condensed 6-hydroxy-
coumaran and phenyldiethylmalonic ester in diphenylether and
obtained 4',5'-dihydro-4-hydroxy-3-phenylfurano-2',3',6,7-
coumarin (XI) which was then dehydrogenated over palladised
charcoal to give 4-hydroxy-3-phenylpsoralene (XII).
Kaufmann and coworkers have developed a new synthetic route to synthesise psoralene. Bromination of ethyl(2-formyl-5-methoxyphenoxy)acetate gave the 4-bromo derivative (XIII) which was saponified and simultaneously cyclised and decarboxylated to 5-bromo-6-methoxybenzofuran (XIV). Lithium bromide interchange and then formylation and
demethylation gave 5-formyl-6-hydroxybenzofuran (XV) which was condensed with diethyl malonate to furnish psoralene (IV), after hydrolysis and decarboxylation of the Knoevenagel product.

Pardanani and Trivedi synthesized psoralene and alkyl psoralene. Pechmann condensation of 2-bromoresorcinol with malic acid gave 7-hydroxy-8-bromocoumarin (XVI), which was allylated to 7-allyloxy-8-bromocoumarin (XVII). This was
refluxed with dimethyl aniline in an atmosphere of nitrogen to give 6-allyl-7-hydroxycoumarin (XVIII). Ozonolysis of (XVIII) gave an acetaldehydo derivative which on cyclisation with o-phosphoric acid gave psoralene (XIXa). (XVIII) on cyclisation with conc. sulphuric acid gave dihydro derivative (XX) which was subsequently dehydrogenated by refluxing with diphenyl ether in the presence of palladised charcoal (10 %) to give 2-methyl-7-oxo-7H-furano(3,2-g)benzopyran (XIXb).

(a) R=®,=£2=H
(b) R=CH3; R1=H2=H
(c) R=H2=H; R1=CH3
(d) R=R1=CH3; R2=H
(e) R=H; R1=C6H5; R2=CH3.
Fechmann condensation of 2-bromoresorcinol with ethyl acetoacetate and ethyl benzoylacetate gave 7-hydroxy-8-bromo-4-methylcoumarin and 7-hydroxy-8-bromo-4-phenylcoumarin respectively. These were subjected to the above series of reactions to give (XIXc, XIXd and XIXe).

Pardanani and Trivedi have also carried out the Fechmann condensation of 2-methylresorcinol with ethyl benzoylacetate to give 7-hydroxy-8-methyl-4-phenylcoumarin (XXI). This on acylation and subsequent Fries migration gave 7-hydroxy-6-acyl-8-methyl-4-phenylcoumarin (XXII), which on condensation with ethyl bromoacetate followed by hydrolysis and cyclisation gave the corresponding psoralene derivative (XXIII).
Shah and Trivedi have recently synthesised 2-methyl-5-phenyl-7H-furan(3,2-g)benzopyran-7-one (XXIV), 9-methyl-5H-benzofuran(6,5-c)benzopyran-5-one (XXV), 9-methyl-1,2,3,4-tetrahydro-5H-benzofuran(6,5-c)benzopyran-5-one (XXVI)
and 8-methyl-1,2,3,4-tetrahydrocyclopenta(2,3)furano(2,3-g)-benzopyran-4-one (XXVII) by the same method as described above.

Dholakia and Trivedi synthesized 4-methoxy-5',8-dimethylpsoralene (XXVIII) and 1-hydroxy-5',8-dimethylpsoralene (XXIX). 2,4-Dihydroxy-3-methylacetophenone (XXX) was allylated with allyl bromide to 4-allyloxy-2-hydroxy-3-methylacetophenone (XXXI) which on condensation with diethyl carbonate in the presence of pulverised sodium yielded 4-hydroxy-7-allyloxy-8-methylcoumarin (XXXII). This was methylated to its methylether derivative (XXXIII) which was subjected to Claisen rearrangement by refluxing it with diethylaniline to give 4-methoxy-6-allyl-7-hydroxy-8-methylcoumarin (XXXIV). The cyclisation of (XXXIV) gave 4-methoxy-5',8-dimethyl-4',5'-dihydropсорalene (XXXV) by triturating it with conc. sulphuric acid which was further dehydrogenated to 4-methoxy-5',8-dimethylpsoralene (XXVIII) by refluxing it with diphenylether in the presence of palladised charcoal (10%).
It underwent demethylation when refluxed with conc. hydrochloric acid to give 4-hydroxy-5',8-dimethylpsoralene (XXIX).
Shaikh and Trivedi prepared 4-hydroxy-4',8-di-methylpsoralene \( (\text{XXXVII}) \) and 4-hydroxy-3,8,4'-trimethylpsoralene \( (\text{XXXVIII}) \). 4,8-Dimethyl-7-hydroxy-6-acylcoumarin \( (\text{XXXVI}) \) on

\[
\begin{align*}
\text{XXXI} & \quad \xrightarrow{\beta\text{H}_2} \quad \text{XXXII} \\
\text{XXXII} & \quad \xrightarrow{10^7^\circ, \text{Na}_2\text{CO}_3} \quad \text{XXXVII} + \text{XXXVIII}
\end{align*}
\]

\[
\begin{align*}
\text{XXXVIII} & \quad \xrightarrow{\text{Na}, \text{Diethyl carbonate}} \\
\text{XXXIX} & \quad \text{R=H} \\
& \quad \text{R=CH}_3
\end{align*}
\]
bromination followed by hydrolysis with sodium carbonate (10%) yielded 3,7-dimethyl-6-hydroxy-5-acylcoumarone (XXXVII) and 3,7-dimethyl-6-hydroxy-5-acylcoumaron-2-carboxylic acid (XXXVIII). (XXXVII), on condensation with diethyl carbonate in the presence of pulversied sodium gave (XXXIXa) and (XXXIXb).

**Esterification of (XXXVIII) with dimethyl sulphate** in the presence of sodium bicarbonate and acetone followed by the condensation with diethyl carbonate in the presence of pulverised sodium gave (XLa) and (Xlb).

Shaikh and Trivedi have also prepared 2,9-dimethyl-7-oxo-7H-furano(3,2-g)benzo(c)benzopyran (XLI), 9-methyl-5,6-cyclohexano-7-oxo-7H-furano(3,2-g)benzopyran (XLII), 2,9-dimethyl-5,6-cyclopentano-7-oxo-7H-furano(3,2-g)benzopyran (XLIII) and 9-methyl-5,6-cyclopentano-7-oxo-7H-furano(3,2-g)benzopyran (XLIV).
Angelicin (XLVII), a naturally occurring furano-coumarin - an angular one of type (G), was first synthesised by Spath and Pailer by condensing sodium salt of umbelliferon-8-aldehyde with iodoacetic ester under pressure and the product thus obtained was subjected to hydrolysis followed by cyclisation.

Naik and Thakore synthesised this using ethyl bromoacetate and acetone. Using the same method Shah and Shah prepared 3-methyl-5-oxo-5H-furano(2,3-h)benzopyran (furano-3'-methyl-4',5',8,7-coumarin) from 7-hydroxy-8-acetylcoumarin.
Limaye synthesized Angelicin by preparing 4-hydroxy-5-formylcoumarone from 4-hydroxycoumarone and subjecting it to Perkin reaction.

Aneja, Mukherjee and Seshadri synthesized angelicin by subjecting first 7-hydroxy-8-allylcoumarin (XLV) to ozonolysis and subsequent cyclisation of 7-hydroxycoumarin-8-acetaldehyde (XLVI) with polyphosphoric acid.

In continuation of the work on the synthesis of furanocoumarins carried out in our laboratory, the following furanocoumarins, both angular as well as linear, are synthesised to study their photodynamic activity.
(1) 7-Hydroxy-2-methyl-6-phenyl-5-oxo-5H-furano(2,3-h)benzopyran (LV).
(2) 7-Hydroxy-2-methyl-6-(p-methoxyphenyl)-5-oxo-5H-furano-(2,3-h)benzopyran (LXIV).
(3) 2,9-Dimethyl-5-hydroxy-6-phenyl-7-oxo-7H-furano(3,2-g)-benzopyran (LXX).

