CHAPTER I.

SECTION I.

STUDIES IN THE SYNTHESIS OF FUROCOUMARINS :

CHAPTER I

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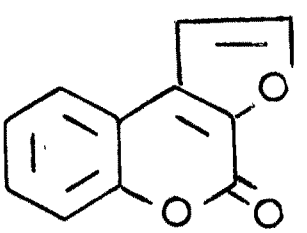
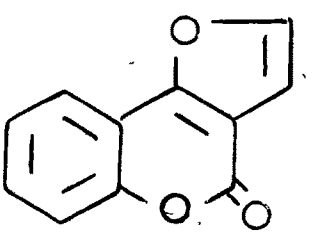
Studies in the synthesis of furocoumarins.

T H E O R E T I C A L

If the furan ring is built on a suitably substituted coumarin derivative, it leads to the synthesis of furocoumarins. Alternatively, one can start with an appropriate coumaran derivative and build up the α-pyrone ring on it. Eight isomeric forms of furocoumarins are found in the literature.



(A)



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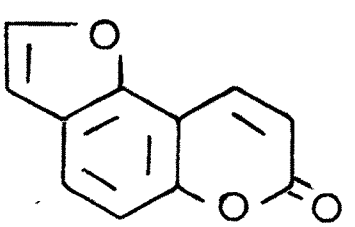

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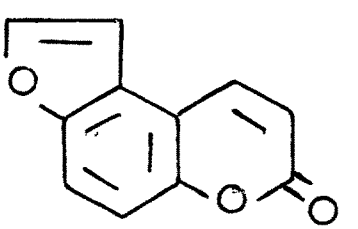

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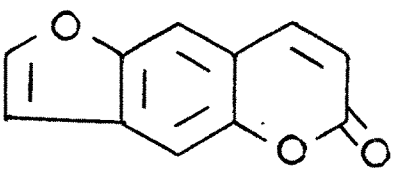

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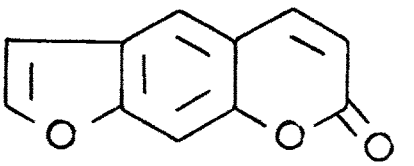

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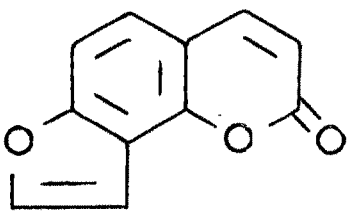

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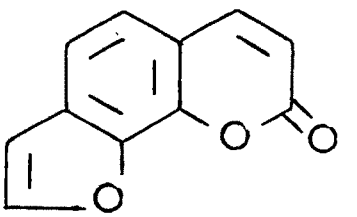
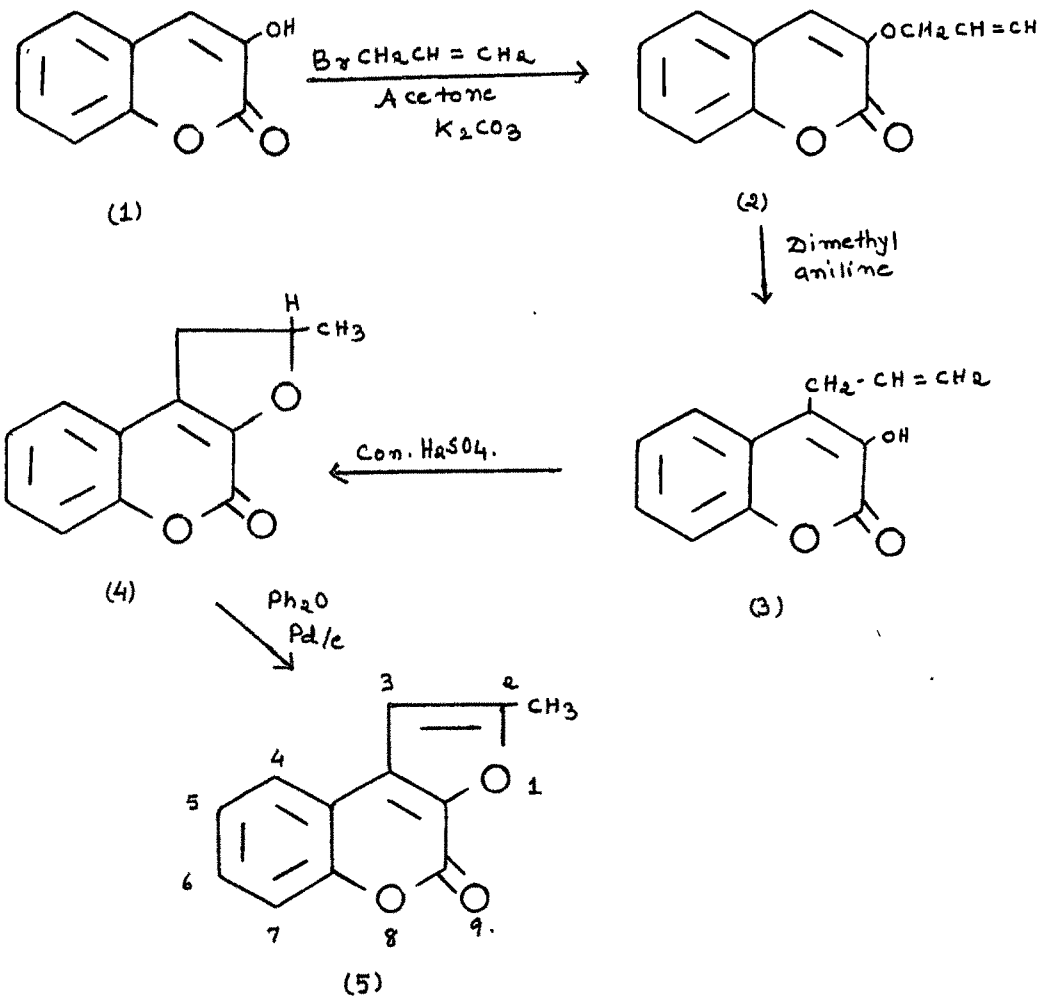


(H)

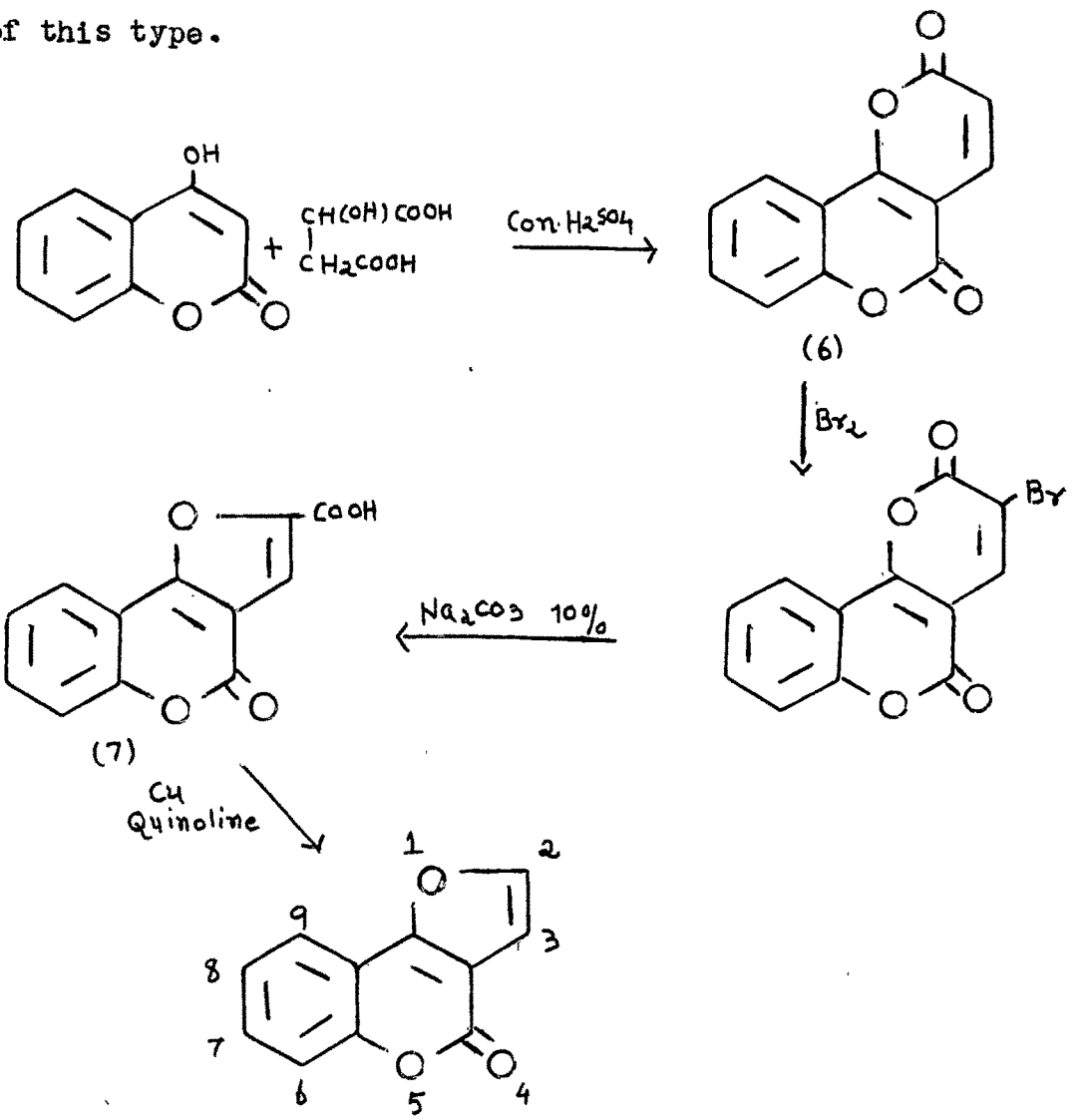
The methods for the synthesis of furocoumarins are briefly reviewed here.

Furocoumarin of type (A) has been recently synthesised for the first time by Shaikh and Trivedi[1]. 3-Hydroxycoumarin (1) was allylated with allyl bromide in

the presence of anhydrous potassium carbonate and dry acetone and the allyl ether (2) on Claisen rearrangement in dimethyl aniline afforded 3-hydroxy-4-allylcoumarin (3) which was cyclised by trituration with conc. sulphuric acid to give 2-methyl-9-oxo-9H-2,3-dihydrofuro(2,3-c)benzopyran (4). This method was found superior to earlier methods[2] which used hydrobromic acid or pyridine hydrochloride. (4) was dehydrogenated with palladised charcoal in boiling diphenyl ether to 2-methyl-9-oxo-9H-furo(2,3-c)benzopyran (5). They have also prepared furocoumarins of this type having substituents in the benzene ring.



Furocoumarins of the type (B) have been synthesised by Dholakia and Trivedi[3]. 4-Hydroxycoumarin was condensed with malic acid in the presence of sulphuric acid to yield 2,5-dioxo-2H,5H-pyrano(3,2-c)benzopyran (6), which on bromination gave 3-bromo derivative. This was hydrolysed with sodium carbonate to furnish 4-oxo-4H-furo(3,2-c)benzopyran-2-carboxylic acid (7), which was decarboxylated with copper and quinoline to yield 4-oxo-4H-furo(3,2-c)benzopyran(8). This is the first synthesis of an unsubstituted furocoumarin of this type.

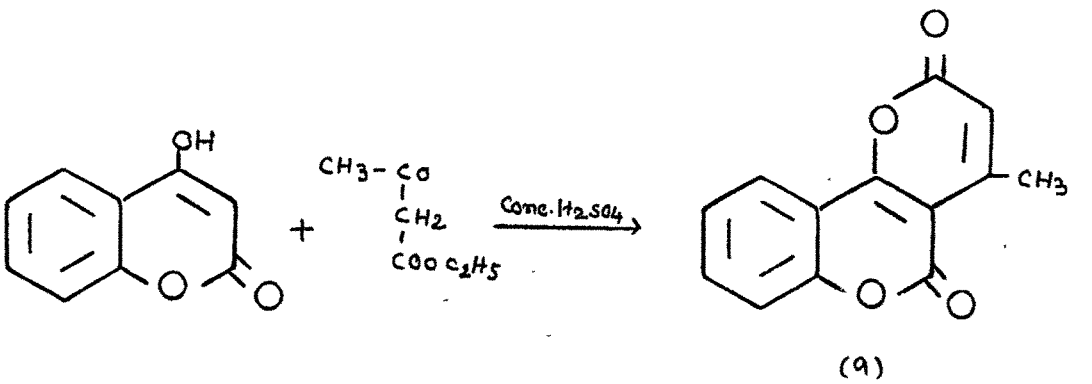


(8)

Similarly, 4-methyl-2,5-dioxo-2H,5H-pyrano(3,2-c) benzopyran (9) on bromination gave 3-bromo derivative (10), which was hydrolysed by refluxing it with 10 % sodium carbonate solution to give 2-(o-hydroxyphynyl)-4-methylfuran--3-carboxylic acid (11) and not the corresponding 3-methyl-4-oxo-4H-furo(3,2-c)benzopyran-2-carboxylic acid as obtained in the previous case of the 4-unsubstituted pyrano benzopyran. This was a typical behaviour observed in the case of 4-methyl pyranobenzopyran derivative. The formation of (11) has been explained as follows :-

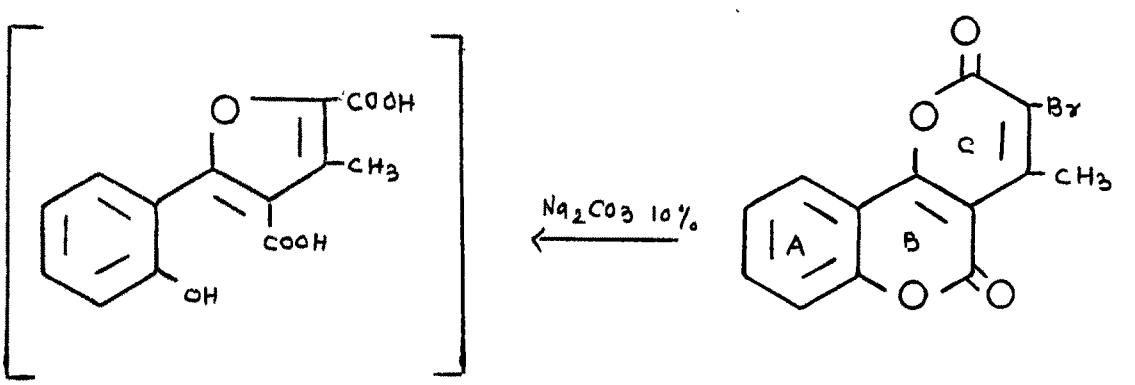
When 4-methyl-3-bromo-2,5-dioxo-2H,5H-pyrano(3,2-c) benzopyran (10) is hydrolysed, the ring contraction of rinc (c) takes place to form a furan ring having a carboxylic group in 2-position, but at the same time α-pyrone ring (B) of the coumarin ring system also opens up to give an intermediate (11) which could not be isolated. This intermediate (11) undergoes decarboxylation to give 2-(o-hydroxypheyl)-4-methyl-furan-3-carboxylic acid (12). This hydroxy acid (12) was cyclised by refluxing it with hydrochlorid acid to 3-methyl-4-oxo-4H-furo(3,2-c)benzopyran (13).

Dholakia and Trivedi[4] also prepared 3-phenyl-4-oxo-4H-furo(3,2-c)benzopyran (16). 4-Hydroxy-3-benzoylcoumarin when condensed with ethyl bromoacetate gave (14). This indicated that the reaction went further involving the ring closure of ethyl-3-benzoyl-4-coumarinyl oxyacetate. The ester (14) was hydrolysed to 3-phenyl-4-oxo-4H-furo(3,2-c)benzopyran-

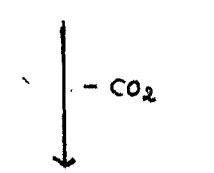

OH
CH3- CO
CH2
COO C2H5
Conc. H2SO4
CH3

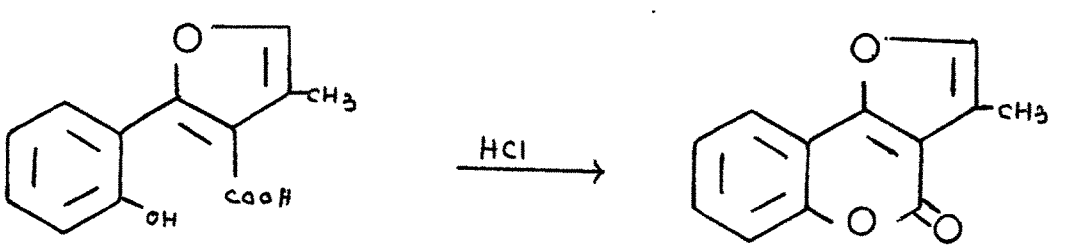
(9)


Br2


COOH
CH3
COOH
OH
Na2CO3 10%
Br
C
CH3
A
B

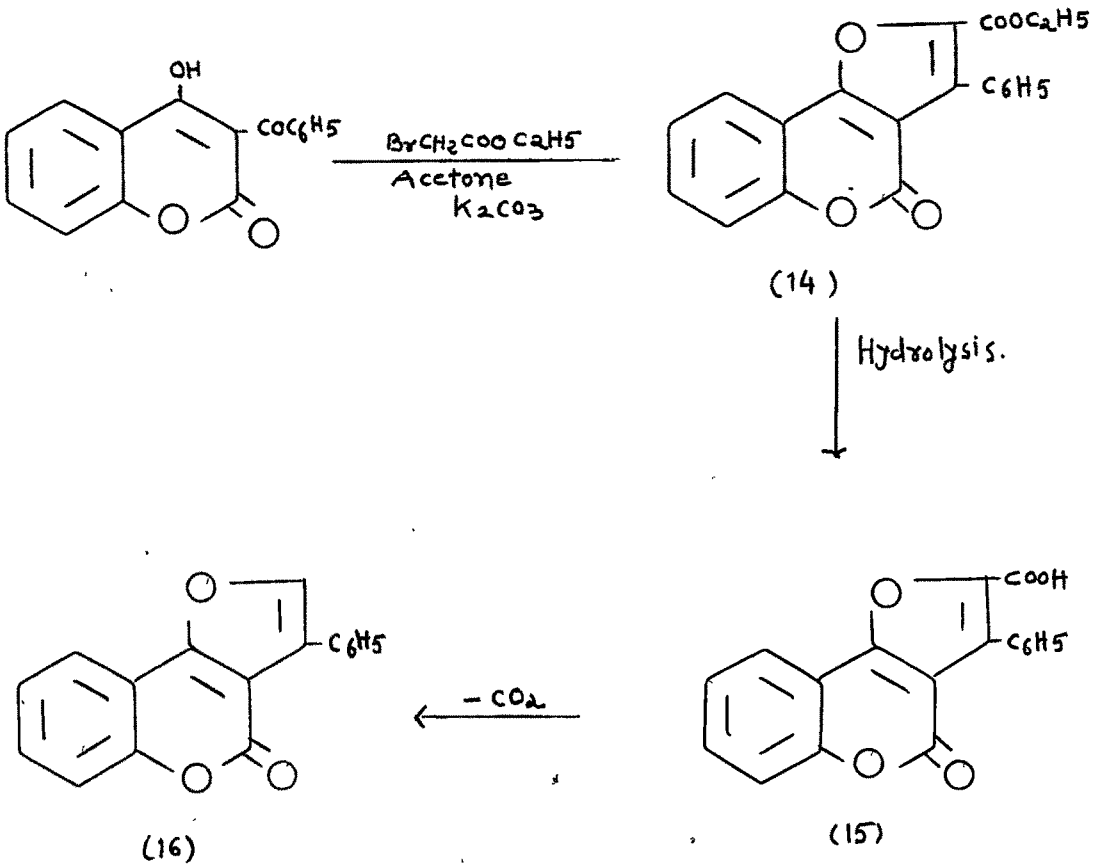
(11) (10)


- CO2


CH3
COOH
OH
HCl
CH3

(12) (13)

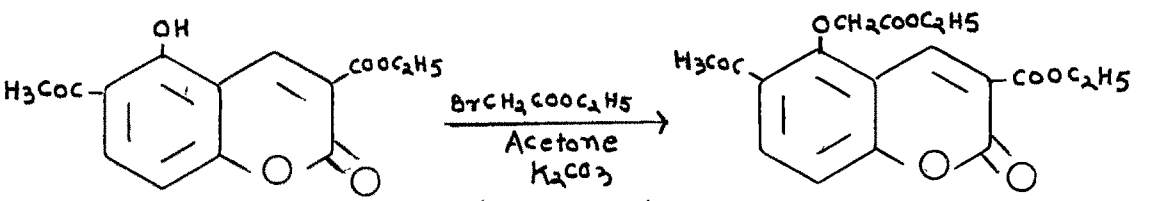
-2-carboxylic acid (15) which was subsequently decarboxylated to give 3-phenyl-4-oxo-4H-furo(3,2-c)benzopyran (16).



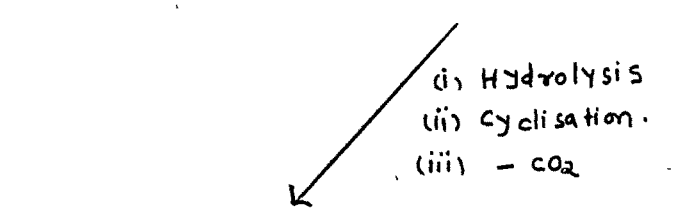
They have also synthesised 2-methyl-4-oxo-4H-furo (3,2-c)benzopyran (19). 4-Hydroxycoumarin on allylation with allyl bromide gave 4-allyloxycoumarin (17) which on Claisen rearrangement gave 2,3-dihydrofuro (3,2-c)benzopyran (18). Dehydrogenation of (18) with palladised charcoal (10 %) gave 2-methyl-4-oxo-4H-furo(3,2-c)benzopyran (19).

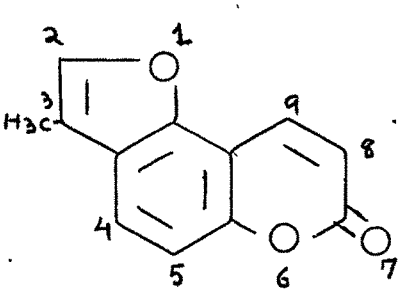
Furocoumarins of type (C) have been synthesised by several workers. Limaye and Sathe[5] subjected 6-hydroxy-7-acetyl-3-methylcoumarone (20) to Kostanecki-Robinson acetylation and obtained 3,9-dimethyl-7-oxo-7H-furo(2,3-f) benzopyran (21) in poor yield along with 3,7-dimethyl-9-oxo-9H-furo(2,3-f)benzopyran (22).

Shah and Shah[6] synthesised 3-alkyl-7-oxo-7H-furo (2,3-f)benzopyran (24) by condensing 5-hydroxy-6-acetyl-3-carboethoxycoumarin (23) with ethyl bromoacetate, followed by hydrolysis, cyclisation and subsequent decarboxylation.



(23)





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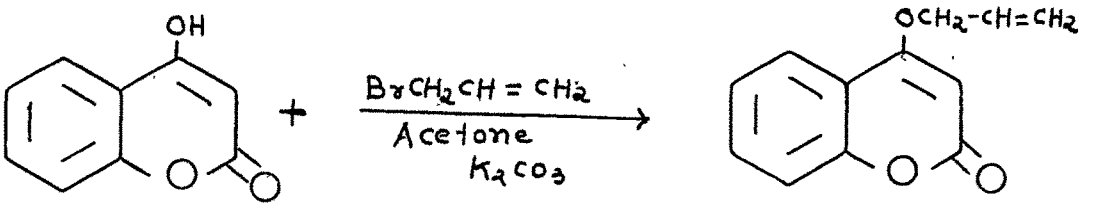
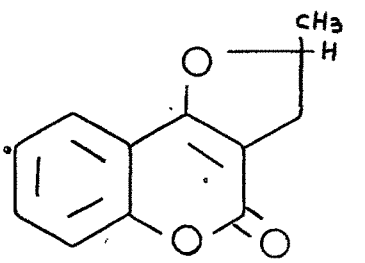


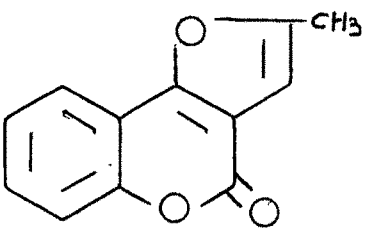
(17)

claisen rearrangement.

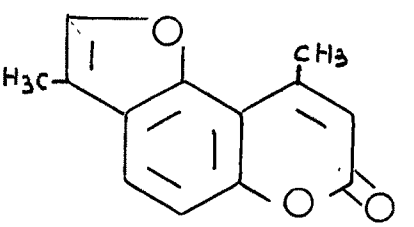


(18)

Ph_2O, Pd/c



(19)



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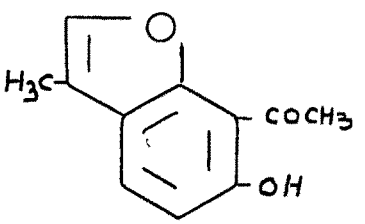
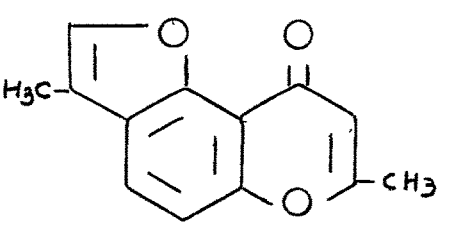


(20)

K.R.
Acetylation.

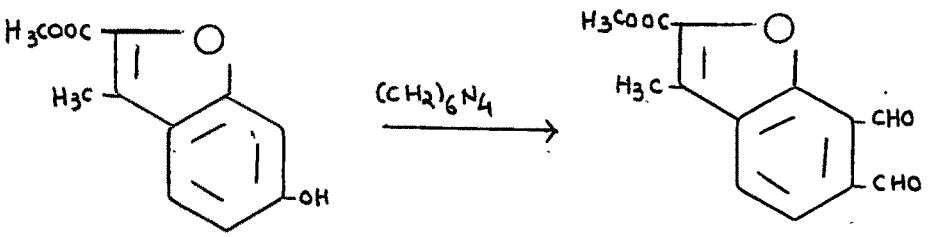
+



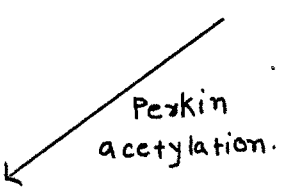
(22)

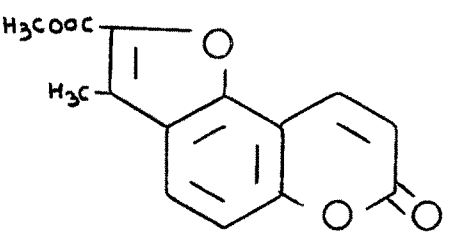
Chudgar and Shah[7] synthesised several 3-alkyl-9-methyl-7-oxo-7H-furo(2,3-f)benzopyran derivatives by condensing 5-hydroxy-6-acyl-4-methylcoumarin with ethyl bromoacetate followed by hydrolysis and subsequent cyclisation.