**Synthesis of 7-hydroxy-2-methyl-6-phenyl-5-oxo-5H-furano(2,3-h)benzopyran**

Using the procedure of Dholakia and Trivedi, synthesis of 7-hydroxy-2-methyl-6-phenyl-5-oxo-5H-furano-(2,3-h)benzopyran (LV) is achieved as under:

2,4-Dihydroxyphenylbenzyl ketone (XLVIII) was allylated with allyl bromide in the presence of anhydrous potassium carbonate in acetone. 4-Allyloxy-2-hydroxyphenylbenzyl ketone (XLIX) was then condensed with diethyl carbonate in the presence of pulverised sodium to give 7-allyloxy-3-phenyl-4-hydroxycoumarin (L). This was then methylated to 7-allyloxy-4-methoxy-3-phenylcoumarin (LI) which on Claisen rearrangement gave three products. The ethereal solution on washing with sodium bicarbonate solution yielded 8-allyl-4,7-dihydroxy-3-phenylcoumarin (LII) on acidification. The ethereal solution on washing with dilute sodium hydroxide solution gave 8-allyl-7-hydroxy-4-methoxy-3-phenylcoumarin (LIII) and the ethereal solution on evaporation gave an original allyloxy derivative (LI). The products (LII and LIII), on cyclisation with conc.
sulphuric acid gave the same product which was soluble in sodium bicarbonate solution, and it was assigned the structure 2,3-dihydro-7-hydroxy-2-methyl-6-phenyl-5-oxo-5H-furano(2,3-h)-benzopyran (LIV). This was refluxed with palladised charcoal (10%) in diphenylether to give 7-hydroxy-2-methyl-6-phenyl-5-oxo-5H-furano(2,3-h)benzopyran (LV). Attempt to carry out oxidative dehydrogenation with palladised charcoal and air of (LIV) to furanocoumestan derivative according to the procedure of Thomas Kappe et al. failed, only (LV) was obtained.
Synthesis of 7-hydroxy-2-methyl-6-(p-methoxyphenyl)-5-oxo-5H-furano(2,3-h)benzopyran

2,4-Dihydroxy(p-methoxyphenyl)benzyl ketone (LVII) was condensed with allyl bromide in the presence of potassium carbonate to give 4-allyloxy-2-hydroxy(p-methoxy-phenyl)benzyl ketone (LVIII) which was further reacted with ethyl carbonate in the presence of pulverised sodium to give 7-allyloxy-4-hydroxy-3-(p-methoxyphenyl)coumarin (LIX). This was then methylated to 7-allyloxy-4-methoxy-3-(p-methoxyphenyl)coumarin (LX) with dimethyl sulphate. (LX) was subjected to Claisen rearrangement by refluxing it with dimethylaniline. Three products were obtained by separating chemically. The ethereal solution was washed successively with sodium bicarbonate solution and dilute sodium hydroxide solution. Sodium bicarbonate solution on acidification gave 8-allyl-4,7-dihydroxy-3-(p-methoxyphenyl)coumarin (LXI) and sodium hydroxide solution on acidification gave 8-allyl-7-hydroxy-4-methoxy-3-(p-methoxyphenyl)coumarin (LXII). The ethereal solution on evaporation gave unchanged (LX). (LXI and LXII) were triturated with conc. sulphuric acid to give 2,3-dihydro-7-hydroxy-2-methyl-6-(p-methoxyphenyl)-5-oxo-5H-furano(2,3-h)benzopyran (LXIII). This did not undergo dehydrogenation with palladised charcoal (10 %) to give 7-hydroxy-2-methyl-6-(p-methoxyphenyl)-5-oxo-5H-furano(2,3-h)benzopyran (LXIV).
LVI

For CH₂ CH = CH₂
K₂ CO₃, Acetone

LVII

Na
Diethyl carbonate

LVIII

CH₃₂SO₄

LIX

LX
Synthesis of 2,9-dimethyl-5-hydroxy-6-phenyl-7-oxo-7H-
-furano(3,2-g)benzopyran

Condensation of 4-allyloxy-2-hydroxy-3-methyl-
phenylbenzyl ketone (LXV) with diethyl carbonate in the
presence of pulverised sodium gave 7-allyloxy-8-methyl-3-
-phenyl-4-hydroxycoumarin (LXVI). This was methylated to its
4-methoxy derivative (LXVII). The Claisen rearrangement of
7-allyloxy-4-methoxy-8-methyl-3-phenylcoumarin gave three
products. The separation was affected by treating the ethereal
solution of the mixture, first with sodium bicarbonate solution,
which on acidification yielded 6-allyl-1,7-dihydroxy-8-methyl-
-3-phenylcoumarin (LXVIII) and second with sodium hydroxide
solution on acidification gave 6-allyl-7-hydroxy-8-methyl-3-
phenyl-4-methoxycoumarin (LXIX). The ethereal solution on
evaporation gave an unconverted (LXVII). (LXVIII and LXIX)
were then cyclised with conc. sulphuric acid to give 2,9-di-
methyl-5-hydroxy-6-phenyl-2,3-dihydro-7-oxo-7H-furano(3,2-g)-
benzopyran (LXX). This was then dehydrogenated in the presence
of palladised charcoal (10 %) by refluxing it with diphenyl-
ether to give 2,9-dimethyl-5-hydroxy-6-phenyl-7-oxo-7H-furano-
-(3,2-g)benzopyran (LXXI).
\[
\begin{align*}
\text{LXVI} & \xrightarrow{\text{(CH\textsubscript{3})\textsubscript{2}SO\textsubscript{4}}} \\
\text{LXVII} & \xrightarrow{\text{DMA}} \\
\text{LXVIII} & \quad R = H \\
\text{LXIX} & \quad R = \text{CH}_3
\end{align*}
\]
EXPERIMENTAL

7-Hydroxy-2-methyl-6-phenyl-5-oxo-5H-furan(2,3-b)benzopyran (LV) : 7-Allyloxy-3-phenyl-4-hydroxycoumarin (L) :
4-Allyloxy-2-hydroxyphenylbenzyl ketone was prepared by the allylation of 2,4-dihydroxyphenylbenzyl ketone according to the method of Dholakia and Trivedi.

A solution of 4-allyloxy-2-hydroxyphenylbenzyl ketone (2.0 g.) in diethyl carbonate (15 ml.) was added slowly to the pulverised sodium (2.0 g.) and the mixture was heated on a water bath for 12 hr. Alcohol was added to the mixture to decompose the unreacted sodium and the solution was added to the crushed ice. The solution was filtered and the filtrate on acidification gave a solid, 7-allyloxy-3-phenyl-4-hydroxycoumarin, crystallised from chloroform, m.p. 195°. Yield 2.0 g.
Analysis : Found : C, 73.05 ; H, 4.93 %
C_{18}H_{14}O_{4} requires : C, 73.47 ; H, 4.78 %.

Methylation of 7-allyloxy-3-phenyl-4-hydroxycoumarin :
7-Allyloxy-4-methoxy-3-phenylcoumarin (LI) :

7-Allyloxy-3-phenyl-4-hydroxycoumarin (2.0 g.) was refluxed with dimethyl sulphate (2 ml.) and anhydrous potassium carbonate (6.0 g.) in dry acetone (50 ml.) on a water bath for 3 hr. Acetone was removed by distillation and the residue was diluted with water. The solid separated was filtered and crystallised from benzene-petroleum ether mixture,
m.p. 85-86°. Yield 2.0 g.
Analysis: Found: C, 73.52; H, 5.61%
C_{19}H_{16}O requires: C, 73.05; H, 5.19%

Claissen rearrangement of 7-allyloxy-4-methoxy-3-phenylcoumarin:
8-allyl-4,7-dihydroxy-3-phenylcoumarin (LII): 8-allyl-7-
hydroxy-4-methoxy-3-phenylcoumarin (LIII):

7-allyloxy-4-methoxy-3-phenylcoumarin (2.0 g.) was refluxed with dimethylaniline (15 ml.) for 6 hr. The reaction mixture was added to the ice-cold dilute hydrochloric acid solution. The whole solution was then extracted with ether. The ethereal layer was first extracted with sodium bicarbonate solution (3 x 100 ml.) which on acidification with hydrochloric acid gave a solid, 8-allyl-4,7-dihydroxy-3-phenylcoumarin, crystallised from methanol, m.p. 193°. Yield 0.06 g.
Analysis: Found: C, 73.69; H, 4.93%
C_{18}H_{14}O_{4} requires: C, 73.47; H, 4.78%

The ethereal solution was washed with sodium hydroxide solution which on acidification with hydrochloric acid gave 8-allyl-7-hydroxy-4-methoxy-3-phenylcoumarin, crystallised from alcohol, m.p. 191-2°. Yield 0.8 g.

IR (mujol): 3400 cm.{-1} (hydroxyl group), 1680 cm.{-1} (carbonyl stretching frequency), 1610 cm.{-1} (aromatic \text{-C=C- stretching frequency}) and 910 cm.{-1} (\text{>C=CH}_2\text{ stretching frequency}).
The ethereal solution on evaporation yielded unchanged 7-allyloxy-4-methoxy-3-phenylcoumarin. The compound was characterised by its mixed m.p. with the original compound.

Cyclisation of 8-allyl-4,7-dihydroxy-3-phenylcoumarin and 8-allyl-7-hydroxy-4-methoxy-3-phenylcoumarin:

8-allyl-7-hydroxy-4-methoxy-3-phenylcoumarin (0.5 g.) was triturated with sulphuric acid (80%; 5 ml.) on a water bath for 10 minutes and the solution was poured into the crushed ice. The solid separated was filtered and purified by dissolving in sodium bicarbonate solution. The filtrate on acidification gave a solid, 7-hydroxy-2-methyl-6-phenyl-2,3-dihydro-5-oxo-5H-furano(2,3-h)benzopyran (LIV).

8-allyl-4,7-dihydroxy-3-phenylcoumarin also gave the same product (LIV), on treating it with sulphuric acid (80%). The m.p. and mixed m.p. with the above compound remained the same, i.e. 225°.
7-Hydroxy-2-methyl-6-phenyl-5-oxo-5H-furano(2,3-h)benzopyran (IV) :

7-Hydroxy-2-methyl-6-phenyl-2,3-dihydro-5-oxo-5H-furano(2,3-h)benzopyran (0.5 g.) was refluxed with diphenylether (10 ml.) and palladised charcoal (10%; 0.3 g.) for 10 hr. on a wire gauze. The solution was cooled and petroleum ether was added after the removal of the catalyst. The solid separated, 7-hydroxy-2-methyl-6-phenyl-5-oxo-5H-furano(2,3-h)benzopyran, was crystallised from ethyl acetate-petroleum ether mixture, m.p. 208°. Yield 0.2 g.

Analysis: Found: C, 73.50; H, 4.62%
C₁₈H₁₂O₄ requires: C, 73.97; H, 4.19%

7-Hydroxy-2-methyl-6-(p-methoxyphenyl)-5-oxo-5H-furano(2,3-h)-benzopyran (LXIV) :

A solution of 4-allyloxy-2-hydroxy(p-methoxyphenyl)benzyl ketone (2.5 g.) in diethyl carbonate (15 ml.) was added to the pulverised sodium (2.5 g.) and the mixture was heated on a water bath for 12 hr. The mass was diluted with alcohol and the solution was poured into the ice-cold water. The solution was filtered and the filtrate on acidification with hydrochloric acid gave a solid, 7-allyloxy-3-(p-methoxyphenyl)-4-hydroxycoumarin, crystallised from alcohol, m.p. 166-68°. Yield 2.0 g.

Analysis: Found: C, 71.03; H, 4.89%
C₁₉H₁₆O₅ requires: C, 70.40; H, 4.92%
Methylation of 7-allyl-oxy-3-(p-methoxyphenyl)-4-hydroxy-coumarin: 7-Allyloxy-4-methoxy-3-(p-methoxyphenyl)-coumarin (LX):

7-Allyloxy-3-(p-methoxyphenyl)-4-hydroxy-coumarin (2.0 g.) was refluxed with dimethyl sulphate (3 ml.) and anhydrous potassium carbonate (6.0 g.) in dry acetone (50 ml.) for 3 hr. on a water bath. The solid obtained after evaporation of the solvent and subsequent dilution with water, was crystallised from benzene-petroleum ether mixture, m.p. 110°. Yield 2.0 g.

Analysis: Found: C, 71.46; H, 5.62 %
C_{20}H_{18}O_{5} requires: C, 71.00; H, 5.32 %.

Claisen rearrangement of 7-allyloxy-4-methoxy-3-(p-methoxy-phenyl)coumarin: 8-Allyl-4,7-dihydroxy-3-(p-methoxyphenyl)-coumarin (LXI) and 8-allyl-7-hydroxy-4-methoxy-3-(p-methoxy-phenyl)coumarin (LXII):

8-Allyl-7-dihydroxy-3-(p-methoxyphenyl)coumarin (2.0 g.) was refluxed with dimethylaniline (15 ml.) for 6 hr. The mixture was then added to the dilute hydrochloric acid solution and extracted with ether. The ethereal solution was then extracted with sodium bicarbonate solution which on acidification gave 8-allyl-4,7-dihydroxy-3-(p-methoxyphenyl)-coumarin, crystallised from aqueous alcohol, which decomposes at 184° and melts at 210°. Yield 0.4 g.

IR (nujol): 3400 cm\(^{-1}\) (hydroxyl group), 1655 cm\(^{-1}\) (carbonyl stretching frequency) and 940 cm\(^{-1}\) (>C=OH\(_2\) stretching frequency).
The ethereal solution on extraction with sodium hydroxide solution followed by its acidification gave 8-allyl-7-hydroxy-4-methoxy-3-(p-methoxyphenyl)coumarin, crystallised from alcohol, m.p. 207-8°. Yield 0.8 g.

\[ \text{IR (nujol)} : 3400 \text{ cm.}^{-1} \text{ (hydroxyl group)} \text{ and} 1665 \text{ cm.}^{-1} \text{ (carbonyl stretching frequency).} \]

Analysis: Found: C, 71.47; H, 5.34%

C_{20}H_{18}O_{5} requires: C, 71.00; H, 5.32%

The ethereal solution on evaporation gave unchanged 7-allyloxy-4-methoxy-3-(p-methoxyphenyl)coumarin. The compound was characterised by its mixed m.p. with the original compound.

Cyclisation of 8-allyl-4,7-dihydroxy-3-(p-methoxyphenyl)coumarin and 8-allyl-7-hydroxy-4-methoxy-3-(p-methoxy-phenyl)coumarin: 7-Hydroxy-2-methyl-6-(p-methoxyphenyl)-2,3-dihydro-5-oxo-5H-furano(2,3-h)benzopyran (LXIII):

8-ALLYL-4,7-DIHYDROXY-3-(P-METHOXYPHENYL)COUMARIN (0.5 g.) was triturated with sulphuric acid (5 ml.; 80 %) on a water bath for 10 minutes. The solution was then added to the crushed ice and the solid separated was filtered, crystallised from ethyl acetate-petroleum ether mixture, m.p. 212°. Yield 0.2 g.

Similarly, 8-ALLYL-7-HYDROXY-4-METHOXY-3-(P-METHOXY-PHENYL)COUMARIN (0.5 g.) was cyclised by triturating with sulphuric acid (5 ml.; 80 %) and worked out as above. It gave
7-hydroxy-2-methyl-6-(p-methoxyphenyl)-2,3-dihydro-5-oxo-5H-furano(2,3-h)benzopyran, m.p. 210-11°. The mixed m.p. did not depress with the product obtained as above.

Analysis: Found: C, 68.77; H, 5.02 %

C₁₇H₁₆O₅.1/2 H₂O requires: C, 68.46; H, 5.10 %.

Attempted dehydrogenation of 7-hydroxy-2-methyl-6-(p-methoxyphenyl)-5-oxo-5H-2,3-dihydrofuran(2,3-h)benzopyran:

7-Hydroxy-2-methyl-6-(p-methoxyphenyl)5-oxo-5H-furano(2,3-h)-benzopyran (LXIV):

A mixture of 7-hydroxy-2-methyl-6-(p-methoxyphenyl)-2,3-dihydro-5-oxo-5H-furano(2,3-h)benzopyran (0.5 g.) and palladised charcoal (10 %; 0.3 g.) in diphenylether (15 ml.) was refluxed on a wire gauze for longer period. The reaction mixture was filtered hot to remove the catalyst. The mother liquor on dilution with petroleum ether gave the original dihydro derivative which was characterised by its mixed m.p. and TLC.