Salvi and Sethna[8] synthesised furocoumarin of this type starting with a benzofuran derivative. Methyl-6-hydroxy--3-methylcoumarilate (25) on reaction with hexamine gave the 7-formyl derivative (26) which on Perkin acetylation gave 2-carbomethoxy-3-methyl-7-oxo-7H-furo(2,3-f)benzopyran (27).



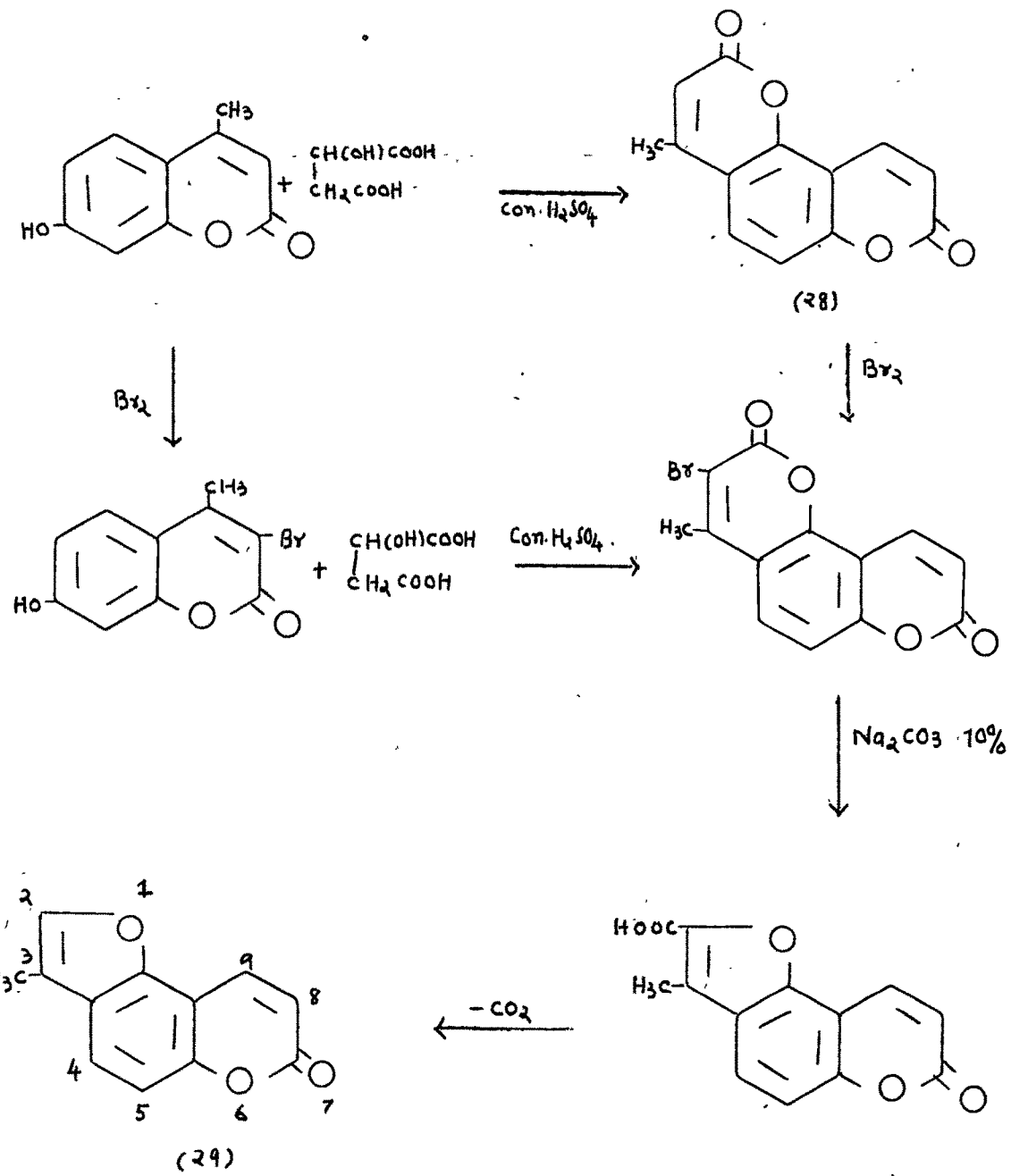
(25) (26)





(27)

Trivedi and Sethna[9] made a new approach to synthesise furocoumarins. They studied the hydrolysis of 3-halogen substituted coumarino-α-pyrones and obtained corresponding furocoumarins. 3-Methyl-7-oxo-7H-furo(2,3-f) benzopyran (29) was prepared from coumarino-α-pyrone derivative (28) through the following sequence of reactions.



Furocoumarin of type (D) form the subject matter of this Chapter, hence it will be discussed later.

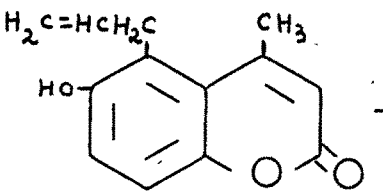
Furocoumarin of type (E) was synthesised by Kaufmann et al[10] as follows :-

5-Allyl-6-hydroxy-4-methylcoumarin (30) was catalytically hydrogenated to 6-hydroxy-4-methyl-5-n-propyl-coumarin (31) which was converted to an allyl ether by reaction with allyl bromide. Refluxing of the allyl ether in dimethyl aniline caused Claisen rearrangement to take place in 7-position, giving 7-allyl-6-hydroxy-5-n-propyl-4-methylcoumarin (32). Ozonolysis, catalytic hydrogenation and heating with o-phosphoric acid gave 8-methyl-9-n-propyl-6-oxo-6H-furo(2,3-g)benzopyran (33).

Furocoumarin of type (F) form the subject matter of this Chapter, hence it will be discussed later.

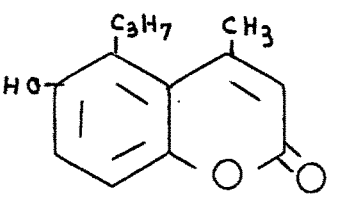
Angelioin is a naturally occuring furocoumarin of type (G). Spath and Pailer[11] synthesised Angelicin by condensing sodium salt of umbelliferon-8-aldehyde (34) with iodoacetic ester under pressure and the product thus obtained was subjected to hydrolysis followed by cyclisation to give angelicin (37).

Naik and Thakor[12] repeated this work using ethyl bromoacetate. They observed that the melting point of 7-(8-formylcoumarinoxy)-acetic acid (35) was 248-49^0 instead of 178-81^0 as reported by Spath and Pailer[11]. They also observed that cyclisation of this product (35) gave angelicin-2-carboxylic acid (36) which was not isolated by Spath and Pailer was obtained



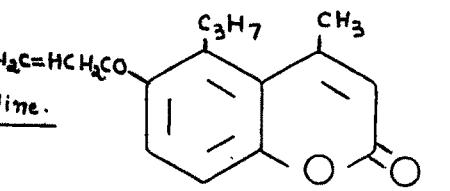
(30)

Catalytic hydrogenation

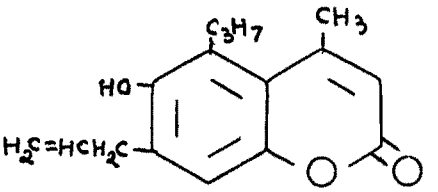


(31)

$BrCH_2CH=CH_2$

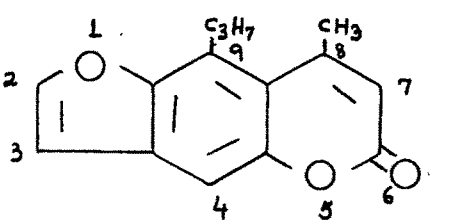


Diethyl aniline.



(32)

(i) O_3
(ii) Hydrogenation.
(iii) O-Phosphoric acid.



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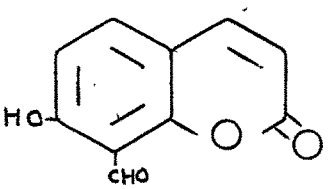
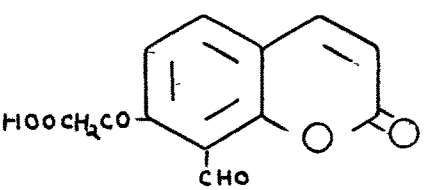


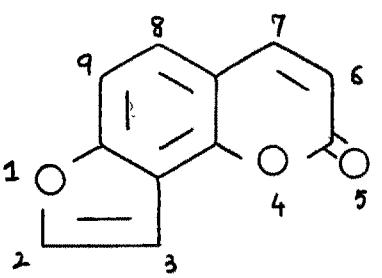
(34)

$BrCH_2COOC_2H_5$



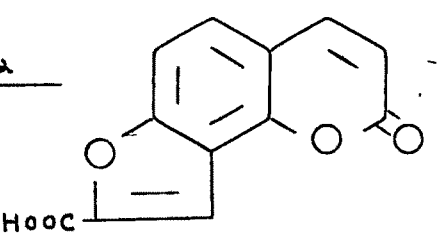
(35)

Cyclisation.



(37)

$-CO_2$



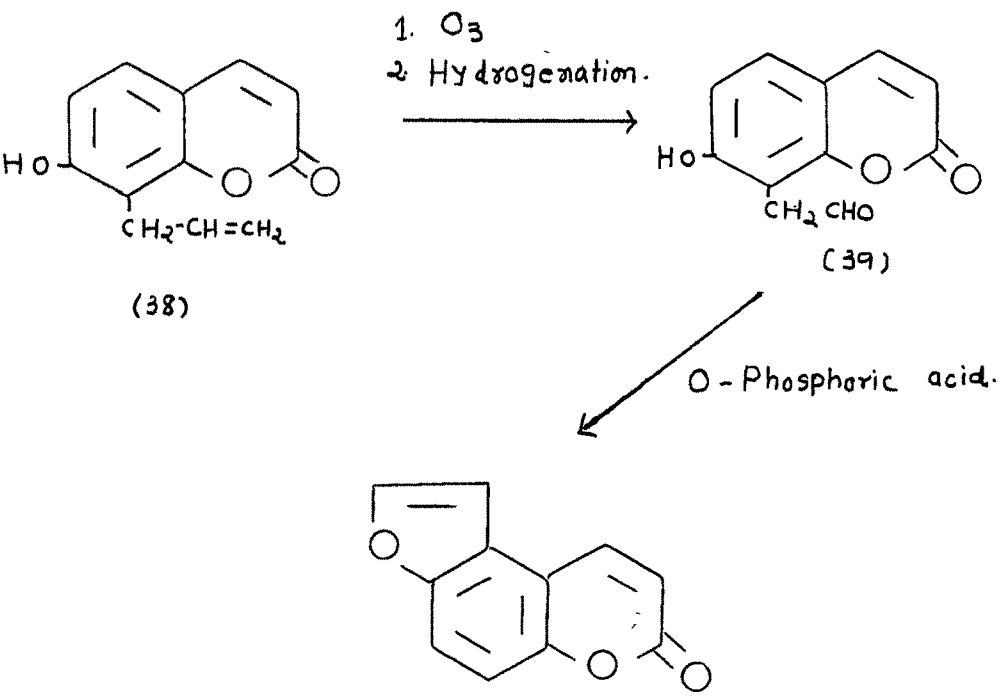
(36)

and it underwent decarboxylation when heated with copper and quinoline to angelicin (37).

Using the same method Shah and Shah[13] synthesised 3-methyl-5-oxo-5H-furo(2,3-h)benzopyran from 7-hydroxy-8-acetylcoumarin.

Limaye[14] synthesised angelicin by first preparing 4-hydroxy-5-formylcoumarone from 4-hydroxycoumarone and then subjecting it to Perkin reaction.

Aneja, Mukherjee and Seshadri[15] synthesised angelicin by subjecting 7-hydroxy-8-allylcoumarin (38) to ozonolysis and subsequent cyclisation of 8-acetaldehyde-7-hydroxycoumarin (39) with o-phosphoric acid.

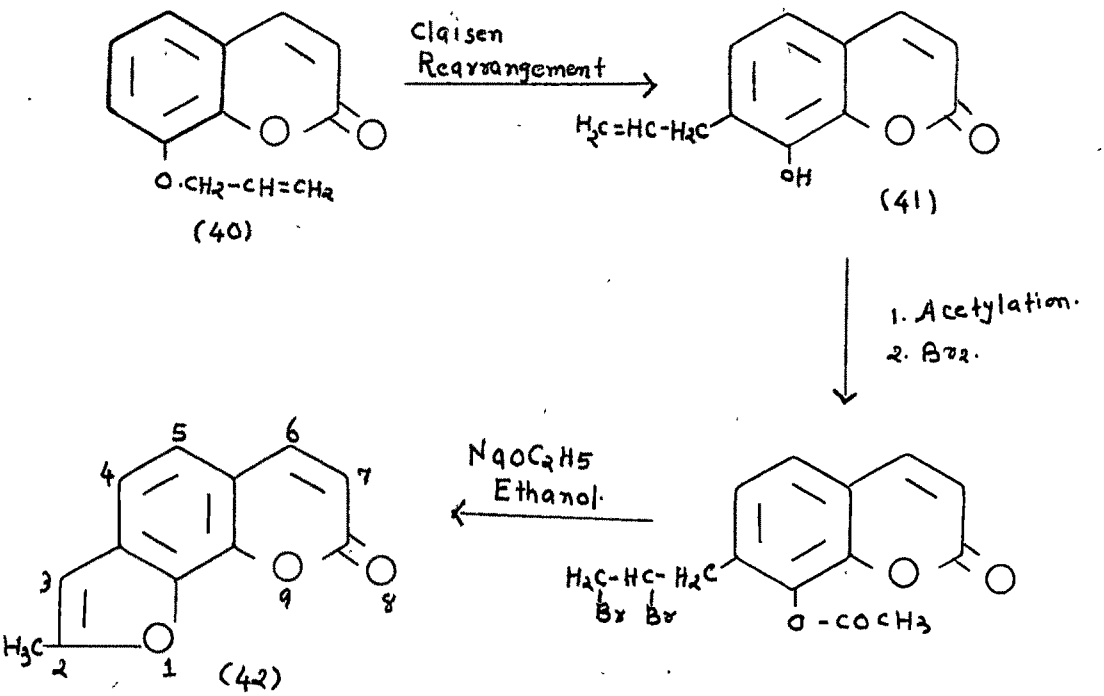


(38)

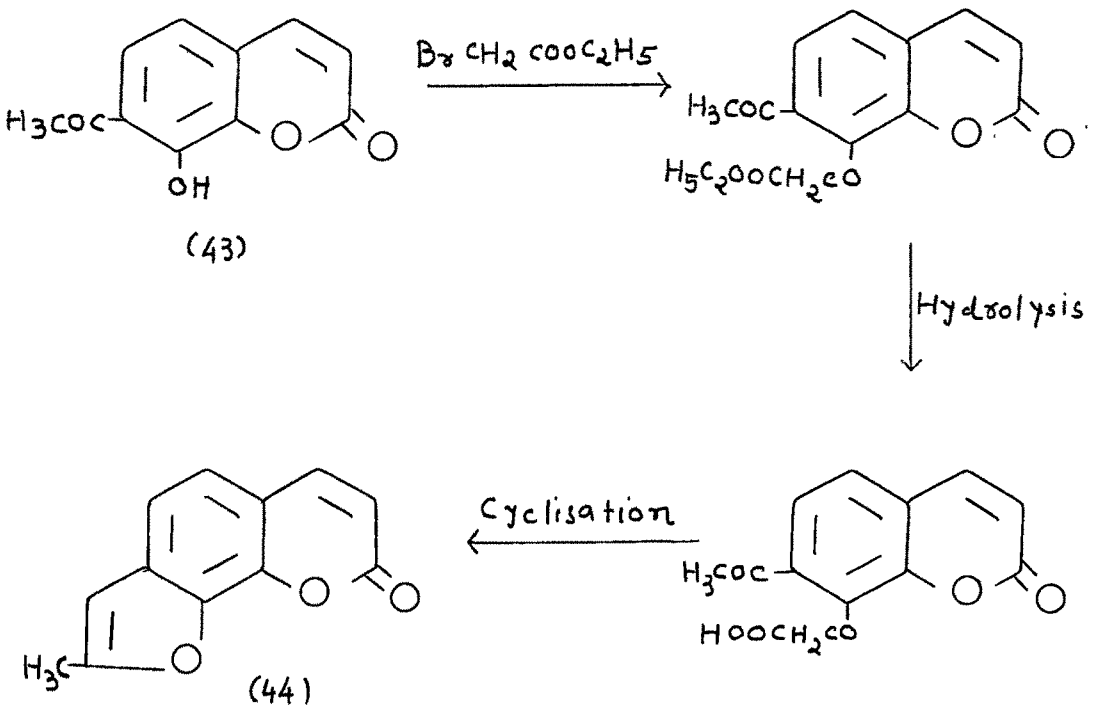
(39)

(37)

Furocoumarin of the type (H) was synthesised by Kaufmann and Russey[16]. They carried out Claisen rearrangement of 8-allyloxycoumarin (40) and obtained 7-allyl-8-hydroxycoumarin (41), which was acetylated and brominated. This bromo derivative underwent cyclisation to 2-methyl-8-oxo-8H-furo(3,2-h)benzopyran (42) when refluxed with sodium ethoxide in absolute alcohol.



Mehta and Sethna[17] synthesised 3-methyl-8-oxo-8H-furo(3,2-h)benzopyran (44) by condensing 8-hydroxy-7-acetylcoumarin (43) with ethyl bromoacetate followed by hydrolysis and cyclisation.



Furocoumarins of type (D) :

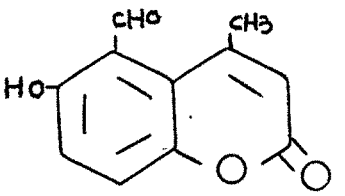
The synthesis of furocoumarins theoretically derivedfrom resorcinol such as Psoralene and isopsoralene, has been extensively investigated because of the photo-sensitizing activity associated with many of those compounds[18]. In contrast, very little has been published concerning the synthesis and natural occurence of furocoumarins derived from hydroquinone[10] and nothing is reported about their biological activity. Three triphenyl furocoumarins have been obtained by a three step process involving condensation of hydroquinone[19] with benzoin followed by

oxidation and treatment with sodium acetate and acetic anhydride. These compounds are not of very much interest as potential photosensitizing agent because Musajo, et al.[20] have reported that the introduction of a phenyl substituent on the furan ring of psoralene eliminates its photosensitizing activity. Although the structure of the naturally occuring compounds Halfordin[21] is still in doubt, it may be another example of furocoumarin theoretically derived from hydroquinone.

Kaufmann et al.[10] synthesised first time the furocoumarin of type (D) by following method. 5-Formyl-6-hydroxy-4-methylcoumarin (45) was condensed with methyl bromoacetate gave methyl-5-formyl-4-methylcoumarin-6-oxy-acetate (46), which was hydrolysed to the corresponding acid (47) by hot 10 % aqueous sulphuric acid. Heating (47) with acetic anhydride and sodium acetate gave 9-methyl-7H-furo[3,2-f] [1] benzopyran-7-one (48) in 31 % yield and its 2-carboxy derivative (49) in 43 % yield.

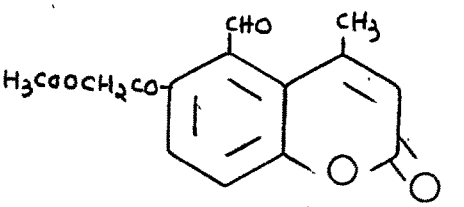
They have synthesised the same furocoumarin, 9-methyl-7H-furo [3,2-f] [1] benzopyran-7-one (48) through an alternative route. 6-Hydroxy-4-methylcoumarin was converted to an allyl ether (50) by reaction with allyl bromide. Claisen rearrangement of (50) gave 5-allyl derivative (51), which was subjected to ozonolysis, catalytic hydrogenation followed by heating with o-phosphoric acid to give the furocoumarin (48).

The above authors prepared 2,9-dimethyl-7H-furo [3,2-f] [1] benzopyran-7-one (52) from 6-hydroxy-5-allyl-4-



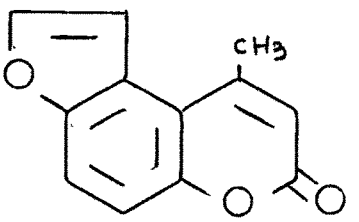
(45)

$BrCH_2COOCH_3$



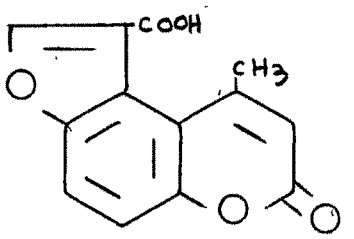
(46)

10% Aq. H_2SO_4.



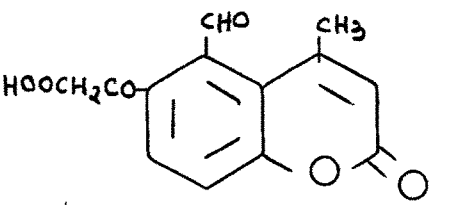
(48)

+

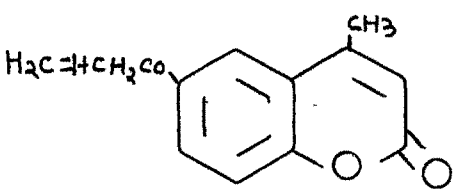


(49)

$(CH_3CO)_2O$
CH_3COONa

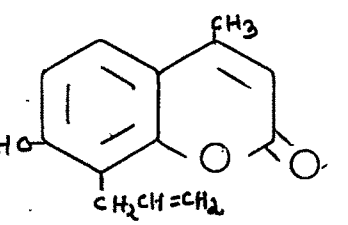


(47)



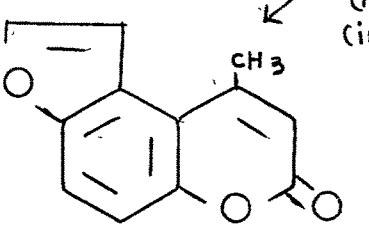
(50)

Claisen Rearrangement



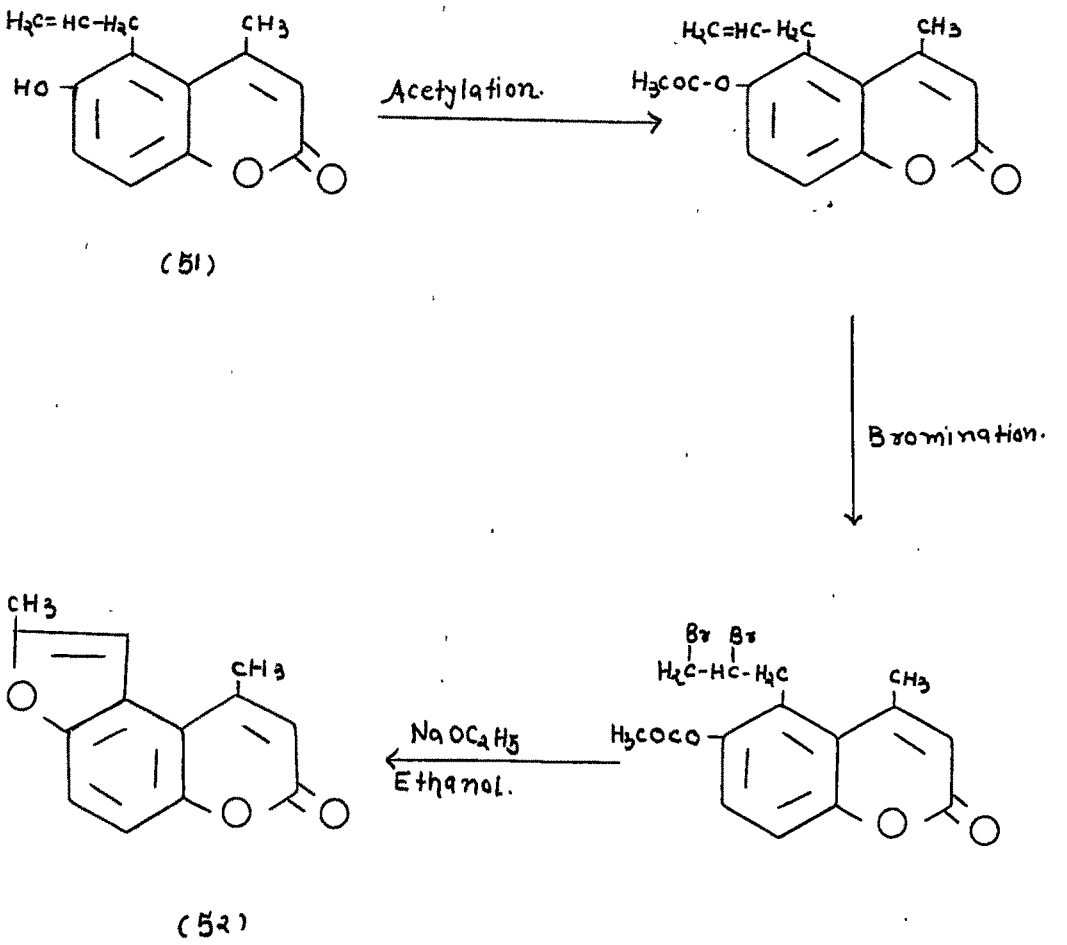
(51)

(i) O_3
(ii) Hydrogenation.
(iii) O-Phosphoric acid



(48

-methylcoumarin (51). The compound (51) was first acetylated and then brominated. The dibromo derivative was cyclised to 2,9-dimethyl-7H-furo [3,2-f] [1] benzopyran-7-one (52), when refluxed with sodium ethoxide in absolute alcohol.

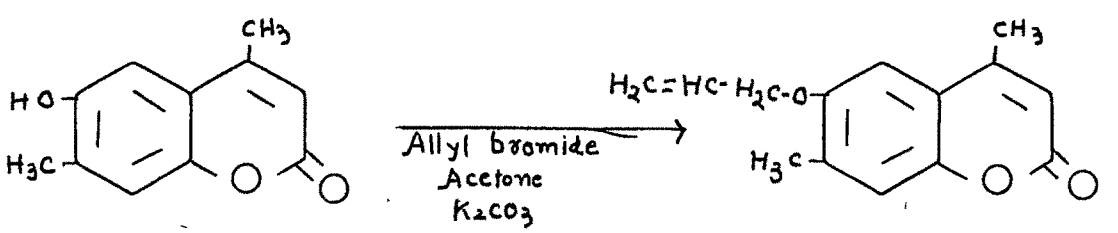


(51)

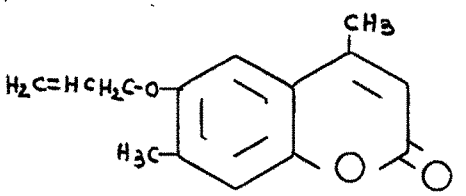
(52)

4,9-Dimethyl-7H-furo [3,2-f] [1] benzopyran-7-one (57) was prepared by the same authors[22] from 2-methyl-hydroquinone. Pechmann condensation of 2-methyl hydroquinone with ethyl acetoacetate gave 4,7-dimethyl-6-hydroxycoumarin. (53), which was converted to its allyl ether (54) by the reaction with allyl bromide and anhydrous potassium carbonate in dry acetone. 4,7-Dimethyl-6-allyloxy coumarin (54) underwent the Claisen rearrangement in boiling diethyl aniline to produce 5-allyl-4,7-dimethyl-6-hydroxycoumarin (55), ozonization, followed by catalytical hydrogenation gave the hemiacetal (56), which was dehydrated to a furocoumarin (57) with hot 85 % o-phosphoric acid.

In another sequence, (55) was acetylated and brominated to obtained 6-acetoxy-5-(2',3'-dibromopropyl)-4,7-dimethylcoumarin (58), which was converted to a trimethyl furocoumarin (59) by treatment with sodium ethoxide in boiling ethanol. Both of these furocoumarins were evaluated for psoralene-like photosensitizing activity and were found to be inactive.

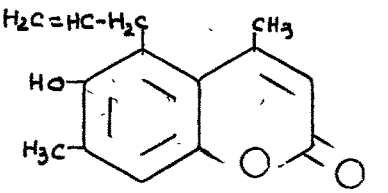


(53) (54)



(54)

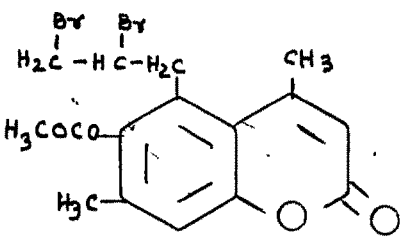
Diethyl aniline.



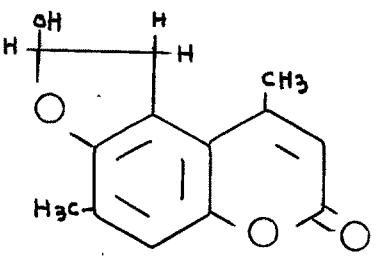
(55)

1. Acetylation.
2. Bromination

1. O_3
2. Hydrogenation



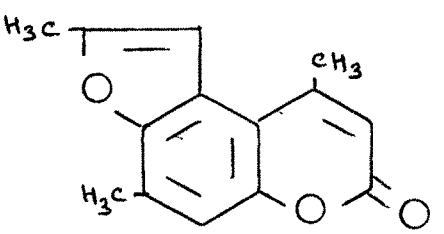
(58)



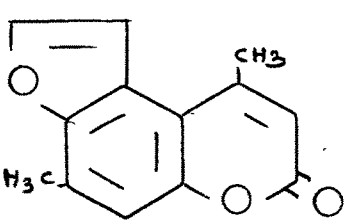
(56)

$NaOC_2H_5$
C_2H_5OH

O-Phosphoric acid.

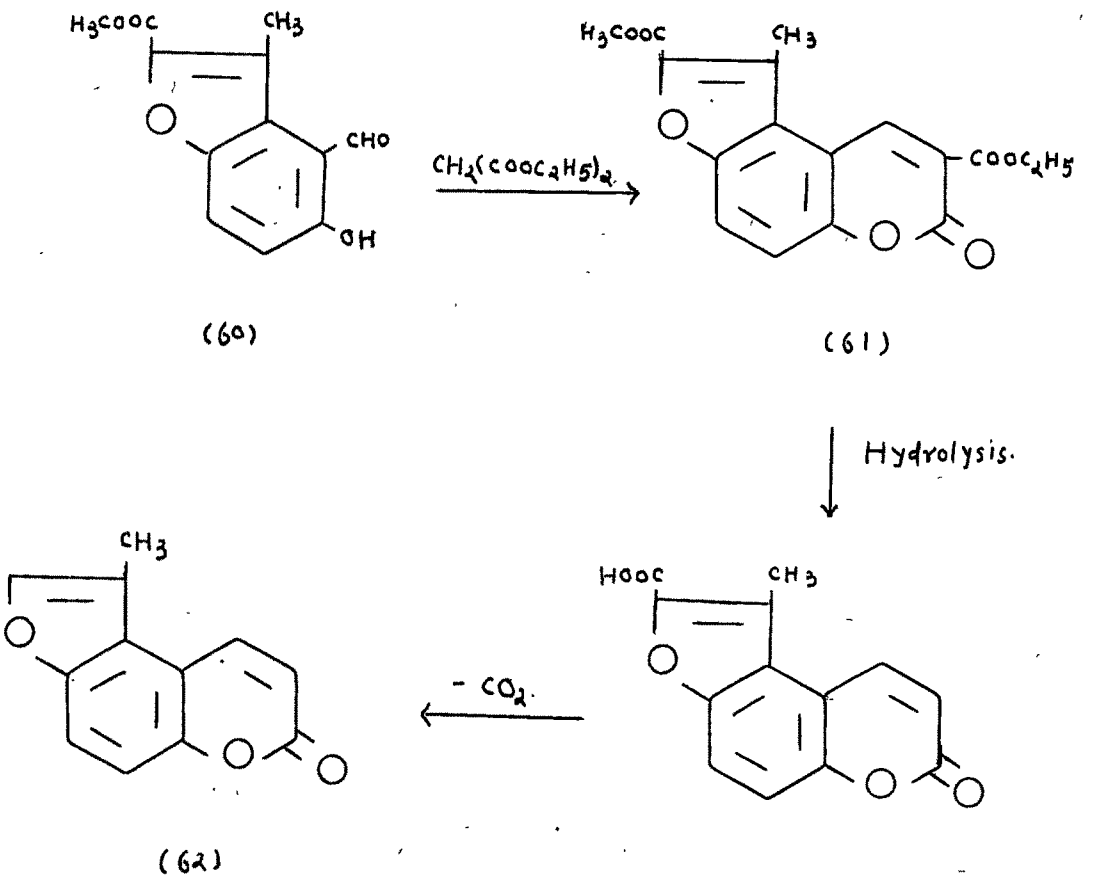


(59)



(57)

Salvi and Sethna[23], first formylated the hydroxy benzofurans and then carried out the synthesis of furocoumarins by Perkin or Knoevenagel reaction. Methyl-4-formyl-5-hydroxy-3-methylcoumarilate (60) on reaction with diethylmalonate gave ethyl-2-carbomethoxy-3-methyl-7H-furo-[3,2-f] [1] benzopyran-7-one (61), which on hydrolysis followed by decarboxylation gave 3-methyl-7H-furo [3,2-f] [1] benzopyran-7-one (62).



(60) (61) (62)

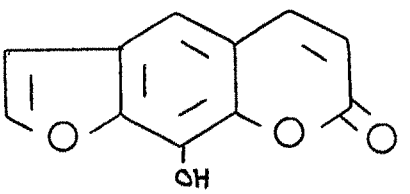
Furocoumarin of type (F) :

Natural furocoumarins are not mere metabolic products of the living cell, but they possess varied and often remarkable physiological activities. The role of certain plant juices and extractions as dermal photosensitizing agents has been known for many years. Juices of various parts of these plants, e.g. Parsley, Celery, Figs and Parship[24], after contact with the skin and exposure to sun light cause changes on mammalian skin manifested by erytherma and increased pigmentation.

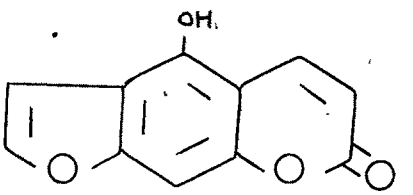
A study of the effect of structural alternations on the erythermal activity of furocoumarins[24,28] indicates that maximum photosensitizing activity lies in the parent compound, psoralene and that the various structurally related compounds have more or less reduced activity, depending on the ring system and the nature of substituents. The presence of a linear unreduced furocoumarin ring system is required for significant activity to be seen. A non-linear angular structure exemplified in isopsoralene does not exhibit any activity. Free phenolic groups inactivate the molecule, Xanthotoxol (63), Bergaptol (64), but the methyl ethers of the two possible phenols are both active Xanthotoxin (65), Bergapten (66). However, the dimethyl ether, Isopimpinellin (67) is inactive. Etherifying groups longer than methyl result in progressive reduction of activity as the size of the group increases. Nuclear substitution with methyl groups can cause the loss of activity to be retained depending on

the position of the group. Thus a methyl at the 4,4',5' or 8-position may or may not inhibit the activity, but a methyl group at the 3-position invariably does so. Little success has been noted with the introduction of nitro, amino or acetylamino group. The order of activity in psoralene type compounds is as follows :-

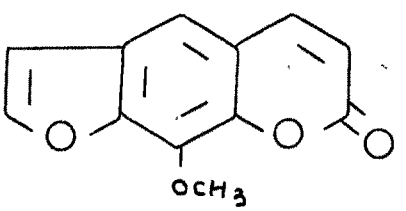
Psoralene > 4,5',8-trimethyl psoralene > 4-methyl-psoralene > 5',8-dimethyl psoralene > 8-methoxy psoralene > 5-methoxy psoralene > 8-isoamylene oxy psoralene.



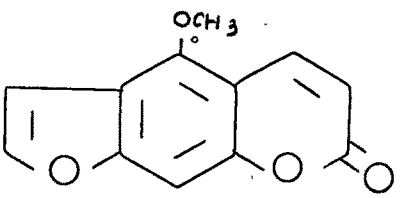
(63)



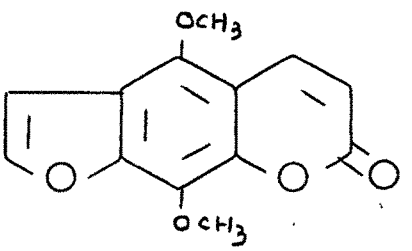
(64)



(65)



(66)



(67)

Leucoderma is characterised by circumscribed patches where the skin stops forming the pigment of the skin. A cure for leucoderma has attracted attention since ancient times. The seeds of Psoralea Corylifolia is widely used in Ayurvedic medicine. Psoralene was isolated as active principles by Jois et al.[26] Mukherjee[27], has given an excellent review of the chemistry, pharmacognosy and therapeutic activity of the indigenous drugs used in leucoderma. Most of them have a furocoumarin structure as an important constituent.

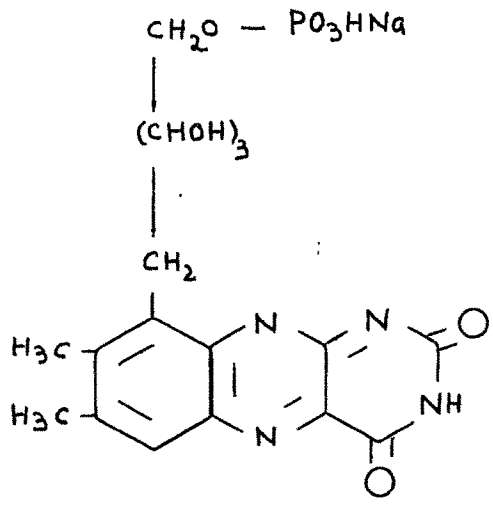
Xanthotoxin or 8-methoxy psoralne is a fish poison[28] but it is relatively non-toxic to mammals[29]. Schonberg and Latif[30] observed that it possesses molluscidal activity. It was demonstrated by Elwi[31] that it produces fatty degeneration of liver and adrenal haemorrhage if it is administered in large doses to mammals. In the case of human beings the compound has found medical acceptance for the treatment of leucoderma[29,32]. The most recent applications have made use of the fact that it alters the erythermal response to ultra-violet light, a property which has been used clinically to prevent sun burn[33]. There is some evidence that xanthotoxin under certain condition may be carcinogenic[34].

In an effort to determine the mechanism of the photodyanamic effect of furocoumarins, Fowks and co-workers[35-37] have studied the effect of furocoumarins on bacteria. It seems that furocoumarins kill bacteria cells. Pathak and Fellamn[38] have studied the activating and fluorescent wave

length of thirty seven furocoumarins and their biological photosensitizing action was also investigated. Furocoumarins which induced definite photosensitised erythermal response on mammalian skin showed activation peaks in the region of 340-380 m and concomitantly the fluorescent peaks in the region of 420-460 m . The inactive furocoumarins did not show the specific activating and fluorescent peaks. Recently Musajo and co-workers[39,40] have observed that flavinmononucleotide (FMN) will react only with the furocoumarins that are photodynamically active and that the reaction products appear to have been modified mainly in the furan ring. Further, they have demonstrated that FMN in large amounts acts against erytherma expected from the psoralene type molecules. Three new coumarin derivatives have been isolated in the bergapton photoreaction, namely, 7-hydroxy--5-methoxycoumarin-6-acetic acid, its methyl or ethyl ester according to the presence of methyl or ethyl alcohol in the irradiated solution, and probably 4', 5'-dihydroxy-4'--oxo-5-methoxy furocoumarin.

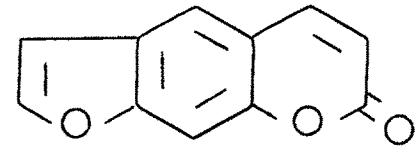
Two substances have been obtained by the photo reaction of FMN and psoralene in a water-methyl alcohol, namely, the methyl ester of 7-hydroxycoumarin-6-acetic acid (a) and 6-formyl-7-hydroxycoumarin (b). No new compounds are formed in the photo reaction of FMN and Xanthotoxin.

Inspite of these findings, the precise mechanism by which furocoumarins function in the treatment of leucoderma is unknown.

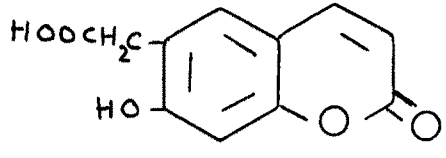


(FMN)

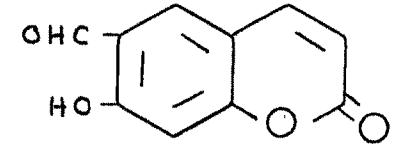
+



(Psoralene)



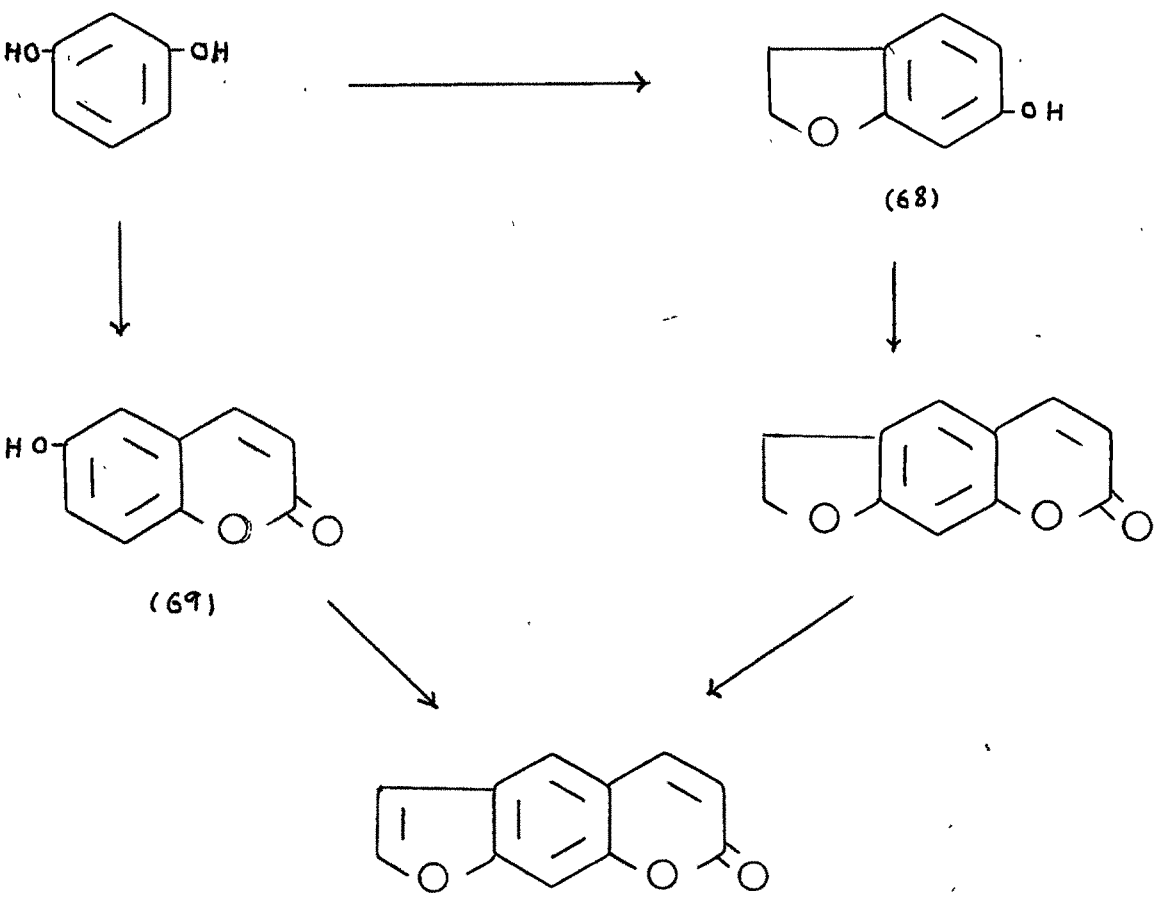
(a)



(b)

Rodighiero and coworkers[41] found that psoralene and Xanthotoxin significantly inhibited the growth of tubercle bacillus. The antifungal activity of furocoumarins has been studied by Chakraborty and co-workers[42] who reported that psoralene and imperatorin were the most effective antifungal agent tested.

Two routes are available for the synthesis of linear furocoumarins of psoralene type either (a) via conversion of 6-hydroxycoumaran (68) or (b) through umbelliferone (69). Both of these can be obtained from resorcinol as follows :-

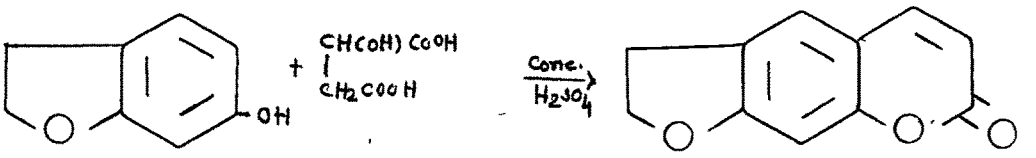


Spath and Pailer[43] carried out the condensation of 6-hydroxycoumaran (68) with malic acid in the presence of conc. sulphuric acid and obtained 2,3-dihydro psoralene (70), which on dehydrogenation gave psoralene (71).

Later Horning and Reisner[44] prepared different 5-substituted 2,3-dihydropsoralene derivative by condensing 6-acetoxycoumaran with a variety of B-ketonic ester in the presence of conc. sulphuric acid. Esse and Chistensen[45] have extended this reaction to obtained 6-alkyl-2,3-dihydro-5-methyl psoralene (73) by condensing appropriate α-alkyl-B-ketonic ester with 6-acetoxycoumaran (72). The main draw-back in the method is that the dehydrogenation of dihydro psoralene derivatives with palladised charcoal gave poor yields of psoralene derivatives.

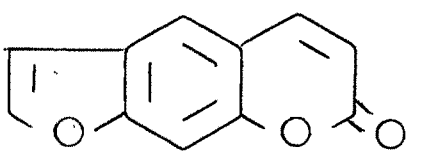
Foster et al.[46] synthesised psoralene by first subjecting 6-hydroxycoumaran (68) to Gattermann aldehyde synthesis and then condensing the 6-hydroxy-5-formylcoumarin (73) with cyanoacetic acid followed by decarboxylation and dehydrogenation.

The problem of furocoumarin synthesis from the coumarin moiety of the psoralene molecule has been approached by Ray and his co-workers[47] who reported the synthesis of 4'-methyl psoralene starting with umbelliferone. In the procedure they carried out cyclisation of 7-acetonyloxy-coumarin (74), obtained by treating umbelliferone with chloracetone in the presence of sodium ethoxide to 4'-methyl psoralene (75).

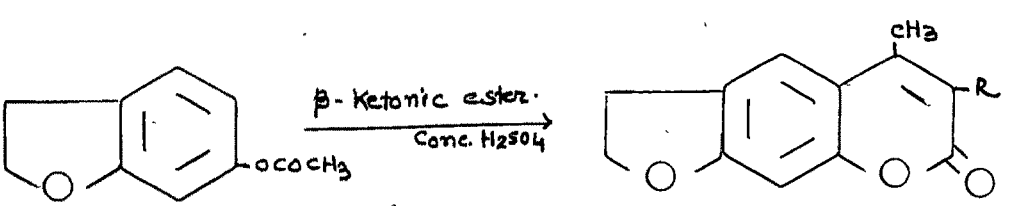


(68) (70)

Dehydrogenation

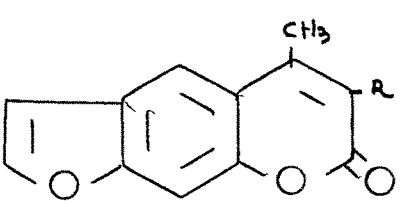


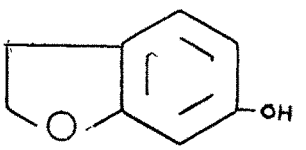
(71)



(72) (73)

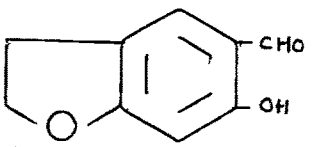
Pd/C





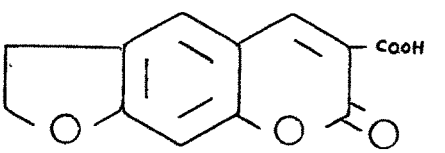
(68)

$Zn(CN)_2$ / HCl



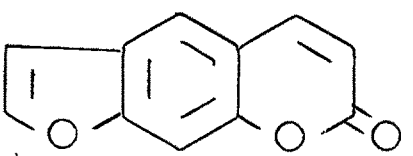
(73)

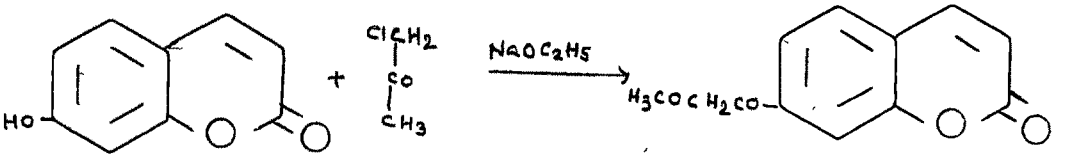
$CNCH_2COOH$



(71)

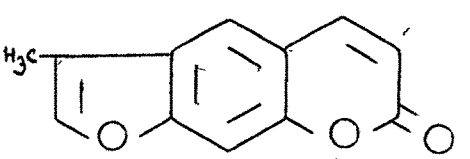
1. Decarboxylation.
2. Dehydrogenation.





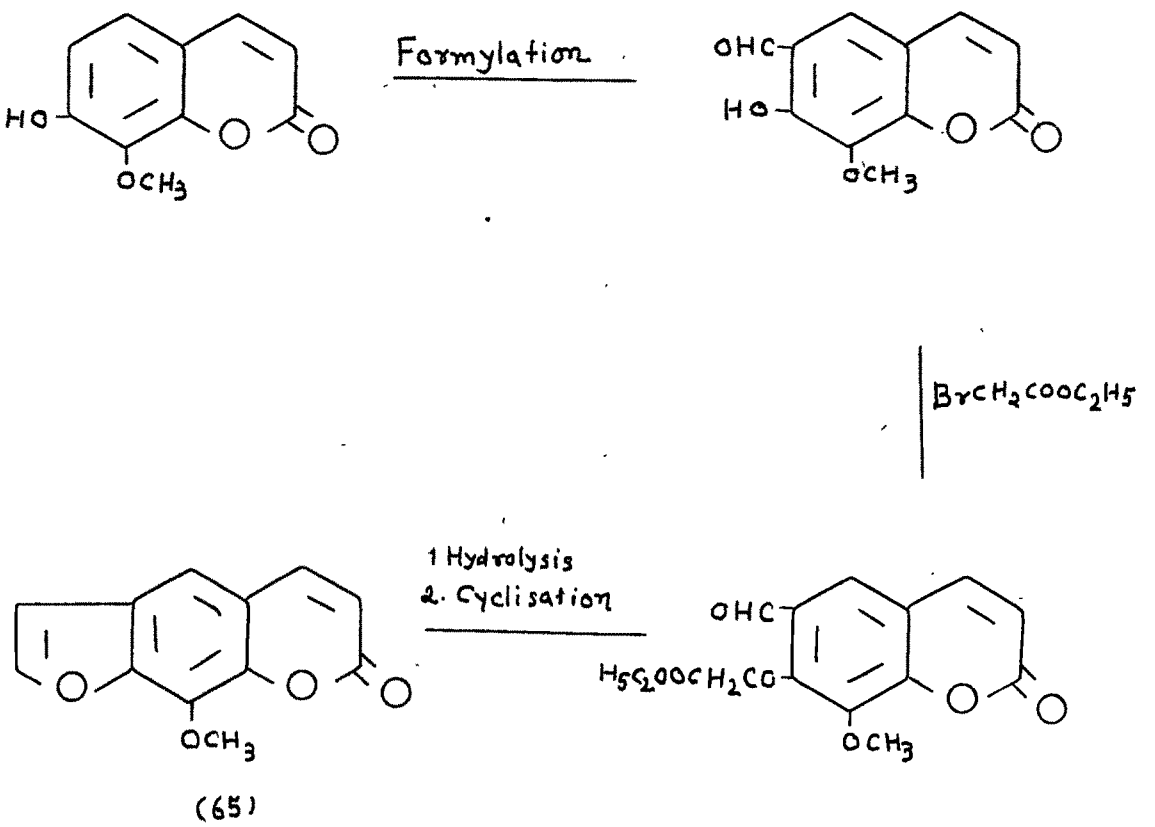
(74)

cyclisation



(75)

Rodighiero and Antonello[48] synthesised xanthotoxin (65) by first preparing 7-hydroxy-8-methoxy-6-formylcoumarin (76) and then treating it with ethyl bromoacetate followed by hydrolysis and cyclisation.