2,9-Dimethyl-5-hydroxy-6-phenyl-7-oxo-7H-furano(3,2-g)benzopyran (LXXI): 7-Allyloxy-8-methyl-3-phenyl-4-hydroxy-coumarin (LXVI):

A solution of 4-allyloxy-3-methyl-3-hydroxyphenyl-benzyl ketone (2.0 g.) in diethyl carbonate (15 ml.) was carefully added to the pulverised sodium (2.5 g.) and the whole mixture was heated on the water bath for 12 hr. Alcohol was added to the reaction mixture to decompose the unreacted
sodium and the solution was added to the ice-cold water. The solution was filtered and the filtrate on acidification gave a solid, 7-allyloxy-8-methyl-3-phenyl-4-hydroxycoumarin, crystallised from benzene-petroleum ether mixture, m.p. 212-14°. Yield 2.0 g.

Analysis: Found: C, 74.49; H, 5.66 %
C_{19}H_{16}O_{4} requires: C, 74.02; H, 5.19 %.

Methylation of 7-allyloxy-8-methyl-3-phenyl-4-hydroxycoumarin:

7-Alllyloxy-4-methoxy-8-methyl-3-phenylcoumarin (LXVII):

7-Alllyloxy-8-methyl-3-phenyl-4-hydroxycoumarin (2.0 g.) was refluxed with dimethyl sulphate (2 ml.) and anhydrous potassium carbonate (6.0 g.) in dry acetone (80 ml.) on a water bath for 40 hr. The acetone was distilled off and the residue was treated with water. The solid separated was filtered and washed with water. The solid, 7-allyloxy-4-methoxy-8-methyl-3-phenylcoumarin, crystallised benzene-petroleum ether mixture, m.p. 130-31°. Yield 1.8 g.

Analysis: Found: C, 74.92; H, 6.02 %
C_{20}H_{18}O_{4} requires: C, 74.53; H, 5.59 %.

Claisen rearrangement of 7-allyloxy-4-methoxy-8-methyl-3-phenylcoumarin:

6-Alllyl-4,7-dihydroxy-8-methyl-3-phenylcoumarin (LXVIII) and 6-allyl-7-hydroxy-4-methoxy-8-methyl-3-phenylcoumarin (LXIX):

7-Alllyloxy-4-methoxy-8-methyl-3-phenylcoumarin (2.5 g.) was refluxed with dimethylaniline (15 ml.) for 6 hr.
The reaction mixture was poured into the ice-cold hydrochloric acid solution. The compound was extracted with ether and the ethereal solution was first washed with sodium bicarbonate solution which on acidification with hydrochloric acid gave 6-allyl-4,7-dihydroxy-8-methyl-3-phenylcoumarin, crystallised from benzene-petroleum ether mixture, m.p. 174-76°. Yield 0.4 g.

Analysis: Found: C, 74.22; H, 5.64%
C₁₉H₁₆O₄ requires: C, 74.02; H, 5.19%.

The ethereal solution was then washed with sodium hydroxide solution which on acidification gave 6-allyl-7-hydroxy-4-methoxy-8-methyl-3-phenylcoumarin, crystallised from benzene-petroleum ether mixture, m.p. 215-16°. Yield 0.6 g.

Analysis: Found: C, 74.42; H, 5.80%
C₂₀H₁₈O₄ requires: C, 74.53; H, 5.59%.

The ether layer on evaporation gave unchanged compound characterised by its mixed m.p. with the original compound.

Cyclisation of 6-allyl-4,7-dihydroxy-8-methyl-3-phenylcoumarin and 6-allyl-7-hydroxy-4-methoxy-8-methyl-3-phenylcoumarin:

2,9-Dimethyl-5-hydroxy-6-phenyl-2,3-dihydro-7-oxo-7H-furano-(3,2-g)benzopyran (LXX):

6-Allyl-4,7-dihydroxy-8-methyl-3-phenylcoumarin (0.5 g.) on triturating with sulphuric acid (10 ml.; 84%)
on a water bath for 10 minutes gave 2,9-dimethyl-5-hydroxy-6-phenyl-2,3-dihydro-7-oxo-7H-furano(3,2-g)benzopyran, crystallised from benzene, m.p. 214-15°. Yield 0.3 g.

Similarly, 6-allyl-7-hydroxy-4-methoxy-8-methyl-3-phenylcoumarin (0.5 g.) was triturated with sulphuric acid (10 ml.; 84%) on a water bath for 10 minutes. The mixture was then poured into the crushed ice and the product separated was crystallised from benzene, m.p. 213-14°. Yield 0.25 g.

Analysis: Found: C, 73.52; H, 5.67%
C₁₅H₁₆O₄ requires: C, 73.02; H, 5.29%

2,9-Dimethyl-5-hydroxy-6-phenyl-7-oxo-7H-furano(3,2-g)-benzopyran (LXXI):

2,9-Dimethyl-5-hydroxy-6-phenyl-2,3-dihydro-7-oxo-7H-furano(3,2-g)benzopyran (0.5 g.) was refluxed with diphenylether (10 ml.) and palladised charcoal (10 %; 0.3 g.) for 10 hr. on a wire gauze. The catalyst was removed by filtration and the filtrate on dilution with petroleum ether gave a solid, 2,9-dimethyl-5-hydroxy-6-phenyl-7-oxo-7H-furano(3,2-g)benzopyran, crystallised from alcohol, m.p. 258°. Yield 0.2 g.

Analysis: Found: C, 74.70; H, 4.66%
C₁₅H₁₄O₄ requires: C, 74.50; H, 4.57%
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CHAPTER II

SECTION III

SYNTHESIS OF PYRANOFLUAROCUMARINS

AND DIFURANOCUMARIN
CHAPTER II

SECTION III

SYNTHESIS OF PYRANO-FURANOCOUMARINS
AND DIFURANO-COUMARIN

THEORETICAL

Furanocoumarins are of interest due to their valuable therapeutic properties and applicability in drugs. Furanocoumarins having furan ring fused with coumarin ring is reviewed in Chapter I, a part of it in Section II of the Chapter II and Chapter III.

Seshadri et al. have synthesised few difuranocoumarin derivatives. They have studied the Claisen migration of 5,7-dihydroxy-4-phenylcoumarin and obtained bis-2'-methyl-dihydrodifurano [4',5': 5,6 and 4',5': 7,8]-4-phenylcoumarin, the structure of which is represented as follows:

![Chemical structure of difuranocoumarin](image-url)
Sanghvi and Trivedi have also synthesised few difuranocoumarin derivatives. 4-Hydroxy-7-allyloxycoumarin (I) on allylation with allyl bromide gave 4,7-diallyloxy-coumarin (II). This was subjected to Claisen rearrangement by refluxing it with dimethylaniline to give (III) which on cyclisation with conc. sulphuric acid followed by dehydrogenation with palladised charcoal (10%) in diphenyl-ether afforded 2,7-dimethyl-4-oxo-1H-difurano(3',2'-c; 2',3'-h)-benzopyran (IV).

\[
\begin{align*}
&\text{I} \\
&\text{II} \\
&\text{III} \\
&\text{IV}
\end{align*}
\]
Similarly, they have synthesised 2,6,8-trimethyl-4-oxo-4H-difurano(3,2-c; 3',2'-g)benzopyran (V) and 2,9-dimethyl-4-oxo-4H-difurano(3,2-c; 3',2'-f)benzopyran (VI).

In the present work the synthesis of few pyranofuranocoumarins and a difuranocoumarin is reported. The following pyranofuranocoumarins and difuranocoumarin derivatives are synthesised:

(1) 2,8,8-Trimethyl-4-oxo-4H-furano(3,2-c)pyrano(2',3'-h)-benzopyran,
(2) 2,8,8-Trimethyl-4-oxo-4H-furano(3,2-c)pyrano(3',2'-g)-benzopyran,
(3) 2,6,8,8,-Tetramethyl-4-oxo-4H-furano(3,2-c)pyrano-(3',2'-g)benzopyran and
(4) 2,3-Dihydro-4-oxo-4H-2,2,3,6,8-pentamethylidifurano-(3,2-c ; 3',2'-g)benzopyran.

Synthesis of 2,8,8-trimethyl-4-oxo-4H-furano(3,2-g)-pyrano(2',3'-h)benzopyran

3,4-Dihydro-2,2-dimethyl-8-hydroxy-6-oxo-6H-pyrano(2,3-h)benzopyran (VII) (prepared as described in Section I) was allylated with allyl bromide in the presence of anhydrous potassium carbonate and acetone to give 8-allyloxy-3,4-dihydro-2,2-dimethyl-6-oxo-6H-pyrano(2,3-h)-benzopyran (VIII). This on Claisen rearrangement by refluxing it with dimethylaniline yielded 2,3,6,7-tetrahydro-2,8,8-trimethyl-4-oxo-4H-furano(3,2-c)pyrano(2',3'-h)benzopyran (IX). This could not be dehydrogenated either with DDQ or palladised charcoal (10%) to 2,8,8-trimethyl-4-oxo-4H-furano(3,2-c)pyrano(2',3'-h)benzopyran (X).

To prepare (X), 2,2-dimethyl-8-hydroxy-6-oxo-6H-pyrano(2',3'-h)benzopyran was allylated with allyl bromide to 8-allyloxy-2,2-dimethyl-6-oxo-6H-pyrano(2',3'-h)benzopyran (XII). This on Claisen migration by refluxing it with dimethylaniline gave 2,3-dihydro-2,8,8-trimethyl-4-oxo-4H-furano(3,2-c)pyrano(2',3'-h)benzopyran (XIII) which could
not be further dehydrogenated to (X). With DDQ or Pd/C.
2-Hydroxy-4-prenyloxyacetophenone (XIV) was condensed with diethyl carbonate in the presence of pulverised sodium to give 4-hydroxy-7-prenyloxycoumarin (XV). This was allylated with allyl bromide to 4-allyloxy-7-prenyloxycoumarin (XVI) which on Claisen rearrangement by refluxing with dimethylaniline gave 2,3-dihydro-2-methyl-7-prenyloxy-1H-furano(3,2-e)benzopyran (XVII). The structure of (XVII) was confirmed by its NMR spectrum in CDCl₃ which showed the signals at δ 1.78, doublet, J=7Hz, methyl group at position-2; 2.00, singlet, geminal dimethyl groups; 3.25, multiplet, methylene group at position-3 of furan ring; 4.80, doublet, J=8Hz, two protons of CH₂=CH group; 5.40, multiplet, one proton at position-2; 5.65, multiplet, one proton of CH₂=CH group and 7.00, 7.70, multiplet, three protons aromatic. This (XVII) on further migration with dimethylaniline gave 2,3,6,7-tetrahydro-2,8,8-trimethyl-1H-furano(3,2-c)pyrano(2',3'-h)benzopyran (IX). This could not be dehydrogenated to (X).
(Fig. 1) : 2,3-Dihydro-2-methyl-7-prenyloxy-4-oxo-4H-furan(3,2-c)benzopyran
Synthesis of 2,8,8-trimethyl-4-oxo-4\(H\)-furano(3,2-\(g\))-pyrano(3',2'-\(g\))benzopyran

3,4-Dihydro-2,2-dimethyl-6-hydroxy-8-oxo-8\(H\)-pyrano(3,2-\(g\))benzopyran (XVIII) was allylated with allyl bromide in the presence of anhydrous potassium carbonate in acetone to give 3,4-dihydro-2,2-dimethyl-6-allyloxy-8-oxo-8\(H\)-pyrano(3,2-\(g\))benzopyran (XIX). This on Claisen rearrangement in dimethylaniline gave 2,3,9,10-tetrahydro-2,8,8-trimethyl-4-oxo-4\(H\)-furan(3,2-\(c\))pyrano(3',2'-\(g\))-benzopyran (XX). This could not give the dehydrogenated product (XXI). The NMR spectrum of (XX) in CDCl\(_3\) showed the following signals:

- \(\delta 1.50\), singlet, geminal dimethyl group at position-8;
- 1.68, doublet, \(J=7Hz\), methyl group at position-2;
- 1.98 and 2.98, two triplets, two methylene groups at position-9 and -10;
- 3.35, doublet, methylene group at position-3;
- 5.35, multiplet, one proton at position-2, and 6.85 and 7.40, two singlets, two protons aromatic at positions-6 and -11. (\(\delta \text{ ppm}\))
To synthesise the dehydrogenated product (XXI), 2,2-dimethyl-6-hydroxy-8-oxo-8H-pyrano(3,2-g)benzopyran (XXII) was first allylated with allyl bromide which gave an oily product (XXIII) which on Claisen migration gave an unidentifiable oily product.
(Fig. 2): 2,3,9,10-Tetrahydro-2,8,8-trimethyl-4-oxo-4H-furano(3,2-c)-pyrano(3',2'-g)-benzopyran.
Synthesis of 2,6,8,8-tetramethyl-4-oxo-4H-furanopyrano(3,2-g)benzopyran

3,4-Dihydro-2,2,10-trimethyl-6-hydroxy-8-oxo-8H-furanopyrano(3,2-g)benzopyran (XXIV) (prepared according to the method described in Section I) was condensed with allyl bromide in the presence of anhydrous potassium carbonate in acetone to give 3,4-dihydro-2,2,10-trimethyl-6-allyloxy-8-oxo-8H-furanopyrano(3,2-g)benzopyran (XXV). This on Claisen rearrangement in dimethylaniline gave 2,3,9,10-tetrahydro-2,6,8,8-tetramethyl-4-oxo-4H-furanopyrano(3,2-g)benzopyran (XXVI). The NMR spectrum in CDCl₃ showed the signals at δ 1.38, singlet, geminal dimethyl group at position-8; 1.55, doublet, J=8Hz, methyl group at position-2; 1.82 and 2.82, two triplets, J=7Hz, two methylene groups at positions-9 and 10; 2.25, singlet, methyl group at position-6; 3.25, multiplet, methylene group at position-3; 5.20, multiplet, one proton at position-2- and 7.20, singlet, one proton aromatic at position-11.

This (XXVI) on refluxing with DDQ in dry benzene gave 9,10-dihydro-2,6,8,8-tetramethyl-4-oxo-4H-furanopyrano(3,2-g)benzopyran (XXVII). The NMR spectrum showed the signals at δ 1.50, singlets, geminal dimethyl group at position-8; 1.90 and 2.98, two triplets, J=7Hz, two methylene group at positions-9 and 10; 2.40, singlet, methyl group at position-6; 2.50, singlet, methyl group at position-2; 6.50, singlet, one proton at position-3 and 7.35, singlet, one
proton aromatic. (Fig. 4). (XXVII) on further refluxion with DDQ in dry benzene gave 2,6,8,8-tetramethyl-4-oxo-4H-furano(3,2-c)pyrano(3',2'-g)benzopyran (XXVIII), which showed two doublets at δ 5.45 and 6.55 having coupling constant J=10 Hz for two protons at positions 9 and 10.
(Fig. 3): 2,3,9,10-Tetrahydro-2,6,8,8-tetramethyl-1-oxo-4H-furan-3',2'H-pyran(3',2'-E)benzopyran.
Fig. 4: 9,10-Dihydro-2,6,8,8-tetramethyl-4H-furano(3,2-c)pyrano(3',2'-g)benzopyran
Synthesis of 2,3-dihydro-4-oxo-4H-2,2',3,6,8-pentamethyl-
-difurano(3,2-c; 3',2'-e)benzopyran

7-Allyloxy-4-hydroxy-8-methyl coumarin (XXIX) was
prepared according to Dholakia and Trivedi. This was
condensed with 1-chloro-3-methyl-but-2-ene in the presence
of anhydrous potassium carbonate and potassium iodide in
acetone to give 7-allyloxy-8-methyl-4-prenyloxycoumarin
(XXX). This on boiling with dimethylaniline gave 2,3-dihydro-
-7-allyloxy-4-oxo-4H-2,2',3,6-tetramethylfurano(3,2-c)benzo-
-pyran (XXXI) and 2,3-dihydro-7-hydroxy-8-allyl-4-oxo-4H-
2,2',3,6-tetramethylfurano(3,2-c)benzopyran (XXXII). The IR
spectrum of (XXXI) in nujol showed the bands at 1720 cm\(^{-1}\)
(\(\alpha\)-pyrone carbonyl stretching frequency), 1620 cm\(^{-1}\) (aromatic
\(\equiv C\equiv\) stretching frequency), 1280 cm\(^{-1}\) (\(\gamma\equiv\)O=O
stretching frequency) and 900 cm\(^{-1}\) (allylic \(\gamma\equiv\)O=O
stretching frequency). The NMR spectrum in CDCl\(_3\) showed the signals, at \& 1.30,
doublet, J=3Hz, methyl group at position-3; 1.38 and 1.42,
two singlets, geminal dimethyl group at position-2; 2.25,
singlet, methyl group at position-6; 3.10, quartate, J=3Hz,
one proton at position-3; 4.55, doublet, two protons of
-CH\(_2\)-CH=; 5.15-5.40, triplet, one proton of -CH\(_2\)-CH=; 6.70
and 7.30, two doublets, J=9Hz, two protons aromatic at
positions-8 and -9. (Figs.)