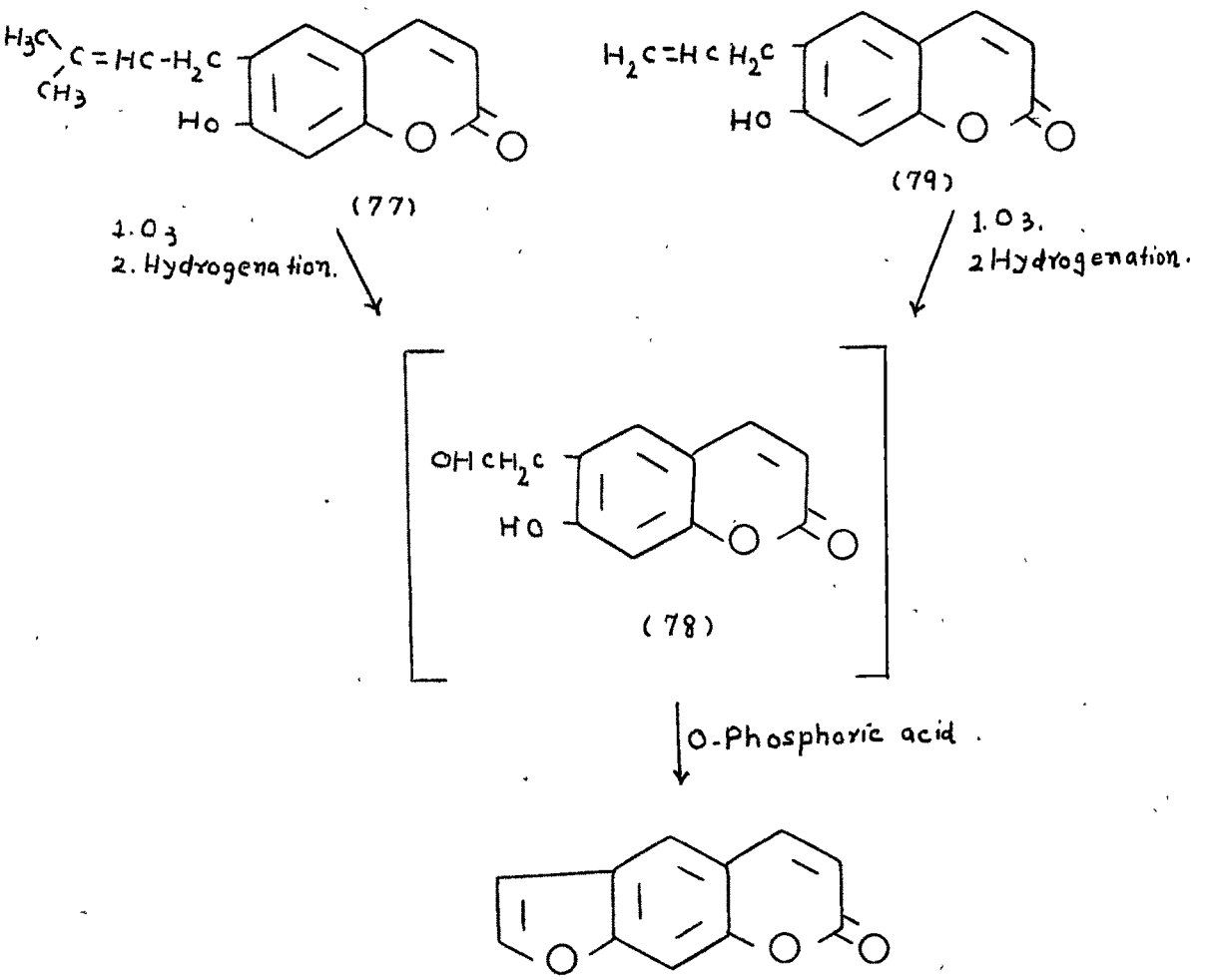


(65)

Limaye and Gangal[49] synthesised 3',4-dimethyl psoralene from 7-hydroxy-6-acetyl-4-methylcoumarin using the same procedure. The synthesis has been successfully used for the preparation of a number of methyl substituted xanthotoxin[50].

Seshadri and co-workers[15] have successfully obtained psoralene by the ozonolysis of 6-dimethyl-allyl--7-hydroxycoumarin (77) followed by cyclisation of the aldehyde (78) formed with o-phosphoric acid.

They have also synthesised psoralene by subjecting 6-allyl-7-hydroxycoumarin (79) to ozonolysis followed by the cyclisation of acetaldehyde coumarin with o-phosphoric acid.



The value of o-allylhydroxycoumarins in the synthesis of furocoumarins has been stressed by Kaufmann[18]. Thus Claisen rearrangement of 7-allyloxycoumarin having the reactive 8-position blocked by a methyl group or acetamido group, resulted in the expected 8-substituted-7-hydroxy-6-allylcoumarin, which were readily converted by the conventional procedure to 8-substituted psoralene derivatives[52-53].

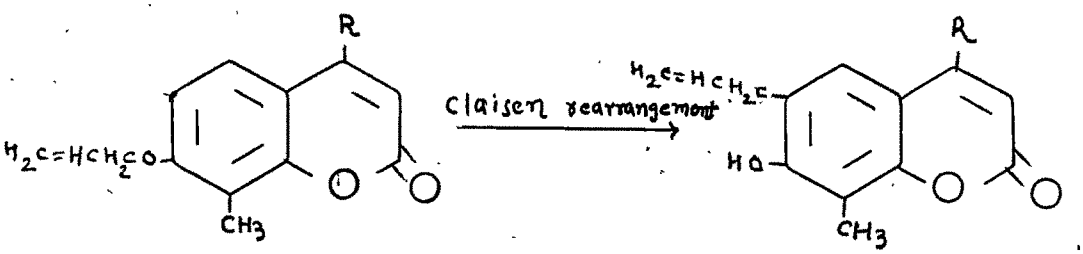
7-Allyloxy-4,8-dimethylcoumarin (80a) and 7-allyloxy--8-methylcoumarin (80b) on Claisen rearrangement gave 7-hydroxy-6-allyl-4,8-dimethylcoumarin (81a) and 7-hydroxy--6-allyl-8-methylcoumarin (81b) respectively. These were then acetylated, brominated and cyclised to obtained 4,5',8-trimethyl psoralene (82a) and 5 ,8-dimethyl psoralene (82b).

Using the same procedure Kaufamann synthesised 4,5'-dimethyl psoralene.

8-Amino psoralene derivative is a valuable starting material for the preparation of several derivatives of psoralene having groups such as Cl, Br, Cn, $N(CH_3)_2$, etc. in 8-position. Kaufamann and co-workers[53] synthesised psoralene derivatives (83) having groups such as Cl, Br, CN, $N(CH_3)_2$ in 8-position using 8-amino psoralene as an intermediate product.

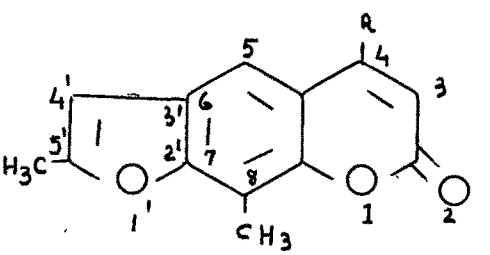
Parekh and Trivedi[54] also synthesised 4,5',8-trimethyl psoralene. The cyclisation of 7-hydroxy-6-allyl-4,8-dimethylcoumarin (84) by triturating it with conc. sulphuric acid afforded 4,5',8-trimethyl-4',5'-dihydro psoralene.(85), which on dehydrogenation with palladised charcoal in diphenyl

ether gave 4,5 ,8-trimethyl psoralene (86) in about 76 % yield.



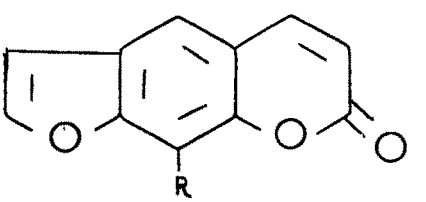
(80) (81)

(i) Acetylation.
(ii) Bromination.
(iii) Cyclisation.



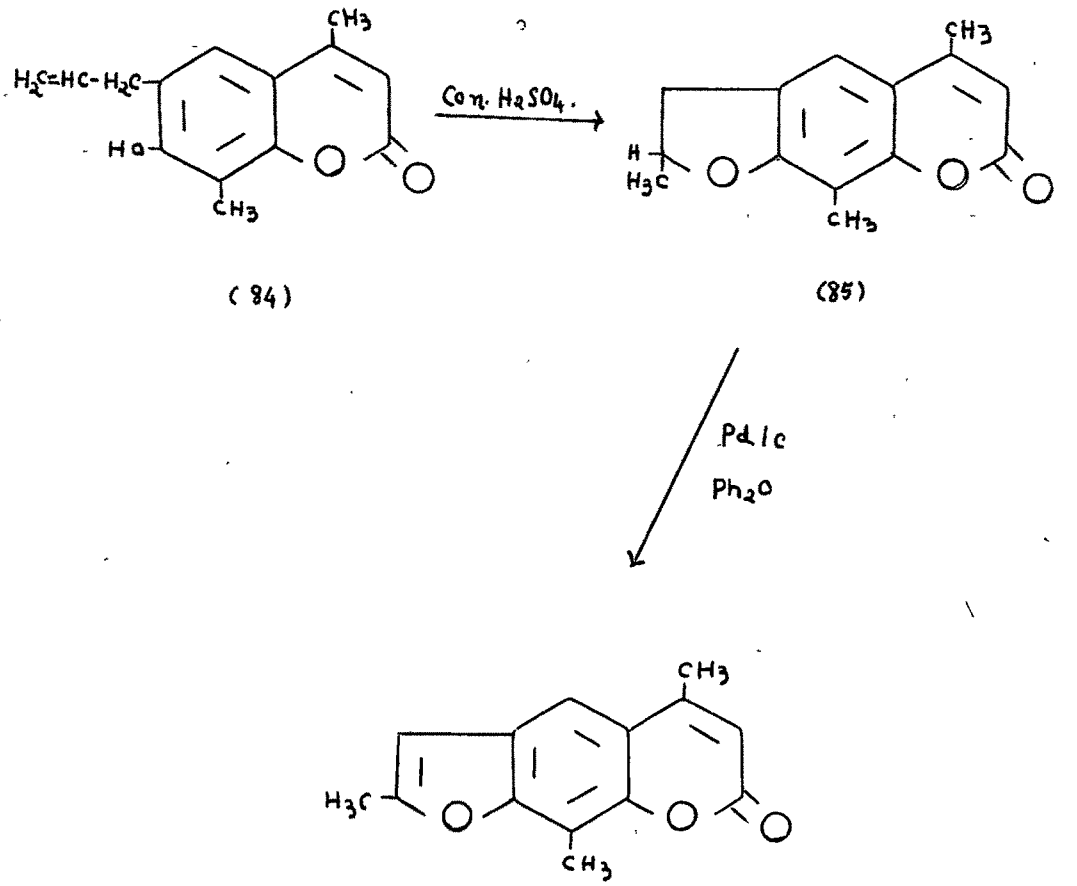
a: R = CH_3
b: R = H

(82)



R = Cl, Br, CN, $N(CH_3)_2$, NH_2 etc.

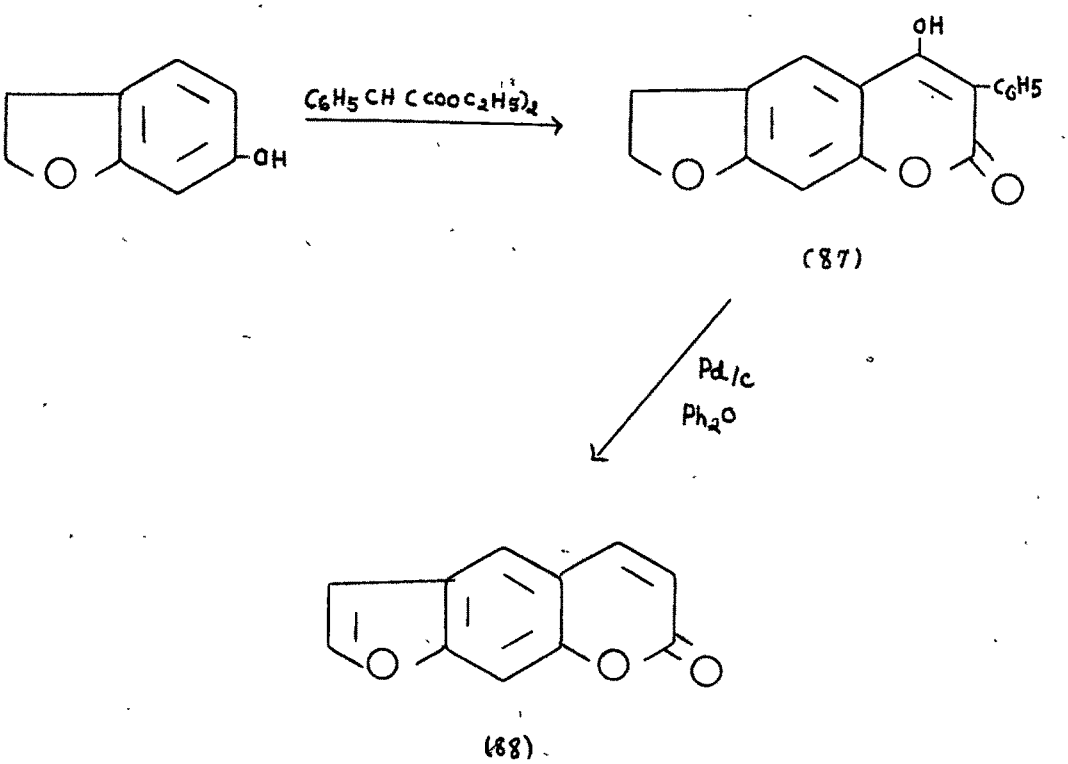
(83)



(84) (85)

Goudou and Blanchecotte[55] have condensed 6-hydroxy-coumaran and phenyl diethyl malonic ester in diphenyl ether and obtained 4',5'-dihydro-4-hydroxy-3-phenyl-furo-2',3',6,7-coumarin (87), which was then dehydrogenated with palladised charcoal to give 4-hydroxy-3-phenyl psoralene (88).

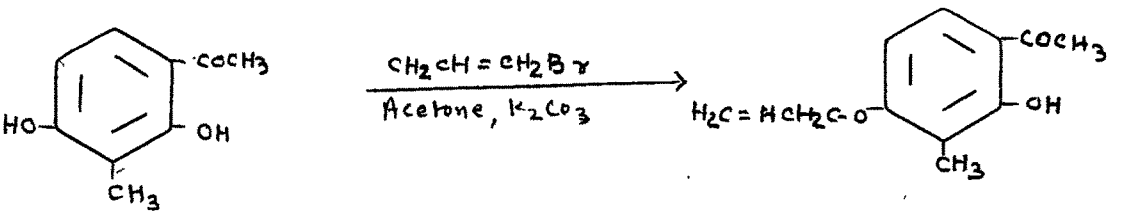
Dholakia and Trivedi[56] also synthesised 4-methoxy-5',8-dimethyl psoralene (95) and 4-hydroxy-5',8-dimethyl psoralene (96). 2,4-Dihydroxy-3-methyl acetophenone (89) was



(87)

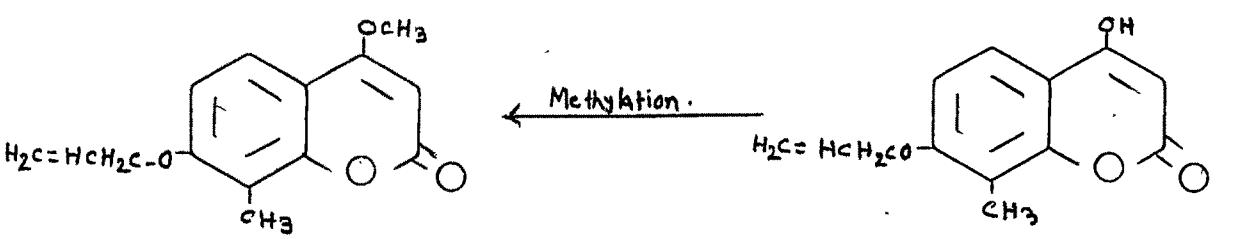
(88)

allylated with allyl bromide to 4-allyloxy-2-hydroxy-3-methyl acetophenone (90), which was treated with pulverised sodium and diethyl carbonate to give 4-hydroxy-7-allyloxy-8-methyl-coumarin (91). This coumarin (91) was methylated and the methyl ether (92) was subjected to Claisen rearrangement by refluxing it with diethylaniline to yield 4-methoxy-6-allyl--7-hydroxy-8-methylcoumarin (93). Cyclisation of (93) by triturating it with conc. sulphuric acid gave 4-methoxy-5',8-dimethyl-4',5'-dihydro psoralene (94), which on dehydrogenation with palladised charcoal afforded 4-methoxy-5',8-dimethyl psoralene (95). It underwent demethylation to 4-hydroxy-5',8-dimethyl psoralene (96) when refluxed with conc. hydrochloric acid.



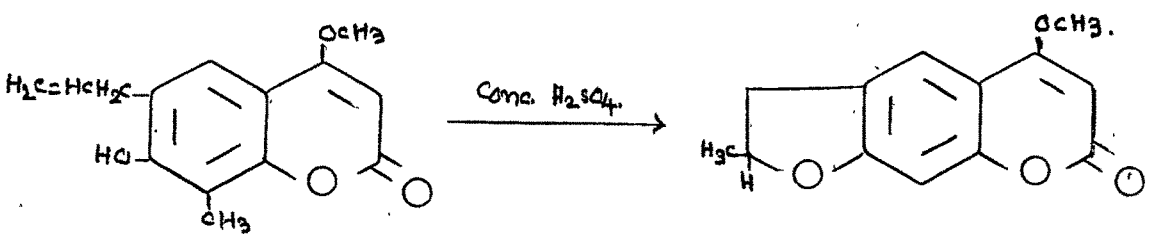
(89) (90)

Diethyl Carbonate
Na

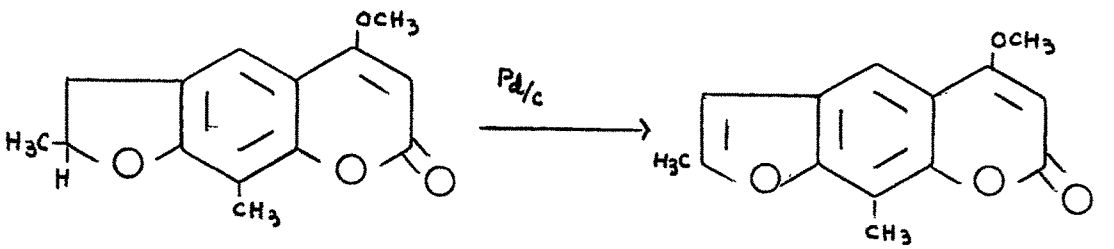


(92) (91)

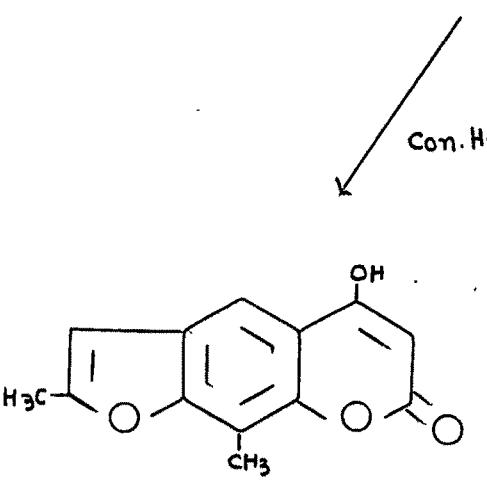
Diethyl aniline.



(93) (94)

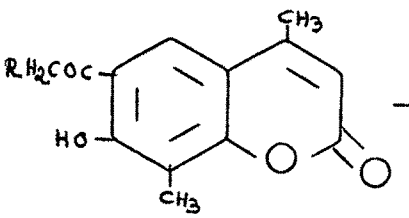


(94) (95)



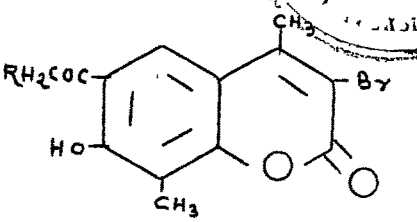
(96)

Shaikh and Trivedi[57] prepared 4-hydroxy-4',8-dimethyl-psoralene (100a) and 4-hydroxy-3,8,4'-trimethyl psoralene (100b). 4,8-Dimethyl-7-hydroxy-6-acylcoumarin (97) on bromination followed by hydrolysis with sodium carbonate solution gave 3,7-dimethyl-6-hydroxy-5-acylcoumarone (98) and 3,7-dimethyl-6-hydroxy-5-acylcoumarone-2-carboxylic acid (99). (98)When heated with pulverised sodium and ethyl carbonate afforded (100a) and (100b).



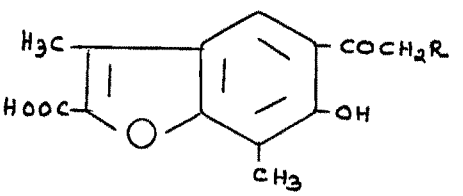
(97)

Bromination



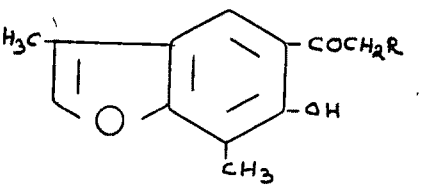
Hydrolysis

Na_2CO_3 10%



(99)

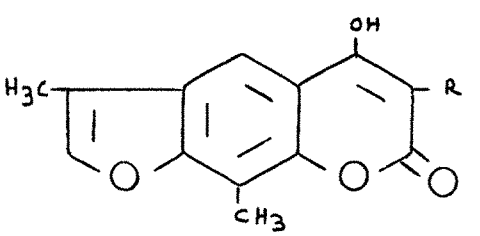
+



(98)

Diethyl Carbonate

Na.

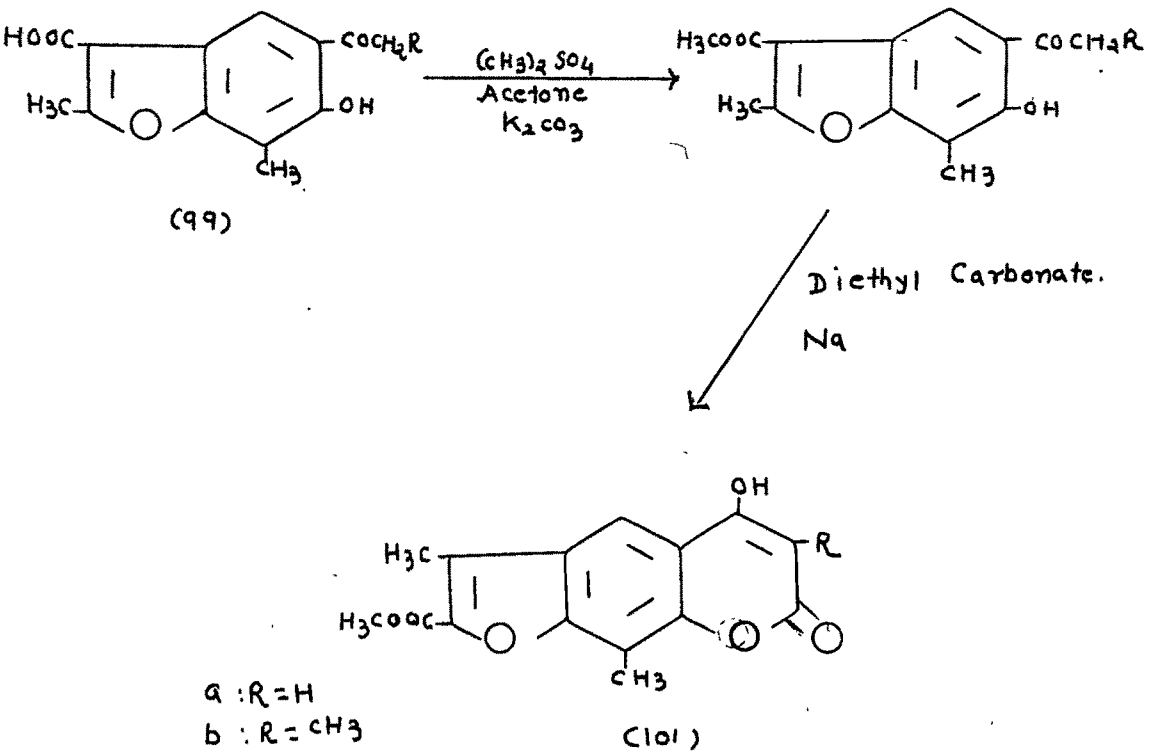


a: R = H

b: R = CH_3

(100)

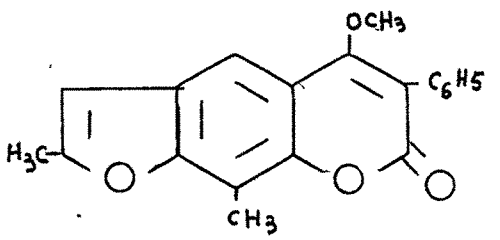
Esterification of (99) with dimethyl sulphate in the presence of sodium bicarbonate and acetone followed by reaction with pulverised sodium and diethyl carbonate yielded (101a) and (101b) as follows :-



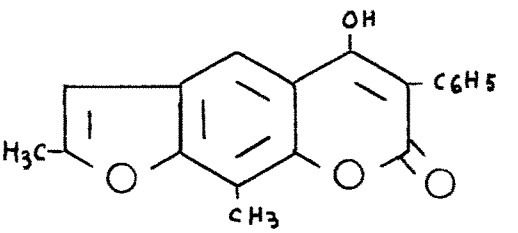
They have also prepared 2,9-dimethyl-5-methoxy-6-phenyl-7-oxo-7H-furo(3,2-g)benzopyran (102) and 2,9-dimethyl-5-hydroxy-6-phenyl-7-oxo-7H-furo(3,2-g)benzopyran (103) using the procedure of Dholakia and Trivedi[76].

By using the same procedure they have synthesised 2,9-dimethyl-7-oxo-7H-furo(3,2-g)benzo (c)benzopyran (104), 9-methyl-5,6-cyclohexeno-7-oxo-7H-furo(3,2-g)benzopyran (105),

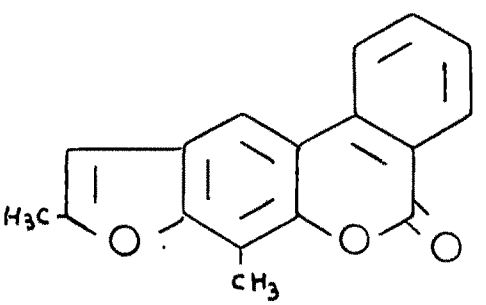
2,9-dimethyl-5,6-cyclopenteno-7-oxo-7H-furo(3,2-g)benzopyran (106) and 9-methyl-5,6-cyclopenteno-7-oxo-7H-furo(3,2-g)benzopyran (107).



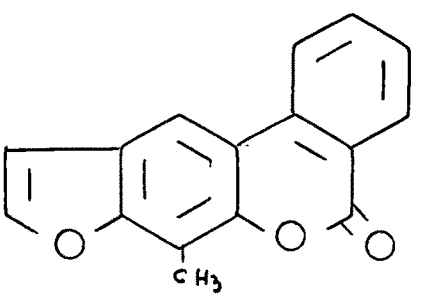
(102)



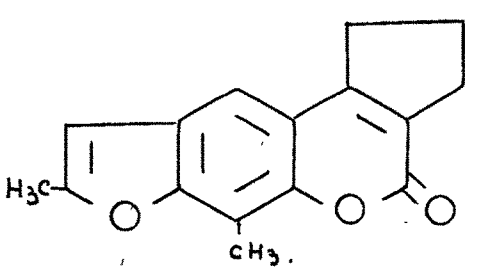
(103)



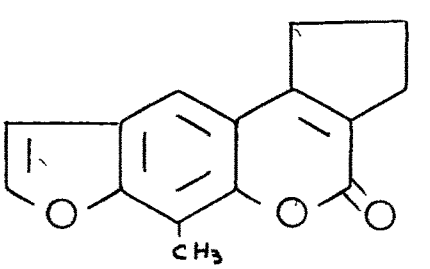
(104)



(105)

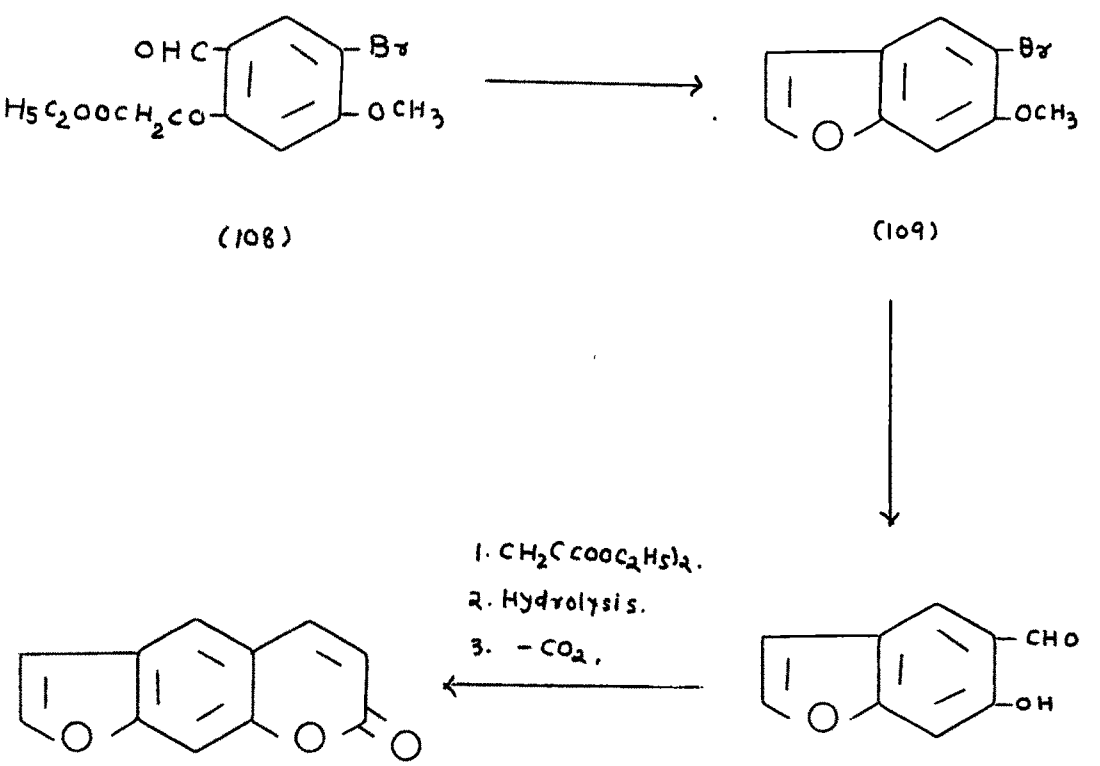


(106)



(107)

Kaufmann and co-workers[58] have developed a new synthetic route to synthesise psoralene. Bromination of ethyl(2-formyl-5-methoxyphenoxy)acetate gave the 4-bromo derivative (108) which was saponified and simultaneously cyclised and decarboxylated to 5-bromo-6-methoxybenzofuran (109). Lithium bromide interchange and then formylation and demethylation gave 5-formyl-6-hydroxybenzofuran (110) which was condensed with diethyl malonate to furnish psoralene, after hydrolysis and decarboxylation of the Knoevenagel product.

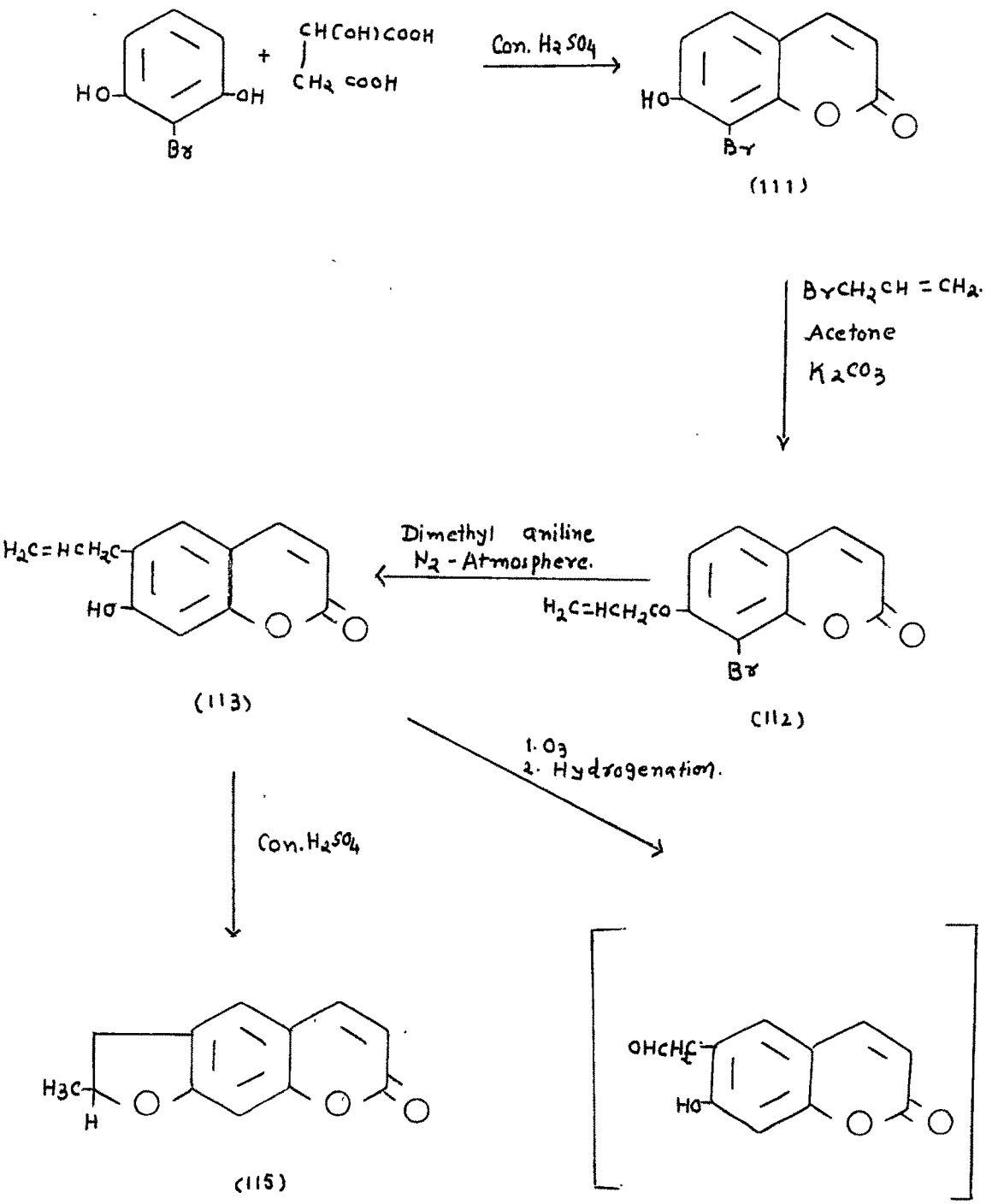


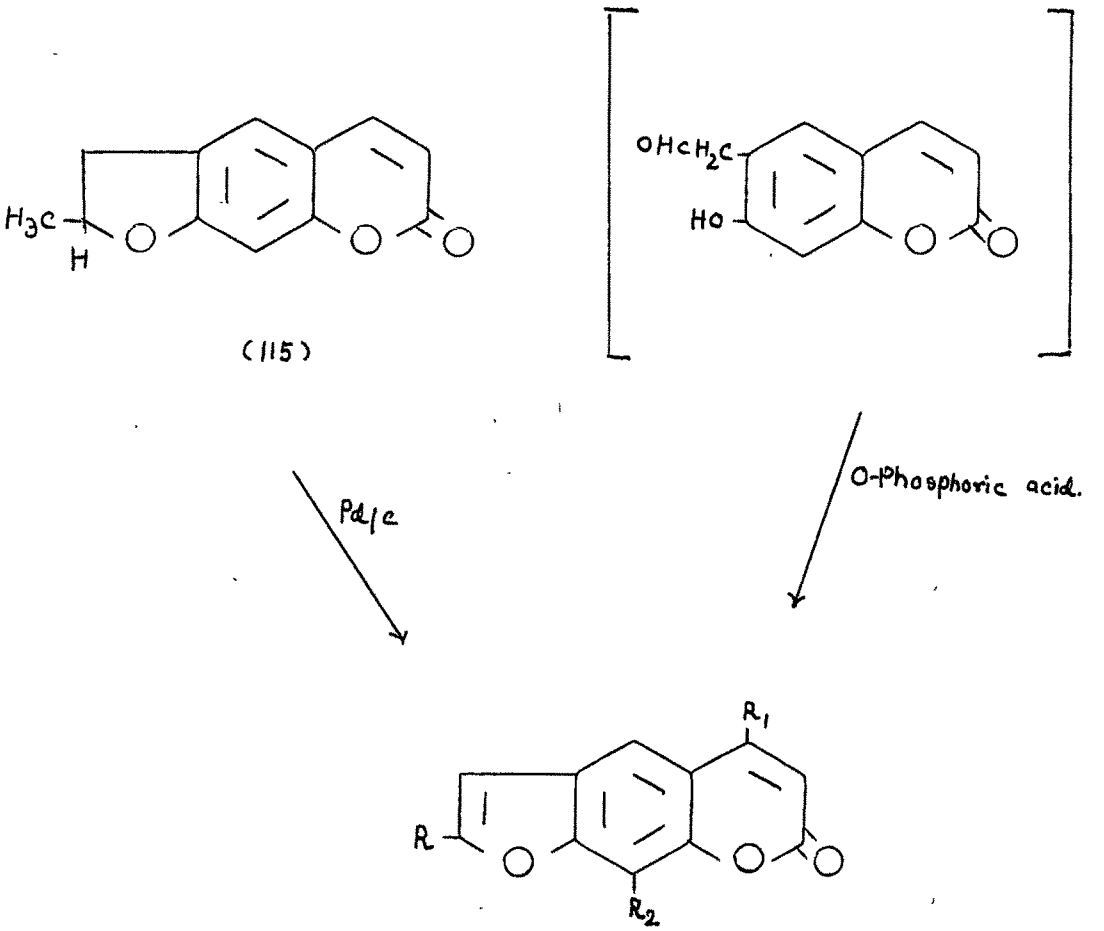
(108) (109)

Recently Pardanani and Trivedi[59] have synthesised psoralene and alkyl psoralenes using 2-bromo-resorcinol as the starting material. Pechmann condensation of 2-bromo-resorcinol with malic acid gave 7-hydroxy-8-bromocoumarin (111) which on allylation with allyl bromide afforded 7-allyloxy-8-bromocoumarin (112). This when refluxed with dimethyl aniline in an inert atmosphere of nitrogen underwent Claisen rearrangement to give 6-allyl-7-hydroxycoumarin (113). The structure of which was confirmed on the basis of NMR and Infra-red spectra. Ozonolysis of (113) gave an acetaldehydo derivative which when cyclised with o-phosphoric acid gave psoralene (114a). (113) was also cyclised with conc. sulphuric acid to give dihydro psoralene derivative (115), which was dehydrogenated with palladised charcoal in diphenyl ether to furnish 2-methyl-7-oxo-7H-furo(3,2-g)benzopyran (114b). Pechmann condensation of 2-bromo-resorcinol with ethylacetoacetate and ethyl benzoylacetate gave 7-hydroxy-8-bromo-4-methylcoumarin and 7-hydroxy-8-bromo-4-phenylcoumarin respectively, when when subjected to the above series of reactions gave (114c), (114d) and (114e).

They[60] have also synthesised psoralene derivatives by a different method. Pechmann condensation of 2-methyl-resorcinol with ethylbenzoyl acetate gave 7-hydroxy-8-methyl-4-phenylcoumarin (116) which on acylation followed by Fries migration, gave 7-hydroxy-6-acyl-8-methyo-4-phenyl-coumarin (117). Condensation of (117) with ethyl bromo acetate, followed by hydrolysis and cyclisation gave the corresponding

psoralene derivatives (118).





(115)

(114)

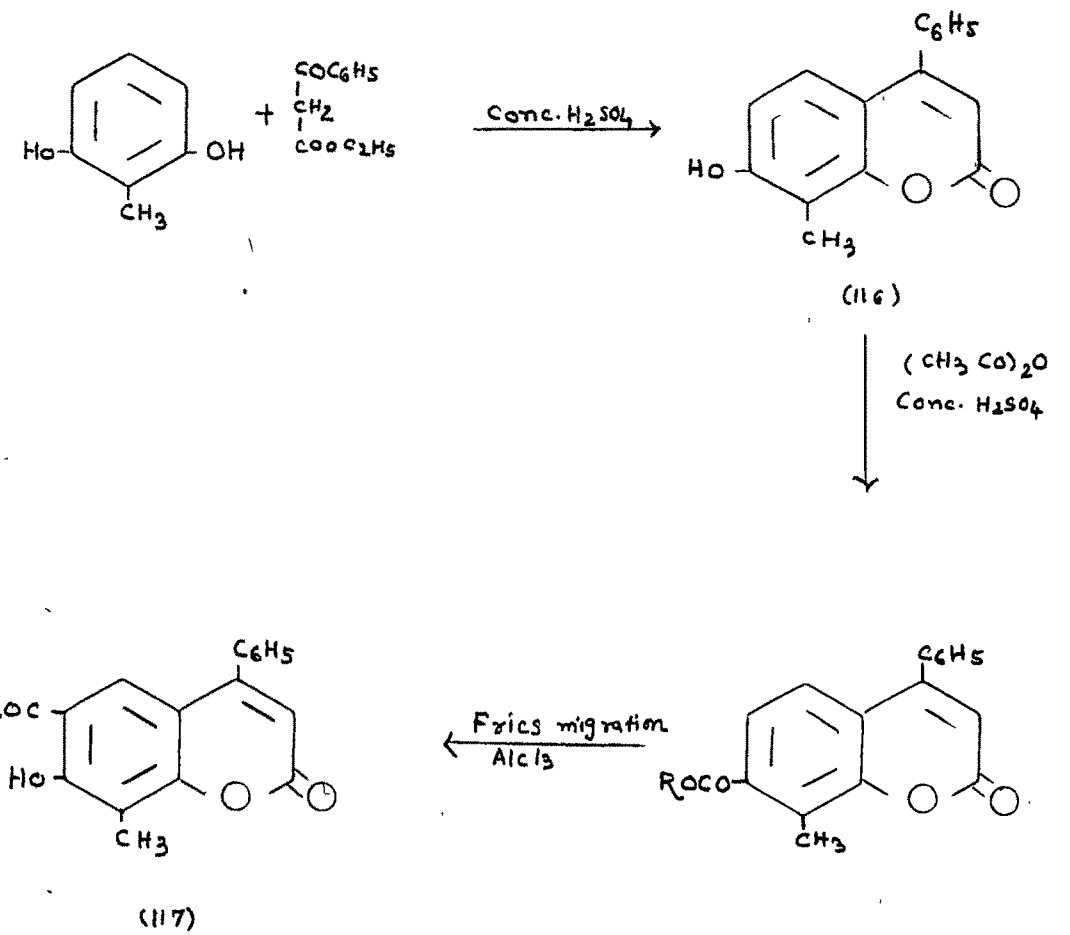
114 a, R = R_1 = R_2 = H.

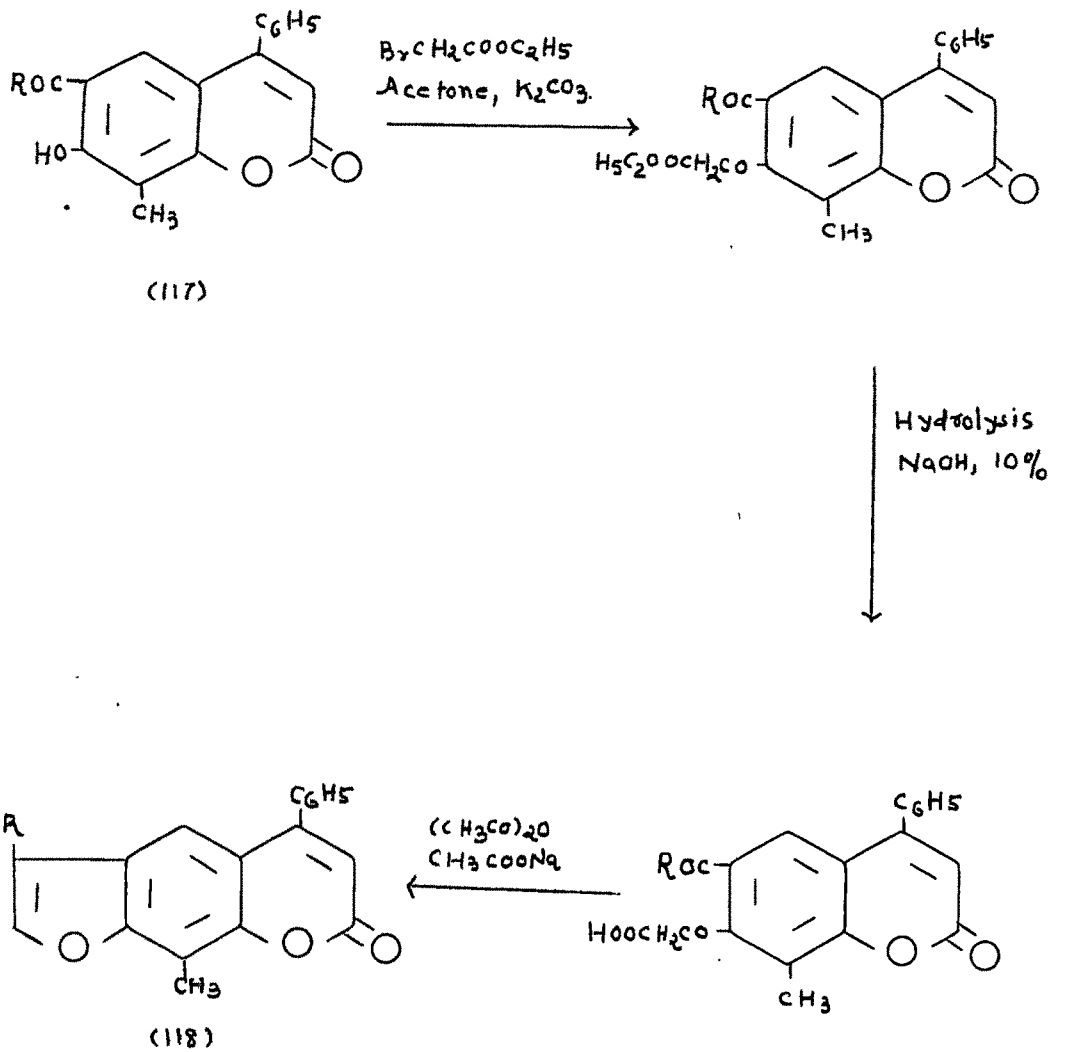
b, R = $-CH_3$; R_1 = R_2 = H.

c, R = R_2 = H; R_1 = $-CH_3$.

d, R = R_1 = $-CH_3$; R_2 = H.

e, R = H; R_1 = $-C_6H_5$; R_2 = $-CH_3$.


HO
OH
CH3
COC6H5
CH2
COOC2H5
Conc. H2SO4
C6H5
HO
CH3
(116)
(CH3CO)2O
Conc. H2SO4
C6H5
ROCO
CH3
Fries migration
AlCl3
C6H5
ROC
HO
CH3
(117)



From the above review, it sis evident that the synthesis of furocoumarin of type (D), having no substituent has not been reported still. It was therefore, thought of interest to prepare (122) by route developed by Seshadri and co-workers and to evaluate its psoralene-like photo-sensitizing activity.

Synthesis of 7H-furo[3,2-f][1]benzopyran-7-one (122) :

6-Hydroxycoumarin[61] (119) on allylation with allyl bromide in the presence of potassium carbonate in dry acetone afforded 6-allyloxycoumarin (120) which on refluxing with dimethyl aniline in an atomosphere of nitrogen underwent Claisen rearrangement to furnish 5-allyl-6-hydroxycoumarin (121). Two ortho position are free for allyl migration. The migrated compound was assigned as 5-allyl-6-hydroxycoumarin structure. This structure was supported by its nuclear magnetic resonance spectrum.(Fig. 1), which showed the following signals :

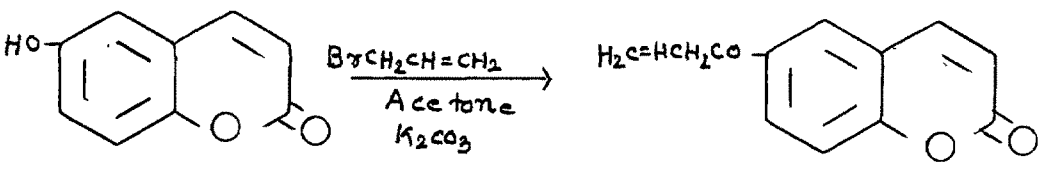
Chemical Shift (δ)	Coupling constant J(Cps)	Signals	Assignments
9.5	---	Singlet	1H, hydroxylic proton at position 6.
7.17 and 7.00	8	Doublet	2H, aromatic proton at H7 and H8.
6.35	10	Doublet	2H, proton at H3 and H4.
7.95	10	Doublet	2H, proton at H3 and H4.
6.1-5.7	---	Multiplet	1H, =CH group
5.1	1	Multiplet	2H, $=CH_2$ group
4.82	1	Multiplet	2H, $=CH_2$ group (Visible long range coupling).
3.62	---	Doublet	2H, $-CH_2-CH=$

The two proton doublets at δ 7.17 and δ7.0 indicate that the two aromatic protons at H7 and H8 are reee to couple. If it were 7-allyl-6-hydroxycoumarin (121), NMR spectrum should have shown two singlets for proton at H5 and H8 for that structure.

6-Hydroxy-5-allylcoumarin (121) was dissolved in ethyl acetate and vigorously shaken with osmium tetroxide[62] in water. Working up the reaction mixture, the 5-formylmethyl--6-hydroxycoumarin was obtained, which after purification by running it over alumina was directly cyclised with o-phosphoric acid to 7H-furo [3,2-f] [1] benzopyran-7-one (122). The Infra-red spectrum of aldehyde shows the band at 1700 (aldehyde >C=O group) and a broad band at 3420 cm^{-1} (aromatic hydroxy group)(Fig. 2). The I.R. spectra of (122) showed a strong band at 1740 cm^{-1} (lactonyl >C=O group) and at 890 cm^{-1} (furan ring)(Fig. 3).

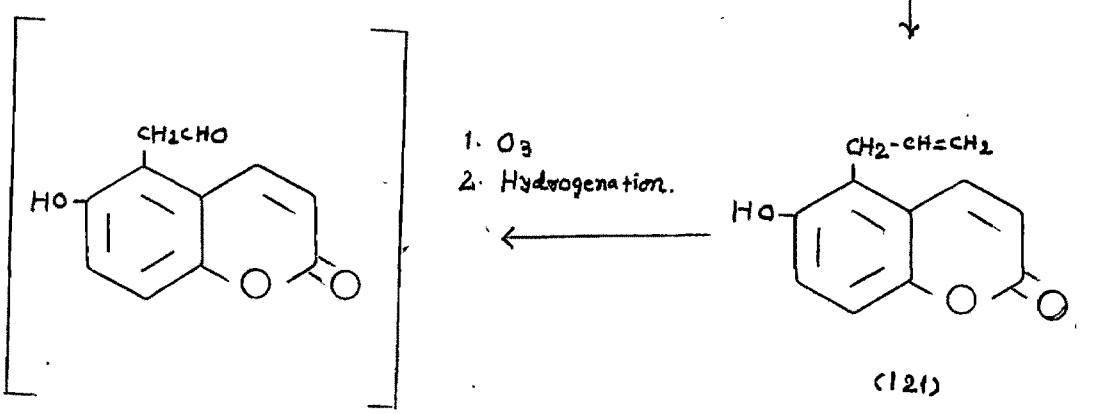
Synthesis of 2-methyl-7H-furo [3,2-f][1] benzopyran-7--one (124). :

6-Hydroxy-5-allylcoumarin (121) on trituration with conc. sulphuric acid gave 2-methyl-2,3-dihydro-7H-furo [3,2-f] [1] benzopyran-7-one (123), which was dehydrogenated to 2-methyl-7H-furo [3,2-f] [1] benzopyran-7-one (124) by refluxing (123) with diphenyl ether using palladised charcoal as catalyst.



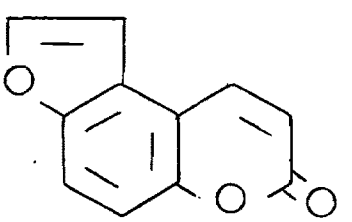
(119) (120)

Dimethyl aniline.