The IR spectrum of (XXXII) showed the bands at
3200 cm\(^{-1}\) (broad), for hydroxyl group, 1695 cm\(^{-1}\) for
Fig. 5: 2,3-Dihydro-7-allyloxy-4-oxo-4H-2,2,3,6-tetramethylfuran(3,2-e)benzopyran
α-pyrone carbonyl stretching frequency, 1370 cm$^{-1}$ for geminal dimethyl group, 1270 cm$^{-1}$ for -C=O- stretching frequency and 930 cm$^{-1}$ for allylic -C=C- stretching frequency.

(XXXII) was cyclised by heating with sulphuric acid (84 %) to 2,3,8,9-tetrahydro-4-oxo-2,2,3,6,8-pentamethylfurano(3,2-c : 3',2'-g)benzopyran (XXXIII). The IR spectrum in nujol showed the bands at 1705 cm$^{-1}$ (α-pyrone carbonyl stretching frequency) and 970 cm$^{-1}$ (furan ring). The NMR spectrum of (XXXIII) in CDCl$_3$ showed the signals at δ 1.30, doublet, J=8Hz, methyl group at position-3; 1.48 and 1.50, two singlets, geminal dimethyl group at position-2; 1.50, doublet, methyl group at position-8; 2.28, singlet, methyl group at position-6; 2.75, quartet, one proton at position-3; 2.97-3.50, multiplet, two protons at position-9; 5.00, quartet, one proton at position-8 and 7.30, one proton aromatic at position-11. (Fig. 6)
(XXXIII) was further refluxed with DDQ in benzene to give 2,3-dihydro-4-oxo-4H-2,2,3,6,8-pentamethyldifuran-3,2'-c : 3',2'-g)benzopyran (XXXIV). The NMR spectrum showed a doublet at δ 2.55, for a methyl group at position -8 and a signal at δ 5.05, as quartate, for one proton at position-9.
Synthesis of 2,3-dihydro-4-oxo-4H-7-hydroxy-2,6-dimethyl-8-prenylfurano(3,2-c)benzopyran

2,4-Dihydroxy-3-methylacetophenone (XXXV) was prenylated with 1-chloro-3-methyl-but-2-ene in the presence of anhydrous potassium carbonate and potassium iodide to 4-prenyloxy-2-hydroxy-3-methylacetophenone (XXXVI). This was further condensed with diethyl carbonate in the presence of pulverised sodium to give 4-hydroxy-8-methyl-7-prenyloxy-coumarin (XXXVII). This was refluxed with allyl bromide in the presence of anhydrous potassium carbonate in acetone to obtain 4-allyloxy-8-methyl-7-prenyloxy-coumarin (XXXVIII). The IR spectrum in nujol showed the bands at 1700 cm\(^{-1}\) (\(\alpha\)-pyrone carbonyl stretching frequency) and 920 cm\(^{-1}\) (allylic C=O stretching frequency). This on refluxing with dimethylaniline gave 2,3-dihydro-4-oxo-4H-7-hydroxy-2,6-dimethyl-8-prenyl-furano(3,2-c)benzopyran (XXXIX). The corresponding cyclised or dehydrogenated product could not be obtained by the usual methods. The NMR spectrum of (XXXIX) in CDCl\(_3\) showed the signals at \(\delta\) 1.50, doublet, methyl group at position-2; 1.60 and 1.70, two singlets, geminal dimethyl group; 2.40, singlet, methyl group at position-6; 2.60-2.80, multiplet, methylene group at position-3 and two protons of \(-\text{CH}_2-\text{CH}\) group; 5.20, triplet, (broad), two protons, \(-\text{CH}_2-\text{OH}\) group and \(-\text{OH}\) group, 6.50, singlet, one proton at position-2 and 7.40, singlet, one proton aromatic at position-9. (Fig. 7)
(Fig. 7) 2,3-Dihydro-1-oxo-4H-7-hydroxy-2,6-dimethyl-8-prenylfurano(3,2-c)benzopyran
EXPERIMENTAL

2,8,8-Trimethyl-4-oxo-4H-furano(3,2-c)pyrano(2',3'-h)benzopyran (X) : 8-Allyloxy-3,4-dihydro-2,2-dimethyl-6-oxo-6H-pyrano(2,3-h)benzopyran (VIII) :

3,4-Dihydro-2,2-dimethyl-8-hydroxy-6-oxo-6H-pyrano(2,3-h)benzopyran (0.8 g.), anhydrous potassium carbonate (2.0 g.) and allyl bromide (0.5 g.) were refluxed in acetone (50 ml.) for 10 hr. The solvent was removed by distillation and the residue was diluted with water. The whole solution was then extracted with ether. A semi solid mass was obtained on evaporating the ether which on passing through alumina and eluting with benzene gave a solid, 8-allyloxy-3,4-dihydro-2,2-dimethyl-6-oxo-6H-pyrano(2,3-h)benzopyran, crystallised from benzene-petroleum ether, m.p. 150-51°. Yield 0.4 g.

Analysis : Found : C, 70.89 ; H, 6.65 %

requires : C, 71.32 ; H, 6.29 %.

Claisen migration of 8-allyloxy-3,4-dihydro-2,2-dimethyl-6-oxo-6H-pyrano(2,3-h)benzopyran : 2,3,6,7-Tetrahydro-2,8,8-trimethyl-4-oxo-4H-furano(3,2-c)pyrano(2',3'-h)-benzopyran (IX) :

8-Allyloxy-3,4-dihydro-2,2-dimethyl-6-oxo-6H-pyrano(2,3-h)benzopyran (0.3 g.) was refluxed with dimethyl-aniline (5 ml.) for 2 hr. The solution was cooled and poured into the dilute hydrochloric acid solution. The solid
separated was filtered, washed with water and crystallised from benzene-petroleum ether, as 2,3,6,7-tetrahydro-2,8,8-trimethyl-4-oxo-4H-furano(3,2-c)pyrano(2',3'-h)benzopyran, m.p. 190°. Yield 0.15 g.

Analysis: Found: C, 70.88; H, 5.89 %

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

2,3-Dihydro-2,8,8-trimethyl-4-oxo-4H-furano(3,2-c)pyrano-(2',3'-h)benzopyran (XII):

2,2-Dimethyl-8-hydroxy-6-oxo-6H-pyrano(2',3'-h)benzopyran (0.5 g.) was refluxed with allyl bromide (0.3 g.) and anhydrous potassium carbonate (1.5 g.) in acetone (50 ml.) for 8 hr. The solvent was removed by distillation and the residue was diluted with water. The product obtained was directly refluxed with dimethylaniline (2 ml.) for 4 hr. The reaction mixture was poured into the dilute hydrochloric acid solution. The solid obtained was filtered and washed with dilute sodium hydroxide solution and crystallised from benzene-petroleum ether mixture to give 2,3-dihydro-2,8,8-trimethyl-4-oxo-4H-furano(3,2-c)pyrano(2',3'-h)benzopyran, m.p. 140-42°. Yield 0.20 g.

Analysis: Found: C, 71.33; H, 6.22 %

C_{17}H_{16}O_4 requires: C, 71.83; H, 5.63 %.

4-Hydroxy-7-prenyloxycoumarin (XV):

2-Hydroxy-4-prenyloxyacetophenone (5.0 g.), diethyl carbonate (20 ml.) and pulverised sodium (4.0 g.)
were heated on a water bath for 12 hr. Alcohol (50 ml.) was added to the reaction mixture to decompose the unreacted sodium and the whole solution was added to the ice-cold water. The solution was then extracted with ether and aqueous solution on acidification with hydrochloric acid gave a solid, 4-hydroxy-7-prenyloxycoumarin, crystallised from alcohol, m.p. 183-84°. Yield 0.3 g.