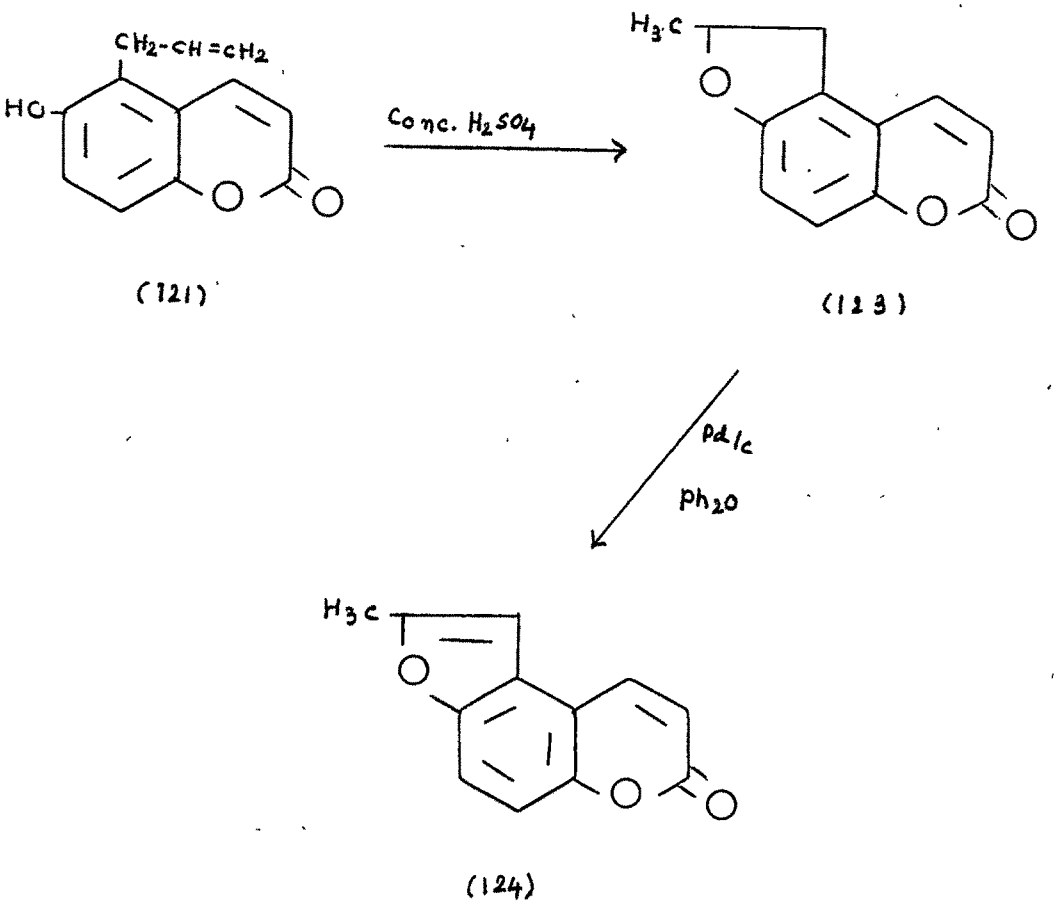


(121)

O-Phosphoric acid



(122)



(121) (123)

(124)

From the theoretical part review, it is also evident that furo benzo-α-pyrone, particularly of type (F) are of immense importance due to their valuable therapeutic properties and applicability.

The synthesis of linear furocoumarins is not easy because whenever substitution reaction is carried out on benzofuran, 2-position being very reactive is invariably attacked, while in the case of umbelliferone, 8-position is

attacked. It has been observed by Krishnaswamy and Seshadri[63] that Claisen rearrangement of 7-allyloxy-coumarin and 7-allyloxy-4-methylcoumarin gives exclusively 8-allyl isomer. It was therefore, thought of interest to study Claisen rearrangement of 7-hydroxycoumarins in which 8-position is blocked by a removable group like bromine, so that migration takes place to 6-position.

In continuation of work carried out by Pardanani and Trivedi[59] for the synthesis of psoralene derivatives using 2-bromo-resorcinol as the starting material, the present work was undertaken as an extension for the synthesis of several other psoralene derivatives using the same starting material 2-bromo-resorcinol.

The following psoralene derivatives were synthesised :

1. 2-Methyl-5-phenyl-7H-furo [3,2-g][1] -benzopyran-7-one (129).
2. 9-Methyl-5H-benzofuro [6,5-c][1] benzopyran-5-one (134).
3. 9-Methyl-1,2,3,4-tetrahydro-5H-benzofuro [6,5-c][1] benzopyran-5-one (137).
4. 8-Methyl-1,2,3,4-tetrahydro cyclopenta [c] furo [3,2-g] benzopyran-4-one (144).

<u>Synthesis of 2-methyl-5-phenyl-7H-furo[3,2-g][1] benzo-pyran-7-one</u> (129) :

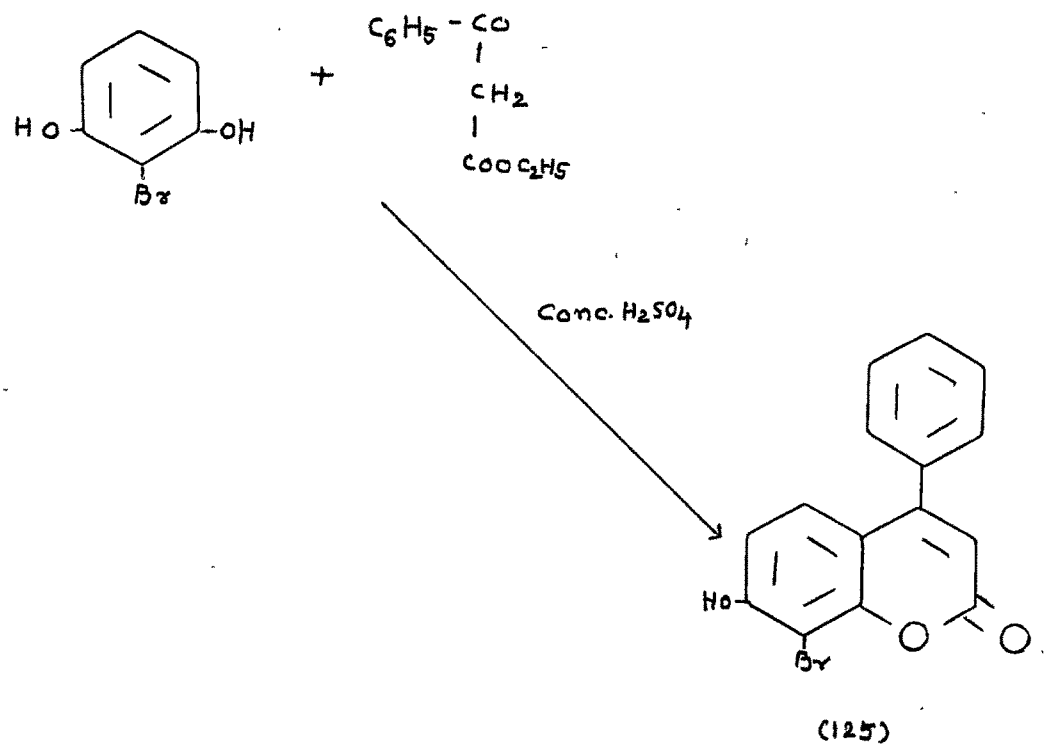
Pechmann condensation of 2-bromo-resorcinol[64] with ethyl benzoyl acetate in the presence of conc. sulphuric acid as condensing agent gave 7-hydroxy-8-bromo-4-phenyl-coumarin (125), which on allylation with allyl bromide in

the presence of anhydrous potassium carbonate and dry acetone afforded 7-allyloxy-8-bromo-4-phenylcoumarin (126). The I.R. spectrum of (126) showed a band at 1720 $cm.^{-1}$ (lactonyl>C=O group) at 1270 $cm.^{-1}$ (aromatic ether linkage) and at 940 $cm.^{-1}$ ($=CH_2$ group). (Figure 4). 7-Allyloxy-8-bromo-4-phenyl-coumarin (126) was subjected to Claisen rearrangement by refluxing it with dimethyl aniline in an inert atmosphere of nitrogen. It was observed that the product, which was obtained after Claisen rearrangement was soluble in alkali and did not show the presence of bromine. The compound was assigned the structure 6-allyl-7-hydroxy-4-phenylcoumarin (127), on the basis of its NMR spectra (Fig. 5). The NMR spectra of (127) ($CDCl_3$-Me_2SO) are as follows :-

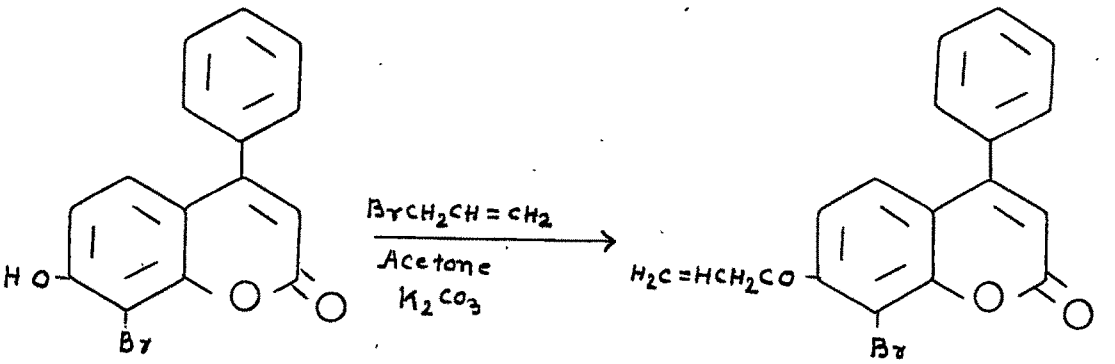
Chemical Shift (δ)	Coupling constant J(Cps)	Singnals	Assignments
10.15	-	Singlet	1H, hydroxylic proton at position 7.
7.52	-	Singlet	5H, Phenyl group at position 4.
7.2	-	Singlet	1H, at position 5
6.8	-	Singlet	1H, at position 8
6.1	-	Singlet	1H, at position 3
5.9-5.75	-	Multiplet	1H, = CH group.
5.1-4.8	1	Doublet	2H, = CH_2 group.
3.35	-	Doublet	2H, = $CH\underline{CH_2}$ group.

The I.R. spectrum of (127) showed the sharp band in the carbonyl region, viz., 1680 $cm.^{-1}$ (lactonyl >C=O group), broad band at 3500 $cm.^{-1}$ (aromatic hydroxyl group)(Fig. 6).

7-Hydroxy-6-allyl-4-phenylcoumarin (127) on trituration with conc. sulphuric acid gave 2-methyl-5-phenyl-2,3-dihydro-7H-furo [3,2-g] [1] benzopyran-7-one (128), which was dehydrogenated to 2-methyl-5-phenyl-7H-furo [3,2-g] [1] benzopyran-7-one (129) by refluxing (128) with diphenyl ether and palladised charcoal. The I.R. spectrum of (129) showed the band at 1710 $cm.^{-1}$ (lactonyl >C=O group) and at 870 $cm.^{-1}$ (furan). (Fig.7)

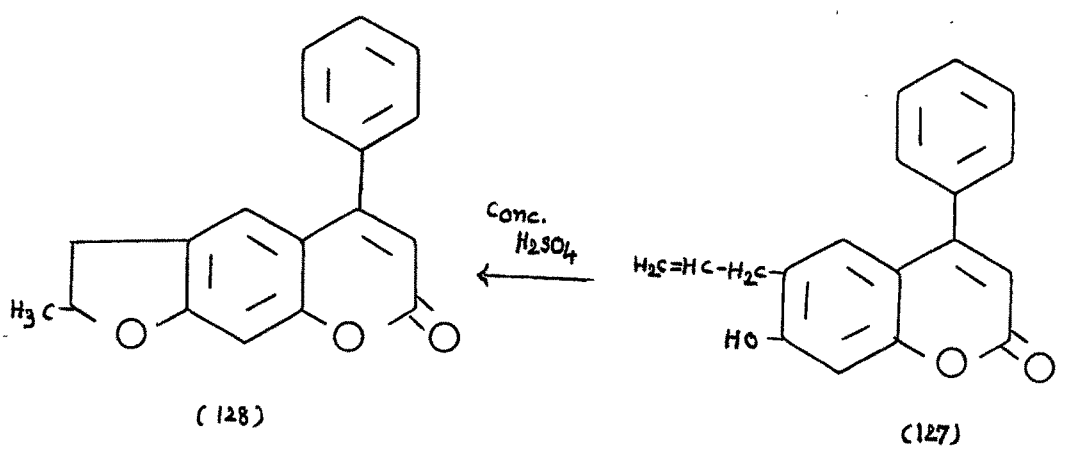


(125)

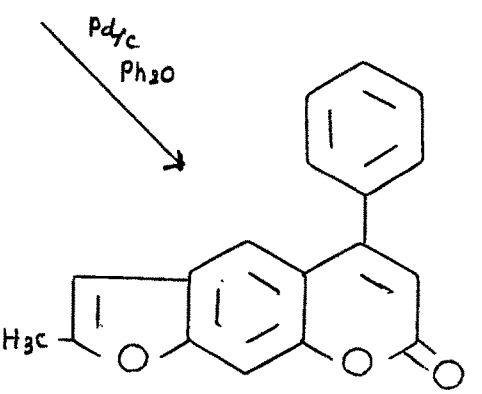


(125) (126)

Di methyl aniline.
N_2- atmosphere.



(128) (127)



(129)

Synthesis of 9-methyl-5H-benzofuro [6,5-c] [1] benzopyran -5-one (134) :

Pechmann condensation of 2-bromo-resorcinol with ethyl-2-oxo-cyclohexane-carboxylate in the presence of conc. sulphuric acid gave 4-bromo-3-hydroxy-7,8,9,10-tetrahydro-6H-dibenzo [b,d] pyran-6-one (130). This on alkylation with allyl bromide in the presence of anhydrous potassium carbonate and dry acetone gave 3-allyloxy-4-bromo-7,8,9,10-tetrahydro-6H-dibenzo [b,d] pyran-6-one (131). 3-Allyloxy-4-bromo-7,8,9,10-tetrahydro-6H-dibenzo [b,d] pyran-6-one on Claisen rearrangement in the presence of nitro atmosphere gave 2-allyl-3-hydroxy-7,8,9,10-tetrahydro-6H-dibenzo [b,d] pyran-6-one (132). The structure of (132) was supported by its NMR spectrum ($CDCl_3$), which shows the following signals (Fig. 8)

Chemicals shifts (δ) ppm.	Coupling constant J (Cps).	Signals	Assignments
1.7	-	Singlet	4H(2 x 2H) at position 8 and 9.
3.42	-	Triplet	2H, at position 7.
7.0	-	Singlet	1H, aromatic proton at position 1.
7.2	-	Singlet	1H, aromatic proton at position 4.
5.0	9Hz	Doublet	2H, Ar-CH_2CH=$\underline{CH_2}$
5.8	-	Multiplet	1H, Ar-$CH_2\underline{CH}$=CH_2
2.6	-	Doublet	4H(2 x 2H); 2H, Ar-$\underline{CH_2}$CH=CH_2. 2H of cyclohexane at position 10.

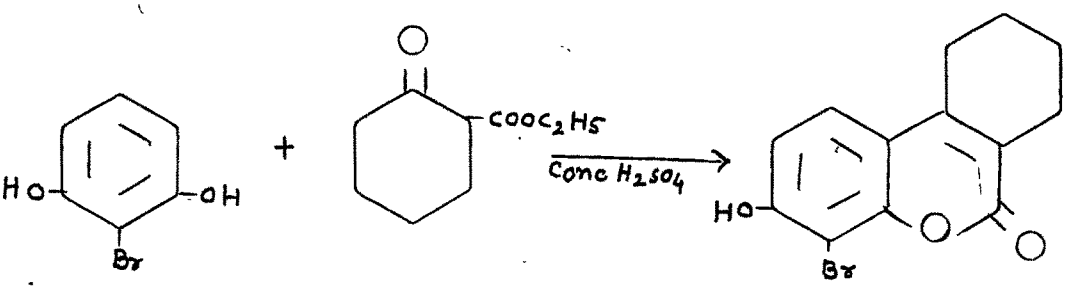
The compound (132), on ring closure with conc. sulphuric acid gave 9-methyl-1,2,3,4,9,10-hexahydro-5H-benzofuro [6,5-c] [1] benzopyran-5-one (133), which was dehydrogenated by refluxing it in diphenyl ether and palladised charcoal to 9-methyl-5H-benzofuro [6,5-c] [1] benzopyran-5-one (134).

Synthesis of 9-methyl-1,2,3,4-tetrahydro-5H-benzofuro [6,5,-c] [1] benzopyran-5-one (137) :

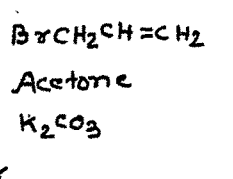
When the dehydrogenation of (133) was carried out with palladised charcola, dehydrogenation of dihydrofuran ring as well as dehydrogenation of cyclohexene ring also took place simultaneously, hence the compound (137) was prepared according to the Kaufmann s method[35], which comprised of acetylation of 2-allyl-3-hydroxy-7,8,9,10-tetrahydro-6H,dibenzo [b,d] pyran-6-one (132) to 2-allyl--6-oxo-7,8,9,10-tetrahydro-6H-dibenzo [b,d] pyran-3-yl acetate (135), addition of bromine to the allylic double bond and subsequent ring closure of 2-(2',3'-dibromopropyl)--6-oxo-7,8,9,10-tetrahydro-6H-dibenzo [b,d] pyran-3-yl acetate (136), with ethanolic potassium hydroxide.

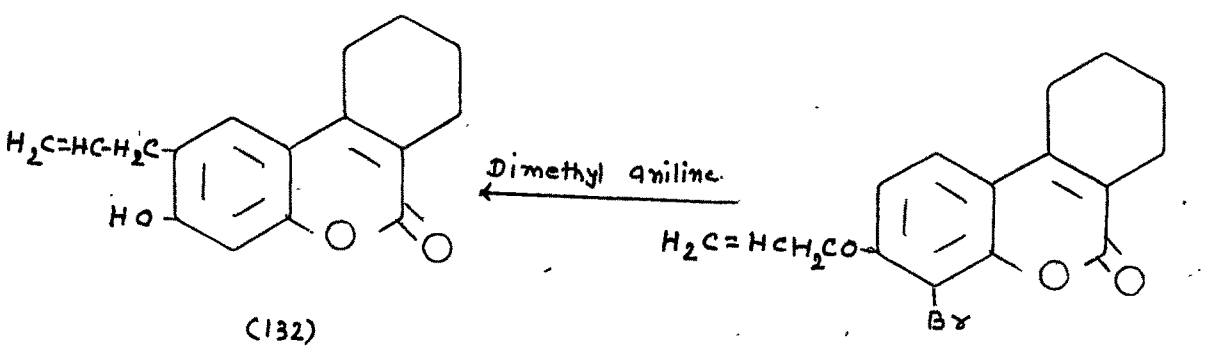
Synthesis of 8-methyl-1,2,3,4-tetrahydrocyclopenta [c] furo [3,2-g] [1] benzopyran-4-one (144) :

2-Bromo-resorcinol on similar condensation with ethyl-2-oxo-cyclopentane-carboxylate, gave 6-bromo-7-hydroxy-1,2,3,4-tetrahydrocyclopenta [c] [1] benzopyran--4-one (138), which on allylation with allyl bromide in anhydrous potassium carbonate and dry acetone afforded



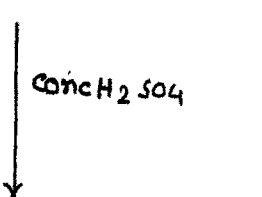
(130)

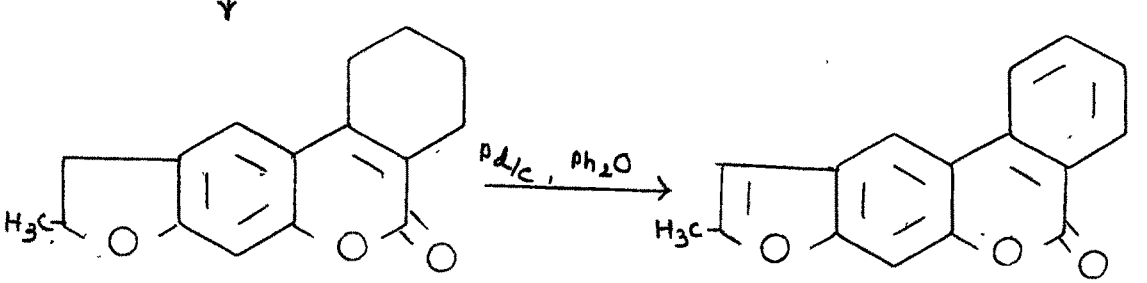




(132)

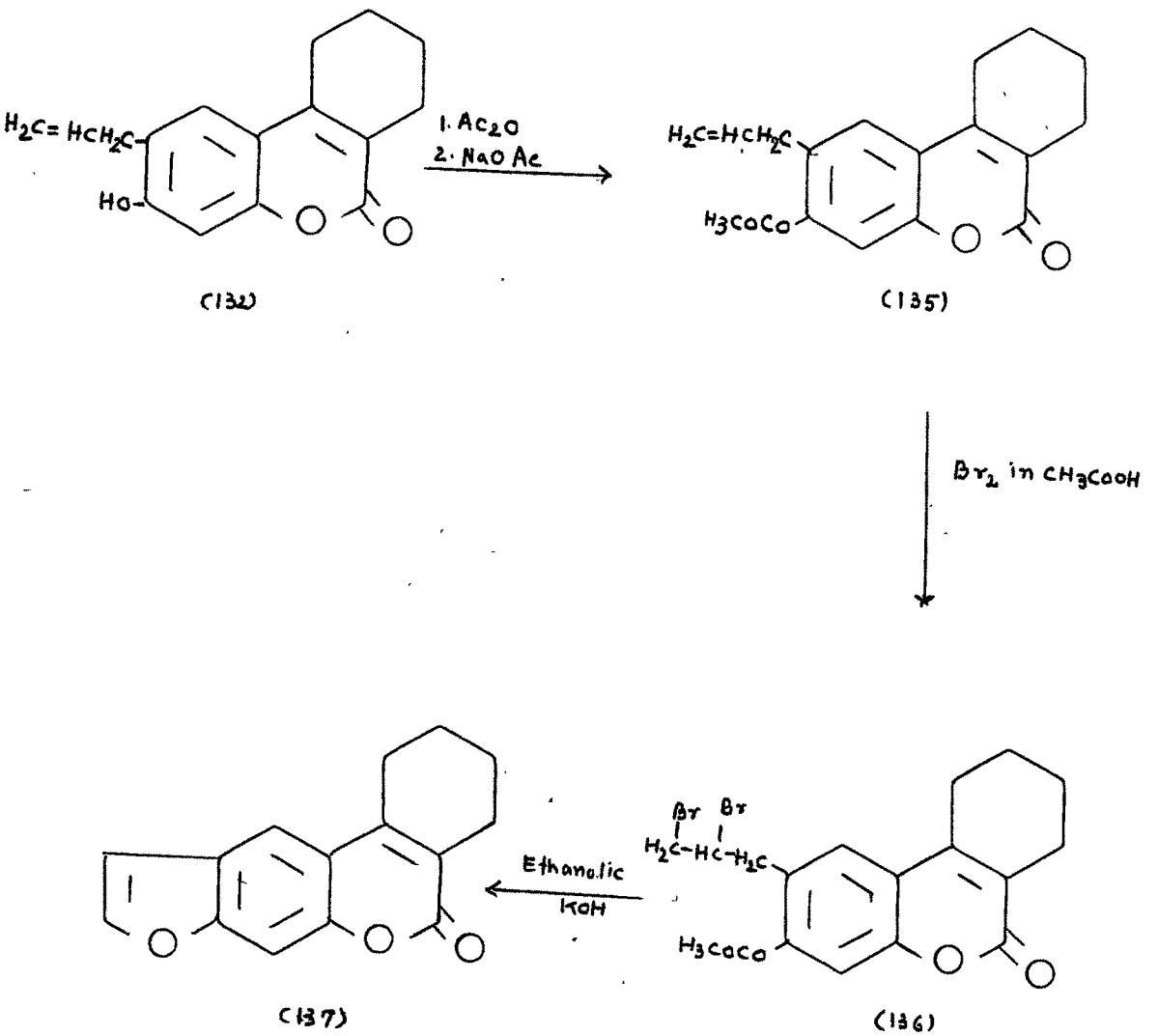
(131)





(133)

(134)



(132) (135) (136) (137)

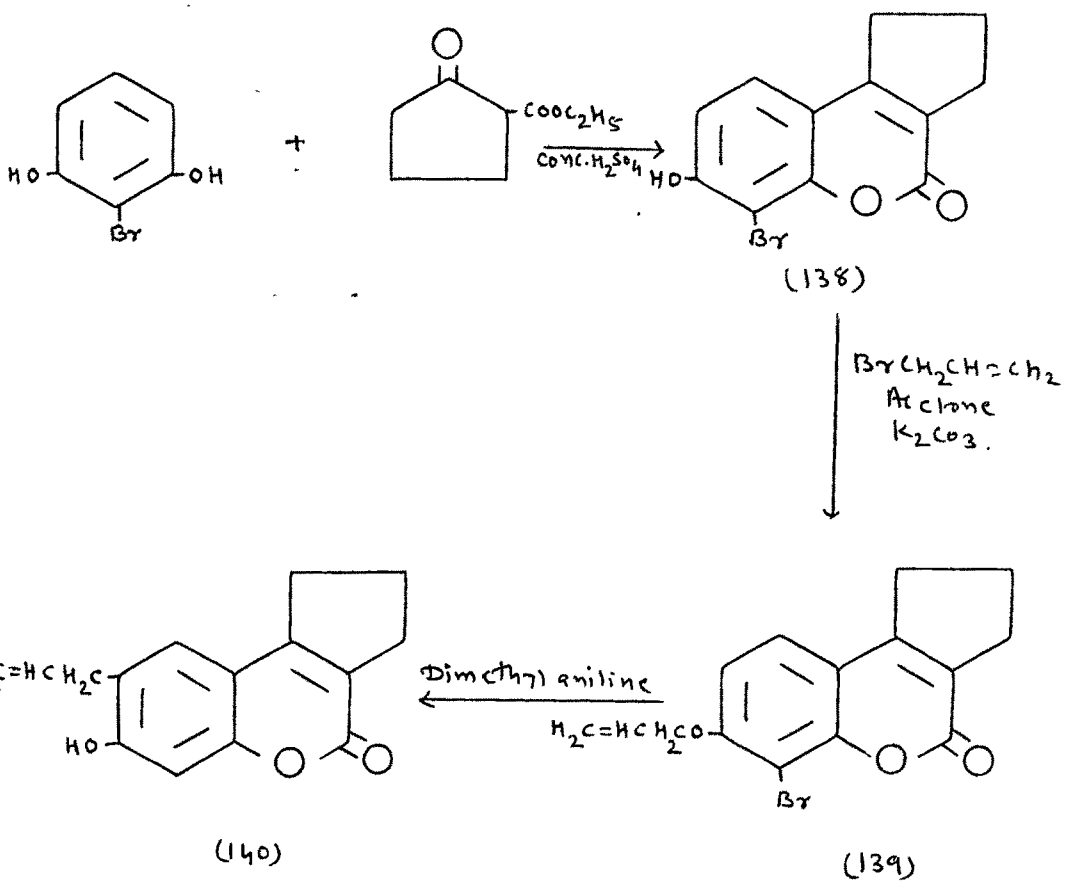
7-allyloxy-6-bromo-1,2,3,4-tetrahydrocyclopenta [c] [1] benzopyran-4-one (139), which on Claisen migration afforded 8-allyl-7-hydroxy-1,2,3,4-tetrahydrocyclopenta [c] [1]benzo-pyran-4-one (140). The NMR spectrum of (140) showed the following signals which confirmed the structure of (140)

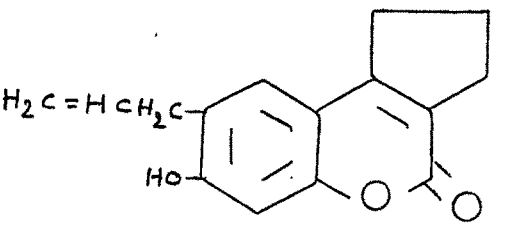
as 8-allyl-7-hydroxy-1,2,3,4-tetrahydrocyclopenta [c] [1] benzopyran-4-one. (Fig.9)

Chemicals Shifts (δ) ppm.	Coupling constant J (Cps).	Signals	Assignments
2.2	7Hz	Triplet	2H at position 1.
3.4	7Hz	Triplet	2H at position 3.
6.8	-	Singlet	1H at position 9.(aromatic)
7.1	-	Singlet	1H at position 6. (aromatic)
2.5-3.0	-	Multiplet	4H, 2H at position 2 and 2H of allyl group at position 8, Ar-$\underline{CH_2}$-CH=CH_2.
5.1	2Hz	Doublet	2H of allyl group at position 8, Ar-CH_2-CH=$\underline{CH_2}$.
5.7-612	12Hz	Multiplet	1H of allyl group at position 8 Ar-CH_2-$\underline{CH}$=CH_2.

The compound (140) on ring closure with conc. sulphuric acid gave 8-methyl-1,2,3,4,8,9-hexahydrocyclopenta [c] furo [3,2-g] [1] benzopyran-4-one (141). The compound (141) did not undergo dehydrogenation with palladised charcoal in diphenyl ether as it gave the original compound back and hence the desired compound 8-methyl-1,2,3,4-tetrahydrocyclopenta [c] furo [3,2-g] benzopyran-4-one (144) was prepared according to the method of Kaufmann[36]. The migrated compound (140) was acetylated with acetic anhydride and sodium acetate 8-allyl-4-oxo-1,2,3,4-tetrahydrocyclopenta [c] benzopyran-7-yl acetate (142), which showed two band in I.R. spectrum, viz., 1760 $cm.^{-1}$ (acetoxy group at position 7) and at 1710 $cm.^{-1}$ (lactonyl >C=O group).(Fig. 10).

The compound (141) on bromination with bromine in acetic acid gave 8-(2',3'-dibromopropyl)-4-oxo-1,2,3,4-tetrahydrocyclopenta [c] benzopyran-7-yl acetate (143), which on ring closure with ethanolic potassium hydroxide furnished 8-methyl-1,2,3,4-tetrahydrocyclopenta [c] furo [3,2-g] [1] benzopyran-4-one (144). The I.R. spectrum of (144) showed the sharp band at 1700 cm^{-1} (lactonyl >C=O group) and at 860 cm^{-1} (furan). (Fig. 11).

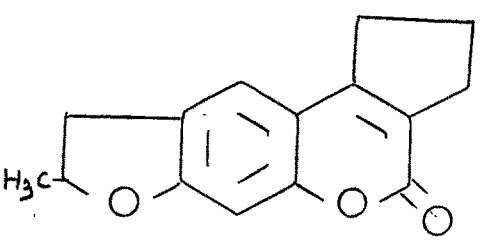




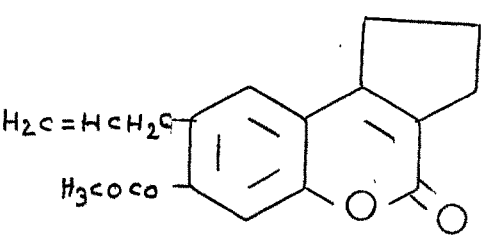
(140)

Conc. H_2SO_4

Ac_2O NaOAc.



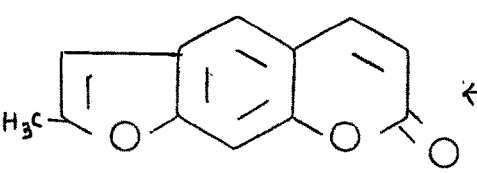
(141)



(142)

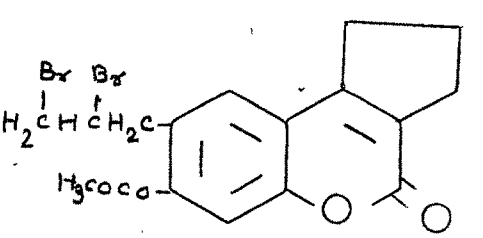
$Pd/_C$ Ph_2O

Br_2 in Acetic Acid



(144)

Ethanolic KOH



(143)

EXPERIMENTAL.

The I.R. spectra were recorded on Perkin-Elmer 457 granting spectrophotometer in nujo.

The U.V. spectra were recorded on Beckmann DU-2 spectrophotometer.

The NMR spectra were recorded on Varian A-60 spectrophotometer using $CDCl_3$ (Fig. 8) and $CDCl_3$ + Me_2SO (Fig. 1, 5, 9) solvents with TMS as internal standard.

Synthesis of 7H-furo [3,2-f] [1] benzopyran-7-one (122) :

Allylation of 6-hydroxycoumarin : 6-Allyloxycoumarin (120) :

6-Hydroxycoumarin was prepared according to G.Bergillini and L. Monti[61].

Coumarin (4.7 g.) was dissolved in sodium hydroxide (5 g.; 50 ml.) by heating on steam bath. The solution was then cooled and potassium persulphate (7.5 g. in 150 ml.water) added gradually from a separated funnel during 3 hr. The solution was mechanically stirred and the temperature was not allowed to raise 10^{0}. After the addition was completed reaction mixture was stirred for half an hour more and left overnight. Next day it was just acidified and extracted with ether twice. The ether extract gave negligible quantity of the starting material. Excess of hydrochloric acid (conc. 100 ml.) was then added to the aqueous layer and the mixture was heated on steam bath for half an hour. The solid was separated during heating was filtered. After cooling, the solution, more product was obtained on extraction of the

filtrate with ether. It was recrystallised from alcohol, m.p. 250°.

A mixture of 6-hydroxycoumarin (2 g.), allyl bromide (2 ml.) and anhydrous potassium carbonate (6 g.) was refluxed in dry acetone (50 ml.) for 10 hr. After the evaporation of acetone, the residue was treated with water. The compound was filtered, washed with dilute hydroxide to remove unreacted product, dried and crystallised from benzene-petroleum ether, m.p. 90°. Yield 1.5 g.

Analysis : Found : C, 71.58; H, 4.83 %

$C_{12}H_{10}O_3$: requires : C, 71.28% H, 4.95 %.

I.R. spectrum 1720 cm^{-1} (lactonyl >C=O group), 1265 cm^{-1} (aromatic ether linkage).

Claisen rearrangement of 6-allyloxycoumarin : 6-Hydroxy-5-allylcoumarin (121) :

6-Allyloxycoumarin (1 g.) was refluxed with dimethylaniline (6 ml.) for 6 hr. in nitrogen atomosphere. The reaction mixture was poured into conc. hydrochloric acid (100 ml.) containing pieces of ice. The product was filtered and treated with sodium hydroxide solution, acidified and filtered. The product was dried and purified by passing its chloroform solution over a short column of alumina. It crystallised from chloroform, m.p. 172°. Yield 0.8 g.

Analysis : Found : C, 71.19 ; H, 4.80 %

$C_{12}H_{10}O_3$ requires : C, 71.28 ; H, 4.95 %.

I.R.spectrum : 1680 cm^{-1} (lactonyl >C=O group) and at 3300 cm^{-1} (aromatic hydroxy group).

7H-furo [3,2-f][1] benzopyran-7-one (122) :

A solution of 6-hydroxy-5-allylcoumarin (0.5 g.) in ethyl acetate was vigorously shaken with 50 mg. Osmium tetraxide in water (100 ml.). Potassium periodate (2 g. in 100 ml. water) was added during the period of two hr. Ethyl acetate layer was separated, dried and evaporated. The residue was dissolved in benzene and passed over alumina. Evaporation of solvent left a residue. This was treated with o-phosphoric acid (5 ml.) on a water bath for 1 1/2 hr. The contents were poured into ice water. The product extracted with ethyl acetate, washed with dilute sodium hydroxide solution and finally purified by chromatographing over alumina. It crystallised from benzene-petroleum ether, m.p. 231°. Yield 0.2 g.

Analysis : Found : C, 71.44 ; H, 3.67 %

$C_{11}H_6O_3$: requires: C, 70.98 ; H, 3.22 %.

I.R.specturm : 1740 cm^{-1} (lactonyl >C=O group), and at 890 cm^{-1} (furan ring).

$\lambda^{Methanol}_{max.}$: 252 nm (log e 3.96) and 300 nm (log e 3.64).

Synthesis of 2-methyl-7H-furo [3,2-f][1] benzopyran-7-one (124). : Cyclisation of 6-hydroxy-5-allylcoumarin : 2-Methyl-2,3-dihydro-7H-furo [3,2-f][1] benzopyran-7-one (123) :

6-Hydroxy-5-allylcoumarin (0.5 g.) was triturated

with conc. sulphuric acid for 1 hr. at room temperature. The contents were poured into crushed ice. The separated product was filtered, washed with dilute sodium hydroxide solution to remove original compound, and dried. It was purified by passing the benzene solution of it over a short column of alumina. The compound was crystallised from benzene-petroleum ether mixture, m.p. 104°. Yield 0.3 g.

Analysis : Found : C, 71.27 ; H, 4.84 %

$C_{12}H_{10}O_3$: requires : C, 71.28 ; H, 4.95 %.

Dehydrogenation of 2-methyl-2,3-dihydro-7H-furo [3,2-f] [1] benzopyran-7-one : 2-Methyl-7H-furo [3,2-f] [1] benzopyran-7-one (124) :

A mixture of 2-methyl-2,3-dihydro-7H-furo [3,2-f] [1] benzopyran-7-one (0.5 g.), palladised charcoal (0.3 g., 10 %) and diphenyl ether (5 ml.) was refluxed for 20 hr. The reaction mixture was filtered hot. The product separated on cooling, which was filtered and crystallised from diphenyl ether, m.p. 161°. Yield 0.3 g.

Analysis : Found : C, 71.58 ; H, 3.84 %

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

$\lambda_{max.}^{Methanol}$ 318 nm (log e 4.20).

Synthesis of 2-methyl-5-phenyl-7H-furo [3,2-g] [1] benzopyran-7-one (129) : Pechmann condensation of 2-bromo-resorcinol with ethyl benzoyl acetate : 8-Bromo-7-hydroxy-4-phenylcoumarin (129) :

2-Bromo-resorcinol was prepared according to Davi

and Havvington[64] as follows :

Liquid bromine (100 g.: 3 mole) was added dropwise constant stirring to a solution of resorcinol (22 g.) in water (500 ml.) kept in freezing mixture. The mixture was further stirred for 15 minutes after the addition of bromine was complete. The separated tribromo-resorcinol was filtered and washed with water. The crude product was stirred vigorously with a saturated solution of sodium sulphite (125 g.) for 1 hr. The solution after cooling was acidified with conc. hydrochloric acid and exttracted with ether. Evaporation of ether gave a liquid, which was warmed with chloroform. The chloroform layer was decanted to which petroleum ether was added. On cooling, 2-bromo-resorcinol separated out, which was filtered and washed with chloroform. Recrystallisation from chloroform gave pure 2-bromo-resorcinol, m.p. 101°. Yield 3.5 g.

The the ice cold mixture of 2-bromo-resorcinol (5 g.) and ethyl benzoyl acetate (5 g.), cold conc. sulphuric acid (80 %; 45 ml.) was added with constant stirring. The reaction mixture was kept at room temperature for 24 hr. It was poured into crushed ice. The separated product was filtered and washed with water. It crystallised from alcohol, m.p. 267°. Yield 4.5 g.

Analysis : Found : C, 56.50 ; H, 2.80; Br, 25.40 %

$C_{15}H_9O_3Br$: requires : C, 56.70 ; H, 2.80; Br, 25.20 %.

Allylation of 7-hydroxy-8-bromo-4-phenylcoumarin : 7-Allyloxy--8-bromo-4-phenylcoumarin (126) :

A mixture of 7-hydroxy-8-bromo-4-phenylcoumarin (5 g.), allyl bromine (2 g.) and anhydrous potassium carbonate (10 g.) was boiled under reflux for 8 hr. in dry acetone (200 ml.) on a water bath. After the evaporation of acetone, the residue was treated with water and the compound was filtered, washed with dilute sodium hydroxide solution to remove unreacted compound. After drying, the compound was crystallised from benzene, m.p. 138°. yield 3.5 g.

Analysis : Found : C, 60.30; H, 3.60; Br, 22.10 %

$C_{18}H_{13}O_3Br$: requires : C, 60.50; H, 3.60; Br, 22.40 %.

I.R.Spectrum : 1720 cm^{-1} (lactonyl >C=O group), at 1270 cm^{-1} (aromatic ether linkage) and at 940 cm^{-1} ($=CH_2$ group).

Claisen rearrangement of 7-allyloxy-8-bromo-4-phenylcoumarin : 6-Allyl-7-hydroxy-4-phenylcoumarin (127) :

7-Allyloxy-8-bromo-4-phenylcoumarin (2 g.) was refluxed with dimethyl aniline (15 ml.) for 6 hr. under nitrogen. The reaction mixture was cooled and poured into ice-cold hydrochloric acid. The separated product was filtered and treated with dilute sodium hydroxide solution. The solution was filtered and the filtrate was acidified with hydrochloric acid. The separated product was filtered and crystallised from methanol, m.p. 222°. Yield 1 g.

The product did not show the presence of bromine

in Lassaigne's test and no green flame observed when the compound was heated on copper foil.

Analysis : Found : C, 77.60 ; H, 4.60 %

$C_{18}H_{14}O_3$: requires : C, 77.70 ; H, 5.00 %.

I.R.Spectrum : 1680 $cm.^{-1}$ (lactonyl >C=O group), a broad band at 3500 $cm.^{-1}$ (aromatic hydroxy group).

Cyclisation of 6-allyl-7-hydroxy-4-phenylcoumarin : 2-Methyl--5-phenyl-2,3-dihydro-7H-furo [3,2-g] [1] benzopyran-7-one (128) :

6-Allyl-7-hydroxy-4-phenylcoumarin (1 g.) was triturated with conc. sulphuric acid (6 ml.) for 20 minutes. The contents were poured into crushed ice. The separated product was filtered, washed with dilute sodium hydroxide solution to remove uncyclised compound and dried. It crystallised from benzene, m.p. 172°. Yield 0.7 g.

Analysis : Found : C, 77.60 ; H, 4.60 %

$C_{18}H_{14}O_3$: requires : C, 77.70 ; H, 5.00 %.

I.R.Spectrum : 1700 $cm.^{-1}$ (lactonyl >C=O group).

Dehydrogenation of 2-methyl-5-phenyl-2,3-dihydro-7H-furo [3,2-g][1] benzopyran-7-one : 2-Methyl-5-phenyl-7H-furo [3,2-g] [1] benzopyran-7-one (129) :

A mixture of 2-methyl-5-phenyl-7H-2,3-dihydrofuro [3,2-g] [1] benzopyran-7-one (0.5 g.), palladised charcoal (0.3 g.; 10 %) and diphenyl ether (6 ml.) was refluxed for 24 hr. The reaction mixture was filtered hot and diphenyl ether was removed by steam distillation. The separated product was filtered, dried and purified by passing its solution in

benzene through alumina. It crystallised from benzene-petroleum ether mixture, m.p. 179°. Yield 0.3 g.

Analysis : Found : C, 78.30 ; H, 4.30 %

$C_{18}H_{12}O_3$ requires : C, 78.30 ; H, 4.30 %.

I.R. spectrum : 1710 cm^{-1} (lactonyl >C=O group) and at 870 cm^{-1} (furan).

$\lambda^{Chloroform}_{max.}$ 254 nm (log e, 4.24), 330 nm (log e, 3.99).

Synthesis of 9-methyl-5H-benzofuro [6,5,c] [1] benzopyran-5-one (134) : Pechmann condensation of 2-bromo-resorcinol with ethyl cyclohexanone-2-carboxylate : 4-Bromo-3-hydroxy-7,8,9,10-tetrahydro-6H-dibenzo [b,d] pyran-6-one (130) :

To the ice cold mixture of 2-bromo-resorcinol (5 g.) and ethyl cyclohexanone-2-carboxylate (4.5 ml.), cold conc. sulphuric acid (45 ml ; 80 %) was added with constant stirring. The reaction mixture was kept at room temperature for 24 hr. It was poured into crushed ice. The separated product was filtered and washed with water. It crystallised from alcohol, m.p. 260° (decomp.). Yield 4.5 g.

Analysis : Found : C, 52.50; H, 4.00; Br, 27.30 %.

$C_{13}H_{11}BrO_3$ requires : C, 52.80; H, 3.70; Br, 27.10 %.

Allylation of 4-bromo-3-hydroxy-7,8,9,10-tetrahydro-6H-dibenzo [b,d] pyran-6-one : 3-Allyloxy-4-bromo-7,8,9,10-tetrahydro-6H-dibenzo [b,d] pyran-6-one (131) :

A mixture of 4-bromo-3-hydroxy-7,8,9,10-tetrahydro-6H-dibenzo [b,d] pyran-6-one (5 g.), allyl bromide (2 g.)

and anhydrous potassium carbonate (10 g.) was refluxed in dry acetone (200 ml.) on a water bath for 10 hr. The reaction mixture was worked up as before. The product crystallised from benzene, m.p. 183°. Yield 3.5 g.

Analysis : Found : C, 57.00; H, 4.40; Br, 23.50 %

$C_{16}H_{15}BrO_3$ requires : C, 57.30; H, 4.40; Br, 23.80 %.

I.R. spectrum 1710 $cm.^{-1}$ (lactonyl >C=O group) and at 1280 $cm.^{-1}$ (aromatic ether linkage).

Claisen rearrangement of 3-allyloxy-4-bromo-7,8,9,10-tetrahydro-6H-dibenzo [b,d] pyran-6-one :2-Allyl-3-hydroxy-7,8,9,10-tetrahydro-6H-dibenzo [b,d] pyran-6-one (132) :

3-Allyloxy-4-bromo-7,8,9,10-tetrahydro-6H-dibenzo [b,d] pyran-6-one (2 g.) was refluxed with dimethyl aniline (15 ml.) for 6 hr. under nitrogen. The reaction mixture was worked up as before. The product crystallised from benzene, m.p. 166°. Yield 1.2 g.

Analysis : Found : C, 75.00; H, 6.00 %

$C_{16}H_{16}O_3$: requires : C, 75.00; H, 6.20 %.

I.R. spectrum : 1660 $cm.^{-1}$ (lactonyl >C=O group) and a broad band at 3500 $cm.^{-1}$ (aromatic hydroxy group).

Cyclisation of 2-allyl-3-hydroxy-7,8,9,10-tetrahydro-6H-dibenzo[b,d] pyran-6-one : 9-Methyl-1,2,3,4,9,10-hexahydro-5H-benzofuro [6,5-c] [1] benzopyran-5-one (133) :

2-Allyl-3-hydroxy-1,2,3,4-tetrahydro-6H-dibenzo [b,d] pyran-6-one (1 g.) was triturated with conc. sulphuric acid (6 ml.) for 20 minutes. The reaction mixture was worked up as usual. The product crystallised from benzene-petroleum

ether mixture, m.p. 137°. Yield 0.8 g.

Analysis : Found : C, 74.80 ; H, 5.90 %.

$C_{16}H_{14}O_3$: requires : C, 75.00 ; H, 6.20 %.

I.R. spectrum : 1695 $cm.^{-1}$ (lactonyl >C=0 group).

$\lambda^{Methanol}_{max.}$ 242 nm (log e 4.27), 248 nm (log e 4.52), 254 nm (log e 4.57), 260 nm (log e 4.50), 268 nm (log e 4.27), 278 nm (log e 4.21) and at 330 nm (log e 4.30).

Dehydrogenation of 9-methyl-1,2,3,4,9,10-hexahydro-5H-benzofuro [6,5-c] [1] benzopyran-5-one : 9-Methyl-5H-benzofuro [6,5-c] [1] benzopyran-5-one (134) :

A mixture of 9-methyl-1,2,3,4,9,10-hexahydro-5H-benzofuro [6,5-c] [1]benzopyran-5-one (0.5 g.), palladised charcoal (0.3 g.; 10 %) and diphenyl ether (6 ml.) was refluxed for 24 hr. The reaction mixture was worked up as usual. The product crystallised from benzene, m.p. 176°. Yield 0.35 g.

Analysis : Found : C, 77.20; H, 3.80 %.

$C_{16}H_{10}O_3$: requires : C, 76.80; H, 4.00 %.

I.R. spectrum : 1705 $cm.^{-1}$ (lactonyl >C=0 group) and at 880 $cm.^{-1}$ (furan).

$\lambda^{Methanol}_{max.}$ 276 nm (log e 3.88) and 330 nm (log e 4.00).

Synthesis of 9-methyl-1,2,3,4-tetrahydro-5H-benzofuro[6,5-c] [1] benzopyran-5-one (137) : Acetylation of 2-allyl-3-hydroxy-7,8,9,10-tetrahydro-6H-dibenzo [b,d] pyran-6-one : 2-Allyl-6-oxo-7,8,9,10-tetrahydro-6H-dibenzo[b,d] pyran-

3-yl-acetate (135) :

A mixture of 2-allyl-3-hydroxy-7,8,9,10-tetrahydro-6H-dibenzo b,d pyran-6-one (1 g.), acetic anhydride (8 ml.) and fused sodium acetate (1.5 g.) was heated under reflux for 5 hr. The reaction mixture was poured into crushed ice. The compound which separated on standing was filtered and crystallised from alcohol, m.p. 138°. Yield 0.9 g.

Analysis : Found : C, 72.60; H, 6.00 %

$C_{18}H_{18}O_4$: requires : C, 72.50; H, 6.00 %.

I.R. spectrum : 1760 cm^{-1} (acetoxy group at position 7) and at 1710 cm^{-1} (lactonyl >C=O group).

Bromination of 2-allyl-6-oxo-7,8,9,10-tetrahydro-6H-dibenzo [b,d] pyran-3-yl acetate : 2-(2',3'-dibromopropyl)-6-oxo-7,8,9,10-tetrahydro-6H-dibenzo [b,d] pyran-3-yl acetate (136) :

A solution of bromine (1.6 g.; 0.01 m) in acetic acid (25 ml.) was added dropwise to a well stirred solution of 2-allyl-6-oxo-7,8,9,10-tetrahydro-6H-dibenzo [b,d] pyran-6-one (2.9 g.; 0.01 m) in acetic acid (25 ml.) during a period of 1 hr. After being stirred for a further 1 hr., the solution was diluted with ice cold water and allowed to stand. The separated product was collected, dried, dissolved in benzene and passed ower alumina. Evaporation of solvent left a residue, which crystallised from benzene, m.p. 220°. Yield 3.0 g.

Analysis : Found : C, 47.00; H, 3.60; Br, 35.10 %

$C_{18}H_{18}Br_2O_4$: requires : C, 47.10; H, 3.90; Br, 34.90 %.

Cyclisation of 2-(2',3'-dibromopropyl)-6-oxo-7,8,9,10-tetrahydro-6H-dibenzo [b,d] pyran-3yl acetate : 9-Methyl-1,2,3,4-tetrahydro-5H-benzofuro [6,5-c] [1] benzopyran-5-one (137) :

A solution of 2-(2',3'-dibromopropyl)-6-oxo-7,8,9,10-tetrahydro-6H-dibenzo [b,d] pyran-3-yl acetate (2 g.) in ethanolic potassium hydroxide (2.5 g. in 75 ml. absolute alcohol), was heated under reflux for 4 hr. and then concentrated to one-third of its volume. Water (50 ml.) was added and the solution was immediately acidified with dilute hydrochloric acid and extracted with ether. Evaporation of ether gave a light red product which was washed with aqueous ammonia (10 %) and then with water. It crystallised from alcohol, m.p. 184°. Yield 0.6 g.

Analysis : Found : C, 75.50 ; H, 5.50 %.

$C_{16}H_{14}O_3$: requires : C, 75.60 ; H, 5.50 %.

I.R. spectrum : 1700 cm^{-1} (lactonyl >C=0 group) and at 860 cm^{-1} (furan).

$\lambda_{max.}^{Methanol}$ 248 nm (log e 4.45), 290 nm (log e 3.98), 330 nm (log e 3.98).

Synthesis of 8-methyl-1,2,3,4-tetrahydrocyclopenta [c] furo [3,2-g] [1] benzopyran-4-one (144) : Pechmann condensation of 2-bromo-resorcinol with ethyl-cyclopentanone-2-carboxylate : 6-Bromo-7-hydroxy-1,2,3,4-tetrahydrocyclopenta [c] [1] benzopyran-4-one (138) :

To the ice cold mixture of 2-bromo-resorcinol (5 g.) and ethyl cyclopentanone-2-carboxylate (4.3 g.), cold conc.

sulphuric acid (45 ml.; 80 %) was added. The reaction mixture was kept at room temperature for 24 hr. and was worked up as usual. The product crystallised from alcohol, m.p. 284° (decomp.). Yield 4.5 g.

Analysis : Found : C, 51.30; H, 3.00; Br, 28.80 %

$C_{12}H_9BrO_3$ requires : C, 51.20; H, 3.20; Br, 28.50 %.

Allylation of 6-bromo-7-hydroxy-1,2,3,4-tetrahydrocyclopenta [c][1] benzopyran-4-one : 7-Allyloxy-6-bromo-1,2,3,4-tetrahydrocyclopenta [c][1] benzopyran-4-one (139) :

A mixture of 6-bromo-7-hydroxy-1,2,3,4-tetrahydrocyclopenta [c] [1] benzopyran-4-one (5 g.), allyl bromide (2 g.) and anhydrous potassium carbonate (10 g.) was refluxed in dry acetone (200 ml.) for 6 hr. in a water bath. The reaction mixture was worked up as usual. The product crystallised from benzene, m.p. 159°. Yield 3.5 g.