**Analysis**: Found : C, 68.80 ; H, 5.71 %  
C\textsubscript{14}H\textsubscript{12}O\textsubscript{4} requires : C, 68.30 ; H, 5.79 %.

4-Allyloxy-7-prenyloxycoumarin (XVI) :

A mixture of 4-hydroxy-7-prenyloxycoumarin (1.0 g.), anhydrous potassium carbonate (3.0 g.) and allyl bromide (0.5 g.) was refluxed in acetone (50 ml.) on a water bath for 12 hr. The solvent was evaporated and water was added to the residue. The whole solution was extracted with ether and the residue obtained after the evaporation of ether, crystallised from petroleum ether, as 4-allyloxy-7-prenyloxy-7coumarin, m.p. 80-2°. Yield 0.2 g.

**Analysis**: Found : C, 71.25 ; H, 6.29 %  
C\textsubscript{17}H\textsubscript{18}O\textsubscript{4} requires : C, 71.32 ; H, 6.29 %.

**Claisen migration of 4-allyloxy-7-prenyloxycoumarin** :

2,3-Dihydro-2-methyl-7-prenyloxy-1-oxo-4\textsuperscript{H}-furan(1,2-c)-benzopyran (XVII) :

4-Allyloxy-7-prenyloxycoumarin (0.15 g.) was refluxed with dimethylaniline (3 ml.) for 2 hr. The solution
was added to the dilute hydrochloric acid solution and the solid obtained was filtered and crystallised from benzene-petroleum ether mixture to give 2,3-dihydro-2-methyl-7-prenyloxy-4-oxo-4H-furano(3,2-c)benzopyran, m.p. 126-27°. Yield 0.05 g.

Analysis: Found: C, 71.52; H, 5.91%

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

This on prolonged refluxion with dimethylaniline gave 2,3,6,7-tetrahydro-2,8,8-trimethyl-4-oxo-4H-furano-(3,2-c)pyrano(2',3'-h)benzopyran, m.p. 188°. The mixed m.p. of this compound did not depress with the compound prepared earlier.

2,3,6-Tetrahydro-2,8,8-trimethyl-4-oxo-4H-furano-(3,2-c)pyrano(2',3'-h)benzopyran (XXI) = 6-Allyloxy-3,4-dihydro-2,2-dimethyl-8-oxo-8H-pyrao(3,2-g)benzopyran (XIX):

3,4-Dihydro-2,2-dimethyl-6-hydroxy-8-oxo-8H-pyrao(3,2-g)benzopyran (0.8 g.), anhydrous potassium carbonate (2.0 g.) and allyl bromide (0.5 g.) were refluxed in acetone (50 ml.) for 10 hr. The solvent was evaporated and the water was added to the residue. The solution was extracted with ether and the ether layer on evaporation gave a residue which gave a solid on passing through alumina, was crystallised from benzene-petroleum ether mixture to give 6-allyloxy-3,4-dihydro-2,2-dimethyl-8-oxo-8H-pyrao(3,2-g)benzopyran, m.p. 140-42°. Yield 0.5 g.

Analysis: Found: C, 71.77; H, 6.32%

C_{17}H_{18}O_4 requires: C, 71.32; H, 6.29%.
Claisen migration of 6-allyloxy-3,4-dihydro-2,2-dimethyl-8-oxo-8H-pyrano(3,2-g)benzopyran : 2,3,9,10-Tetrahydro-2,8,8-trimethyl-4H-furano(3,2-c)pyrano(3',2'-g)-benzopyran (XX) :

6-allyloxy-3,4-dihydro-2,2-dimethyl-8-oxo-8H-pyrano(3,2-g)benzopyran (0.2 g.) was refluxed with dimethylaniline (5 ml.) for 2 hr. The mixture was poured into dilute hydrochloric acid solution. The solid separated was filtered and washed and crystallised from benzene-petroleum ether mixture, m.p. 191-92°. Yield 0.1 g.

Analysis : Found : C, 71.41; H, 6.46 %
C17H18O4 requires : C, 71.32; H, 6.29 %.

2,6,8,8-Tetramethyl-4H-furano(3,2-c)pyrano(3',2'-g)-benzopyran (XXVIII) :

3,4-Dihydro-2,2,10-trimethyl-6-allyloxy-8-oxo-8H-pyrano(3,2-g)benzopyran (XXV) :

3,4-Dihydro-2,2,10-trimethyl-6-hydroxy-8-oxo-8H-pyrano(3,2-g)benzopyran (1.0 g.), anhydrous potassium carbonate (2.0 g.) and allyl bromide (0.5 g.) were refluxed in acetone (50 ml.) on a water bath for 10 hr. The solvent was removed by distillation and the residue was extracted with ether. The ether layer was washed with water and the residue, obtained after evaporation of the solvent, was crystallised from petroleum ether to give 3,4-dihydro-2,2,10-trimethyl-6-allyloxy-8-oxo-8H-pyrano(3,2-g)benzopyran, m.p. 171-72°. Yield 0.6 g.
Analysis: Found: C, 72.41; H, 6.59%.
C_{18}H_{20}O_{4} requires: C, 72.00; H, 6.66%.

Claisen migration of 3,10-dihydro-2,2,10-trimethyl-6-allyloxy-8-oxo-8H-pyrano(3,2-g)benzopyran: 2,3,9,10-Tetrahydro-2,6,8,8-tetramethyl-1-oxo-4H-furano(3,2-c)pyrano(3',2'-g)-benzopyran (XXVI):

3,10-Dihydro-2,2,10-trimethyl-6-allyloxy-8-oxo-8H-pyrano(3,2-g)benzopyran (0.5 g.) was refluxed with dimethyl-aniline (5 ml.) for 2 hr. The solution was cooled and poured into the dilute hydrochloric acid solution. The solid separated was filtered and crystallised from benzene-petroleum ether mixture to give 2,3,9,10-tetrahydro-2,6,8,8-tetramethyl-1-oxo-4H-furano(3,2-c)pyrano(3',2'-g)benzopyran, m.p. 140-42°. Yield: 0.3 g.

Analysis: Found: C, 72.36; H, 6.61%.
C_{18}H_{20}O_{4} requires: C, 72.00; H, 6.66%.

2,3,9,10-Tetrahydro-2,6,8,8-tetramethyl-1-oxo-4H-furano(3,2-c)-pyrano(3',2'-g)benzopyran (XXVII):

2,3,9,10-Tetrahydro-2,6,8,8-tetramethyl-1-oxo-4H-furano(3,2-c)pyrano(3',2'-g)benzopyran (0.2 g.) was refluxed in dry benzene with DDQ (0.2 g.) for 40 hr. The solid separated was filtered hot and washed with hot benzene. The filtrate was concentrated and the residue on column chromatography over silica gel gave a solid, 9,10-dihydro-2,6,8,8-tetramethyl-1-oxo-4H-furano(3,2-c)-pyrano(3',2'-g)-
benzopyran crystallised from benzene-petroleum ether mixture, m.p. 159-60°. Yield 0.15 g.

Analysis of this product did not agree with the molecular formulae, but the structure was confirmed on the basis of its NMR spectrum.

2,6,8,8-Tetramethyl-4-oxo-4H-furano(3,2-c)pyrano(3',2'-g)-
-benzopyran (XXVIII) :

9,10-Dihydro-2,6,8,8-tetramethyl-4-oxo-4H-furano-
-(3,2-c)pyrano(3',2'-g)benzopyran (0.1 g.) was refluxed with DDQ (0.1 g.) in dry benzene (10 ml.) for 70 hr. The solid separated was filtered hot and washed with benzene. The filtrate was concentrated and the residue was eluted with benzene over the column of silica gel. The solid, 2,6,8,8-
tetramethyl-4-oxo-4H-furano(3,2-c)pyrano(3',2'-g)benzopyran, crystallised from benzene-petroleum ether mixture, m.p. 177-78°. Yield 0.03 g.

Analysis: Found: C, 72.64; H, 6.26%
C_{18}H_{16}O_4 requires: C, 72.97; H, 5.40%.

2,3-Dihydro-4-oxo-4H-2,2,3,6,8-pentamethyldifurano(3,2-c :
3',2'-g)benzopyran (XXXIV): 7-Alllyloxy-3-methyl-4-prenyl-
-oxycoumarin (XXX): 4-Alllyloxy-3-methyl-2-hydroxyacetophenone (5.0 g.) was heated on a water bath with diethyl carbonate (15 ml.) and pulverised sodium (5.0 g.) for 10 hr. The mixture was added to the cold water and the solution was filtered. The
alkaline filtrate was acidified with dilute hydrochloric acid to give 4-hydroxy-7-allyloxy-8-methyleoumarin (2.0 g.) which was further refluxed with 1-chloro-3-methyl-but-2-ene (2 ml.), anhydrous potassium carbonate (6.0 g.) and potassium iodide (1.0 g.) in acetone (50 ml.) on a water bath for 8 hr. The solvent was removed by distillation and water was added to the residue. The solid separated was filtered and crystallised from benzene-petroleum ether mixture to give 7-allyloxy-8-methyl-4-prenyloxycoumarin, m.p. 142-44°. Yield 1.0 g.

Analysis : Found : C, 72.16 ; H, 6.60 %
C_{18}H_{20}O_{4} requires : C, 72.00 ; H, 6.66 %.

Claisen migration of 7-allyloxy-8-methyl-4-prenyloxycoumarin:
7-Allyloxy-2,3-dihydro-4-oxo-4H-2,2,3,6-tetramethylfurano-(3,2-c)benzopyran (XXXI) : and 8-allyl-2,3-dihydro-7-
hydroxy-4-oxo-4H-2,2,3,6-tetramethylfurano(3,2-c)benzopyran (XXXII) :

7-Allyloxy-8-methyl-4-prenyloxycoumarin (0.8 g.) was refluxed with dimethylaniline (5 ml.) for 3 hr. The solution was added to dilute hydrochloric acid solution and extracted with ether. The ether layer was washed with dilute sodium hydroxide solution which on acidification gave a solid, 8-allyl-7-hydroxy-2,3-dihydro-4-oxo-4H-2,2,3,6-tetramethyl-
furano(3,2-c)benzopyran, crystallised from benzene-petroleum ether mixture, m.p. 180-81°. Yield 0.4 g.
Analysis : Found : C, 72.46 ; H, 6.52 %
C₁₈H₂₀O₄ requires : C, 72.00 ; H, 6.66 %.

The ether layer on evaporation gave a solid, 7-allyloxy-2,3-dihydro-4-oxo-4H-2,2,3,6-tetramethylfuranono-(3,2-c)benzopyran, crystallised from petroleum ether, m.p. 105-6°. Yield 0.1 g.
Analysis : Found : C, 72.11 ; H, 6.59 %
C₁₈H₂₀O₄ requires : C, 72.00 ; H, 6.66 %.

2,3,8,9-Tetrahydro-4-oxo-4H-2,2,3,6-pentamethylfuranono-(3,2-c : 3',2'-g)benzopyran (XXXIII) :

8- Allyl-7-hydroxy-2,3-dihydro-4-oxo-4H-2,2,3,6-
tetramethylfuranono(3,2-c)benzopyran (0.3 g.) was heated with sulphuric acid (94 % ; 5 ml.) on a water bath for 15 minutes. The solution was added to the cold water and the solid separated was filtered and crystallised from benzene-petroleum ether mixture to give 2,3,8,9-tetrahydro-4-oxo-4H-2,2,3,6,8-
pentamethylfuranono(3,2-c : 3',2'-g)benzopyran, m.p. 188-89°. Yield 0.2 g.
Analysis : Found : C, 72.43 ; H, 6.44 %
C₁₈H₂₀O₄ requires : C, 72.00 ; H, 6.66 %.

2,3-Dihydro-4-oxo-4H-2,2,3,6,8-pentamethylfuranono(3,2-c : 3',2'-g)benzopyran (XXXIV) :

2,3,8,9-Tetrahydro-4-oxo-4H-2,2,3,6,8-penta-
methylfuranono(3,2-c : 3',2'-g)benzopyran (0.15 g.) was refluxed with DDQ (0.15 g.) in dry benzene (10 ml.) for 24 hr.
The solution was filtered hot and the residue washed with hot benzene. The solvent was evaporated and the residue was chromatographed over silica gel. Elution with benzene gave a product, 2,3-dihydro-4-oxo-4H-2,2,3,6,8-pentamethyldifuranone-(3,2-c : 3',2'-g)benzopyran, crystallised from benzene-petroleum ether mixture, m.p. 182-83°. Yield 0.07 g.

Analysis: Found: C, 72.23; H, 5.85%
C₁₈H₁₈O₄ requires: C, 72.48; H, 6.02%.

2,3-Dihydro-4-oxo-4H-7-hydroxy-2,6-dimethyl-8-prenylfuranone-(3,2-c)benzopyran (XXXIX): 2-Hydroxy-3-methyl-4-prenyloxyacetophenone (XXXVI):

2,4-Dihydroxy-3-methylacetophenone (5.0 g.), anhydrous potassium carbonate (15.0 g.), potassium iodide (2.0 g.) and 1-chloro-3-methyl-but-2-ene (6 ml.) were refluxed in acetone (100 ml.) for 3 hr. on a water bath. The solvent was evaporated and the residue was diluted with water. The solution was then extracted with ether. The ether layer on evaporation gave a solid, 2-hydroxy-3-methyl-4-prenyloxyacetophenone, crystallised from petroleum ether, m.p. 70°. Yield 4.0 g.

Analysis: Found: C, 70.86; H, 7.70%
C₁₄H₁₈O₃ requires: C, 70.59; H, 7.56%.

4-Hydroxy-8-methyl-7-prenyloxycoumarin (XXXVII):

2-Hydroxy-3-methyl-4-prenyloxyacetophenone (4.0 g.) was dissolved in diethyl carbonate (10 ml.) and the solution
was added to the pulverised sodium (4.0 g.). The whole mixture was then heated on a water bath for 10 hr. The excess of sodium was destroyed by the addition of alcohol (10 ml.) and the mixture was added to the cold water. The solution was filtered and the filtrate, on acidification, gave a solid, 4-hydroxy-8-methyl-7-prenyloxycoumarin, crystallised from ethyl acetate-petroleum ether mixture, m.p. 184-86°. Yield 4.0 g.

4-Allyloxy-8-methyl-7-prenyloxycoumarin (XXXVIII) :

A mixture of 4-hydroxy-8-methyl-7-prenyloxy-coumarin (2.0 g.), anhydrous potassium carbonate (5.0 g.) and allyl bromide (1.5 ml.) in acetone (100 ml.) was refluxed on a water bath for 6 hr. The solvent was evaporated and water was added to the residue. The solid separated was filtered and crystallised from benzene-petroleum ether mixture to give 4-allyloxy-8-methyl-7-prenyloxy-coumarin, m.p. 146-48°. Yield 1.5 g.

Analysis: Found : C, 72.21; H, 6.59 %
C\textsubscript{18}H\textsubscript{20}O\textsubscript{4} requires : C, 72.00 ; H, 6.66 %.

Claisen migration of 4-allyloxy-8-methyl-7-prenyloxy-coumarin :

2,3-Dihydro-4-oxo-4H-7-hydroxy-2,6-dimethyl-8-prenylfuran- -\textsubscript{5}-(3,2-c)benzopyran (XXXIX) :

4-Allyloxy-8-methyl-7-prenyloxy-coumarin (1.0 g.) was refluxed with dimethylaniline (10 ml.) for 6 hr. The solution was added to the dilute hydrochloric acid solution and the whole solution was extracted with ether. The ethereal
layer was first extracted with sodium bicarbonate solution (10%) which on acidification gave a trace of 4-hydroxy-
coumarin derivative. It was again washed with dilute sodium hydroxide solution which on acidification gave a solid,
2,3-dihydro-4-oxo-4H-7-hydroxy-2,6-dimethyl-8-prenylfuran-
-(3,2-c)benzopyran, crystallised from benzene-petroleum ether mixture, m.p. 189-90°. Yield 0.4 g.
Analysis : Found : C, 72.33 ; H, 6.35 %
C_{18}H_{20}O_4 requires : C, 72.00 ; H, 6.66 %.
The ethereal solution on evaporation gave 4-allyloxy-
8-methyl-7-prenyloxy-coumarin.
REFERENCES