Analysis : Found : C, 56.50; H, 4.10; Br, 24.50 %.

$C_{15}H_{13}BrO_3$: requires : C, 56.10; H, 4.00; Br, 24.90 %.

I.R. spectrum : 1710 $cm.^{-1}$ (lactonyl >C=O group) and at 1290 $cm.^{-1}$ (aromatic ether linkage.).

Claisen rearrangement of 7-allyloxy-6-bromo-1,2,3,4-tetrahydrocyclopenta [c][1] benzopyran-4-one : 8-Allyl-7-hydroxy-1,2,3,4-tetrahydrocyclopenta [c] [1] benzopyran-4-one (140) :

7-Allyloxy-6-bromo-1,2,3,4-tetrahydrocyclopenta [c] [1] benzopyran-4-one (2 g.) was refluxed with dimethylaniline (15 ml.) for 6 hr. in an inert atmosphere of nitrogen. The reaction mixture was worked up as usual. The product

crystallised from alcohol, m.p. 184°. Yield 1.3 g.

Analysis : Found : C, 74.50; H, 5.70 %.

$C_{15}H_{14}O_3$: requires: C, 74.40; H, 5.80 %.

I.R. spectrum : 1700 $cm.^{-1}$ (lactonyl >C=0 group) and a broad band at 3440 $cm.^{-1}$ (aromatic hydroxy group).

Cyclisation of 8-allyl-7-hydroxy-1,2,3,4-tetrahydrocyclopenta [c] [1] benzopyran-4-one : 8-Methyl-1,2,3,4,8,9-hexahydrocyclopenta [c] furo [3,2-g] [1] benzopyran-4-one (141) :

8-Allyl-7-hydroxy-1,2,3,4-tetrahydrocyclopenta [c] [1] benzopyran-4-one (1 g.) was triturated with conc. sulphuric acid (6 ml.) for 2 hr. and the reaction mixture was worked up as before. The product crystallised from benzene-petroleum ether, m.p. 155°. Yield 0.6 g.

Analysis : Found : C, 74.20 ; H, 5.90 %

$C_{15}H_{14}O_3$: requires : C, 74.40 ; H, 5.80 %.

I.R. spectrum : 1710 $cm.^{-1}$ (lactonyl >C=0 group).

$\lambda_{max.}^{Methanol}$ 256 nm (log e 4.95), 280 nm (log e 4.95), 340 nm.(log e 4.23).

Acetylation of 8-allyl-7-hydroxy-1,2,3,4-tetrahydrocyclopenta [c] benzopyran-4-one : 8-Allyl-4-oxo-1,2,3,4-tetrahydrocyclopenta [c] benzopyran-7-yl acetate (142) :

A mixture of 8-allyl-7-hydroxy-1,2,3,4-tetrahydrocyclopenta [c] benzopyran-4-one (1 g.), acetic anhydride (8 ml.) and fused sodium acetate (1.5 g.) was heated under reflux for 5 hr. The reaction mixture was

worked up as usual. The product crystallised from alcohol, m.p. 158°. Yield 0.9 g.

Analysis : Found : C, 71.80; H, 5.60 %.

$ACL_7H_{16}O_4$: requires : C, 71.80; H, 5.60 %.

I.R.Spectrum : 1760 cm^{-1} (acetoxy group at position 7) and at 1710 cm^{-1} (lactonyl >C=O group).

Bromination of 8-allyl-4-oxo-1,2,3,4-tetrahydrocyclopenta [c] benzopyran-7-yl acetate : 8-(2',3'-dibromopropyl)-4-oxo-1,2,3,4-tetrahydrocyclopenta [c] benzopyran-7-yl acetate (143) :

A solution of bromine (1.6 g.; 0.01 M) in acetic acid (25 ml.) was added dropwise to a well stirred solution of 8-allyl-4-oxo-1,2,3,4-tetrahydrocyclopenta [c] benzopyran-7-yl acetate (2.8 g.; 0.01 M) in acetic acid (25 ml.) during a period of 1 hr. The reaction mixture was worked up as usual. The product crystallised from benzene, m.p. 203°. Yidld 3.0 g.

Analysis : Found : C, 45.70; H, 3.40; Br, 35.90 %.

$C_{17}H_{16}Br_2O_4$: requires: C, 45.90; H, 3.60; Br, 36.00 %.

Cyclisation of 8-(2',3'-dibromopropyl)-4-oxo-1,2,3,4-tetrahydrocyclopenta [c] benzopyran-7-yl acetate : 8-Methyl-1,2,3,4-tetrahydrocyclopenta [c] furo [3,2-g][1] benzopyran-4-one (144) :

A solution of 8-(2',3'-dibromopropyl)-4-oxo-1,2,3,4-tetrahydrocyclopenta [c] benzopyran-7-yl acetate (2 g.) in ethanolic potassium hydroxide (2.5 g. in 75 ml. absolute alcohol) was heated under reflux for 4 hr. The

reaction mixture was worked up as before. The product purified by passing its chloroform solution over a short column of alumina. It crystallised from alcohol, m.p. 202°. Yield 0.5 g.

Analysis : Found : C, 75.30; H, 5.10 %.

$C_{15}H_{12}O_3$: requires: C, 75.00; H, 5.00 %.

I.R.spectrum : 1700 $cm.^{-1}$ (lactonyl >C=0 group) and at 860 $cm.^{-1}$ (furan).

$\lambda^{\text{Methanol}}_{\text{max.}}$ 248 nm (log e 4.40), 296 nm (log e 4.95), 334 nm. (log e 4.94).

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CHAPTER I.

SECTION II.

STUDIES IN THE SYNTHESIS OF DIFUROCOUMARINS

SECTION II.

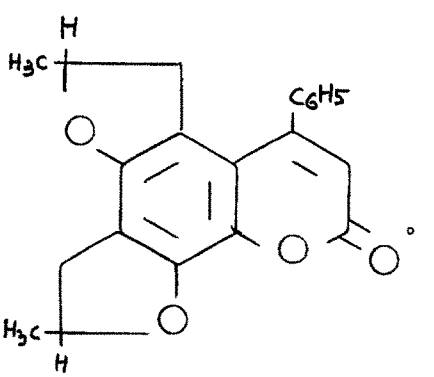
Synthesis of difurocoumarins.

T H E O R E T I C A L.

Furocoumarins are of much importance due to their valuable therapeutic properties and applicability as drugs.

Furocoumarins having one furan ring fused with coumarin ring in different position are known and synthesised by different workers as reviewed in Section I.

Seshadri and co-workers[1] have studied the Claisen migration of substituted 4-phenylcoumarins and obtained the compound bis-2 -methyl-dihydrofurano [4',5': 5,6] and [4',5': 7,8] -4-phenylcoumarin as one product. 5,7-Diallyloxy--4-phenylcoumarin on Claisen rearrangement at 220-40° in the absence of solvent under reduced pressure gave two products, one of which has the structure (1) which is proved by I.R. and NMR spectra.



(1)

It was, therefore, thought of interest to synthesise difurocoumarins for evaluating their furocoumarin like photosensitizing activity.

The synthesis of difurocoumarins has achieved by subjecting diallyloxycoumarin to Claisen migration followed by cyclisation and dehydrogenation with palladised charcoal.

The following difurocoumarin derivatives are synthesised using 4,7-diallyloxycoumarin, 4,7-diallyloxy-8-methylcoumarin and 4,6-diallyloxycoumarin as starting material.

1. 2,7-Dimethyl-4-oxo-4H-difuro (3,2-c; 2',3'-h)benzo-pyran (7).
2. 2,6,8-Trimethyl-4-oxo-4H-difuro(3,2-c; 3',2'-g)benzo-pyran (12).
3. 2,9-Dimethyl-4-oxo-4H-difuro (3,2-c ; 3',2'-f) benzo-pyran (17).

Synthesis of 2,7-dimethyl-4-oxo-4H-difuro (3,2-c ; 2',3'-h)-benzopyran (7) :

4-Hydroxy-7-allyloxycoumarin[2] (2) on allylation with allyl bromide in the presence of anhydrous potassium carbonate and dry acetone afforded 4,7-diallyloxycoumarin (3). Claisen rearrangement of 4,7-diallyloxycoumarin gave two products as shown by thin layer chromatography. The separation was effected by treating the etherial solution of the mixture first with sodium bicarbonate and then with

sodium hydroxide solution. Evaporation of the ether gave the product, which was insoluble either in sodium bicarbonate or sodium hydroxide solution and was found to be 7-allyloxy-2-methyl-2,3-dihydro-4-oxo-4H-furo (3,2-c)benzopyran (4). The I.R. Spectrum of (4) showed a band at 1710 $cm.^{-1}$ (lactonyl >C=O group), at 1275 $cm.^{-1}$ (aromatic ether linkage) and at 875 $cm.^{-1}$ (furan) (Fig.1). The structure of (4) was supported by its NMR spectrum . (Fig. 2).

Chemicals shifts (δ) (ppm).	Coupling constant J (Cps).	Signals	Assignments
1.58	7Hz	Doublet	3H, methyl group at position 2.
3.60	7Hz	Multiplet	2H, $-CH_2$ group at position 3.
4.55	5Hz	Doublet	2H,of allyl group at position 7. $ArO\underline{CH_2}-CH=CH_2$.
5.2	-	Multiplet	1H, at position 2.
5.45	-	Doublet	2H of allyl group at position 7. $ArOCH_2-CH=\underline{CH_2}$.
5.9-6.2	5Hz	Multiplet	1H of allyl group at position 7. $ArOCH_2-\underline{CH}=CH_2$.
6.8-7.6	-	Multiplet	3H, aromatic proton at position 6,8 and 9.

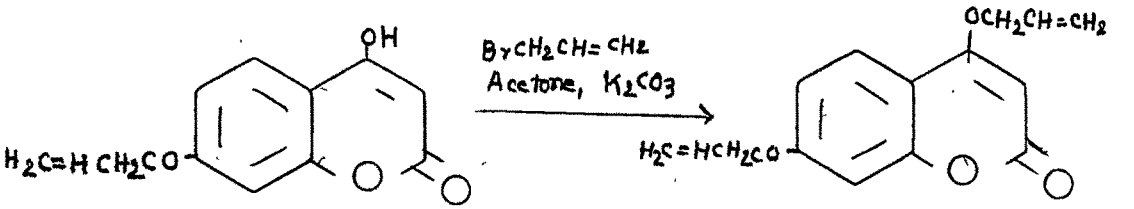
The compound 7-allyloxy-2-methyl-2,3-dihydro-4-oxo-4H-furo (3,2-c) benzopyran on Claisen migration gave 7-hydroxy-6-allyl-2-methyl-2,3-dihydro-4-oxo-4H-furo(3,2-c) benzopyran (5). This compound was found identical with the alkali soluble product, 7-hydroxy-6-allyl-2-methyl-2,3-dihydro-4-oxo-4H-furo (3,2-c) benzopyran which on cyclisation with conc. sulphuric acid gave 2,7-dimethyl-4-oxo-4H-2,3,6,7-tetrahydrodifuro (3,2-c) 2',3'-h)benzopyran (6), the I.R. spectrum of which showed a band at 1720 $cm.^{-1}$ (lactonyl >C=O group), and at 840 $cm.^{-1}$ and also at 905 $cm.^{-1}$ (two furan ring), (Fig.3) (Fig.4). The NMR spectrum of (6) showed the following signals :-

Chemicals shifts (δ) ppm.	Coupling constant J (Cps).	Signals	Assignments
1.5	-	Doublet	3H, $-CH_3$ group at position 7.
1.62	-	Doublet	3H, $-CH_3$ group at position 2.
2.5-3.0	-	Multiplet	2H of cyclic methylene protons at position 6.
3.1-3.5	-	Multiplet	2H of cyclic methylene proton at position 3.
4.9-5.4	-	Multiplet	2H of two cyclic methine protons at position 2 and 7.
6.8	8Hz	Doublet	1H, aromatic proton at position 10.
7.5	8Hz	Doublet	aromatic proton at position 9.

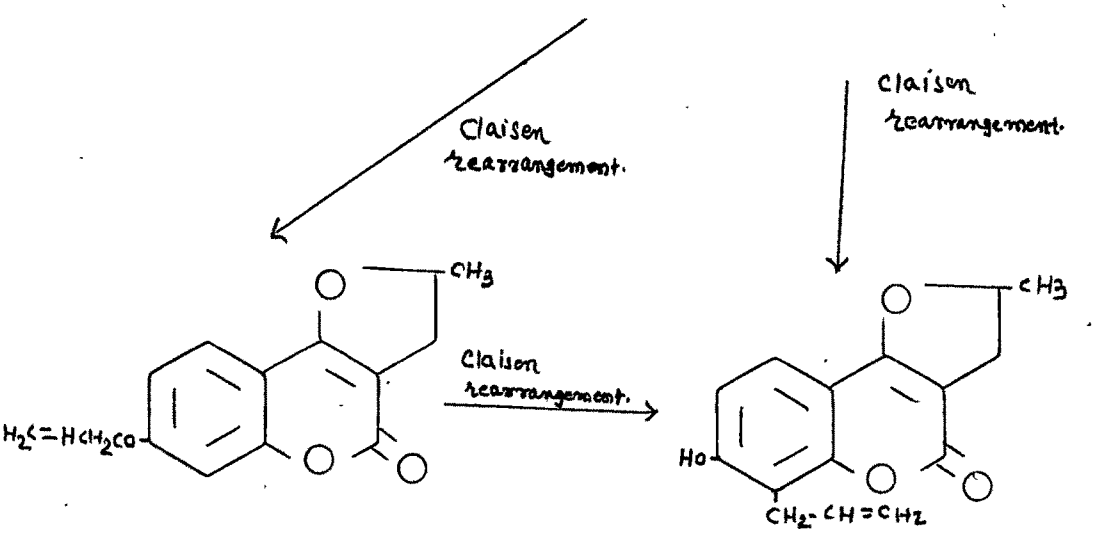
Dehydrogenation of (6) by refluxing it with diphenyl ether in the presence of palladised charcoal gave 2,7-dimethyl-4-oxo-4H-difuro (3,2-c : 2',3'-h) benzopyran (7). The I.R. spectrum of which showed a sharp band at 1730 $cm.^{-1}$ (lactonyl >C=O group) and two bands in furan region, viz., at 800 $cm.^{-1}$ and at 880 $cm.^{-1}$ (furan) (Fig. 5). The acidification of sodium hydroxide extract gave 7-hydroxy-6-allyl-2-methyl-2,3-dihydro-4-oxo-4H-furo (3,2-c) benzopyran identical with (5) by mixed m.p. determination and co-TLC method.

Synthesis of 2,6,8-trimethyl-4-oxo-4H-difuro (3,2-c ; 3',2'-g) benzopyran (12) :

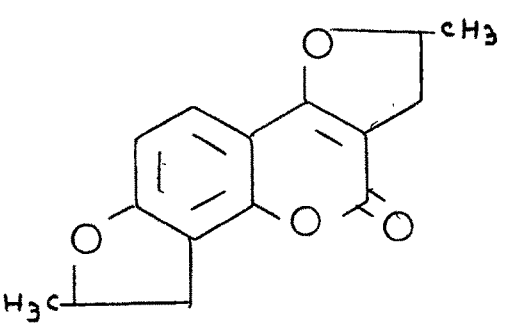
4-Hydroxy-7-allyloxy-8-methylcoumarin (8) on allylation with allyl bromide and anhydrous potassium carbonate in dry acetone gave 4,7-diallyloxy-8-methylcoumarin (9), which on Claisen rearrangement in boiling dimethyl aniline afforded only one product. The etherial solution of the reaction mixture was first treated with sodium bicarbonate and then with sodium hydroxide solution. Evaporation of ether gave no product. Sodium bicarbonate extract, on acidification also gave no product. Acidification of sodium hydroxide solution gave 7-hydroxy-8-allyl-2',6'-dimethyl-2,3-dihydro-4-oxo-4H-furo (3,2-c) benzopyran (10), which on trituration with conc. sulphuric acid gave 2,6,7-trimethyl-4-oxo-4H-2,3,8,9-tetrahydrodifuro (3,2-c : 3',2'-g) benzopyran (11).


OH
$H_2C{=}HCH_2CO$
$BrCH_2CH{=}CH_2$
Acetone, K_2CO_3
$OCH_2CH{=}CH_2$
$H_2C{=}HCH_2CO$

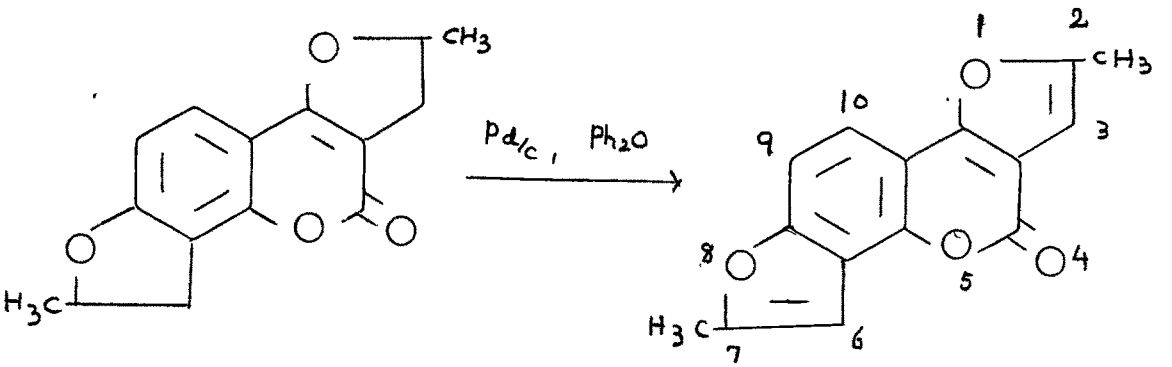
(2) (3)


Claisen rearrangement.
Claisen rearrangement.
CH_3
$H_2C{=}HCH_2CO$
Claisen rearrangement.
CH_3
HO
$CH_2{-}CH{=}CH_2$

(4) (5)


Conc. H_2SO_4
CH_3
H_3C

(6)

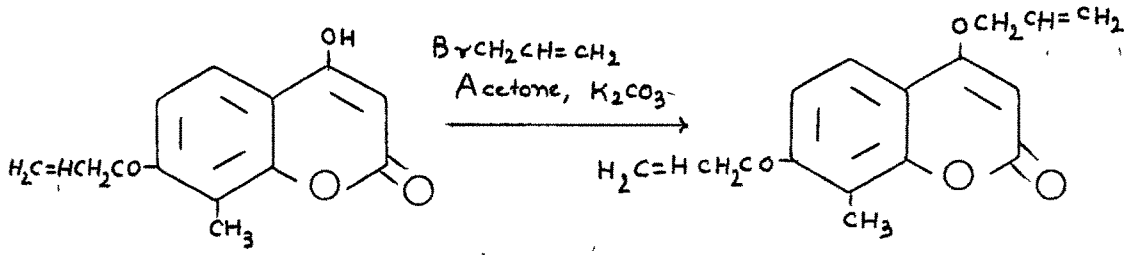


(6) (7)

Dehydrogenation of (11) by refluxing it with diphenyl ether in the presence of palladised charcoal gave 2,6,8-trimethyl--4-oxo-4H-difuro (3,2-c : 3',2'-g) benzopyran (12).

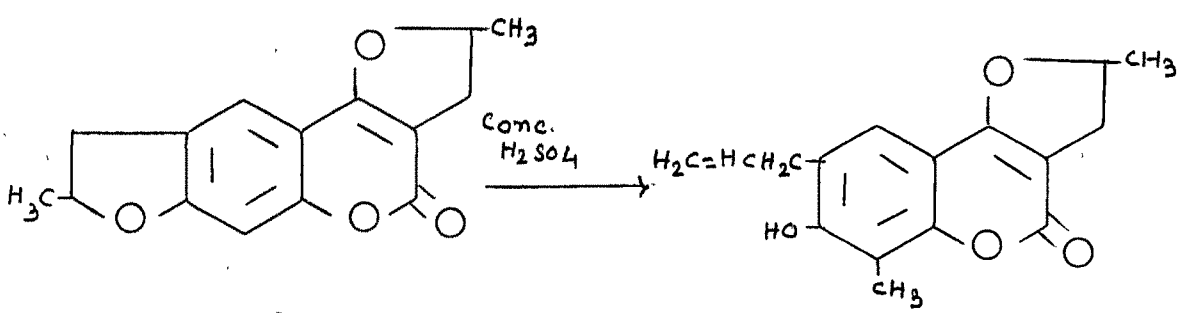
Synthesis of 2,9-dimethyl-4-oxo-4H-difuro (3,2-c : 3',2'-f) benzopyran (17) :

4-Hydroxy-6-allyloxycoumarin (13), on allylation with allyl bromide and anhydrous potassium carbonate in dry acetone gave 4,6-diallyloxycoumarin (14), Claisen rearrangement of which gave only one product. The etherial solution of the reaction mixture was first treated with sodium bicarbonate and then with sodium hydroxide. Evaporation of ether gave no product. Sodium bicarbonate extract on acidification also gave no product. Acidification of sodium hydroxide extract gave 8-hydroxy-9-allyl-2-methyl-2,3-dihydro-



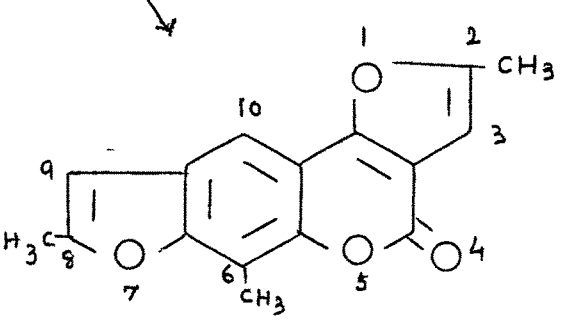
(8)

Dimethyl aniline



(11) (10)

Pd/C
Ph_2O

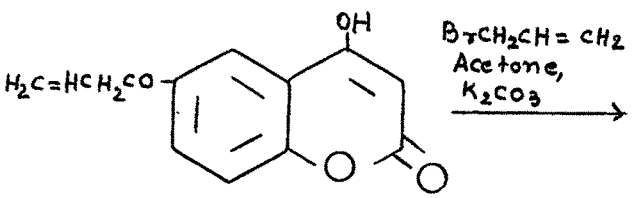


(12)

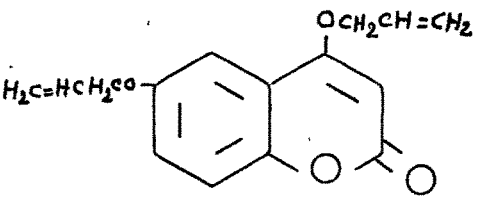
-4-oxo-4H-furo (3,2-c) benzopyran (15), which on cyclisation with conc. sulphuric acid afforded 2,9-dimethyl-2,3,9,10-tetrahydro-4-oxo-4H-difuro (3,2-c : 3',2'-f) benzopyran (16). The structure of (16) was supported by its NMR spectrum, (Fig.4) which showed the following signals :-

Chemical shift (δ) ppm.	Coupling constant J (Cps)	Signals	Assignments.
1.46-1.61	7Hz	Triplet (overlapping two doublets)	6H, two $-CH_3$ groups at position-2 and 9.
2.6-3.8	-	Multiplet	4H, two cyclic methylene groups at position-3 and 10 (overlapping each other).
4.85-5.38	-	Multiplet	2H, two methine protons at position-2 and 9 (overlapping each other).
6.9	9Hz	Doublet	1H, aromatic proton at position-7.
7.15	9Hz	Doublet	1H, aromatic proton at position-6.

Dehydrogenation of (16) by refluxing it with diphenyl ether in the presence of palladised charcoal gave 2,9-dimethyl-4-oxo-4H-difuro (3,2-c : 3',2'-f) benzopyran (17).

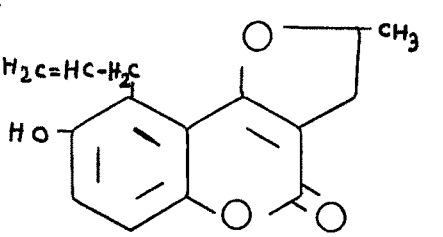


(13)



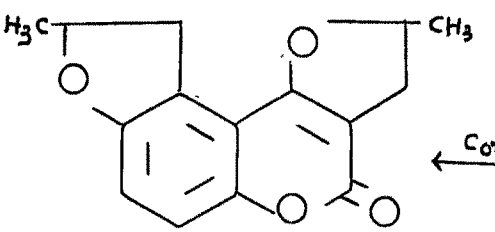
(14)

Dimethyl aniline.



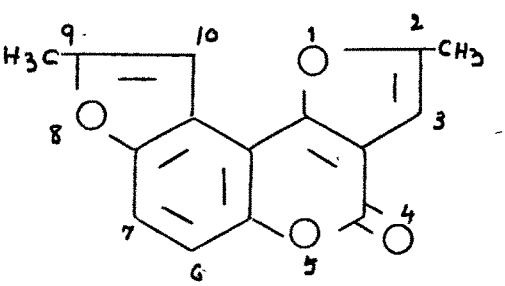
(15)

Conc. H_2SO_4



(16)

Pd/c
Ph_2O



(17)

E X P E R I M E N T A L.

I.R. Spectra were determined with Perkin-Elmer 457 grating spectrophotometer for compound (4). Beckmann IR-20 grating spectrophotometer for compound (7), (10), (11), (12).

NMR spectra were recorded on TPV 60 spectrophotometer using TMS as internal standard. and solvent $CDCl_3$ (Fig. 2, 4, 6)

The U.V. absorption spectra were measured with Beckmann DU - Spectrophotometer.

Synthesis of 2,7-dimethyl-4-oxo-4H-difuro (3,2-c;2',3'-h) benzopyran (7) : Allylation of 4-hydroxy-7-allyloxycoumarin-: 4,7-Diallyloxycoumarin (3) : 4-Hydroxy-7-allyloxycoumarin (3) :

4-Hydroxy-7-allyloxycoumarin was prepared according to Dholakia and Trivedi[2].

4,7-Diallyloxycoumarin (3) :

A mixture of 4-Hydroxy-7-allyloxycoumarin (5 g.), allyl bromide (3 g.) and anhydrous potassium carbonate (10 g.) was boiled under reflux for 8 hr. in dry acetone (200 ml.) on a water bath. After the evaporation of acetone, the residue was treated with water and the compound was filtered, washed with dilute sodium hydroxide solution to remove unreacted compound. It crystallised from alcohol, m.p. 94°. Yield 3.5 g.

Analysis	: Found	:	C, 69.76; H, 5.30 %.
$C_{15}H_{14}O_4$	: requires	:	C, 69.76; H, 5.42 %.

Claisen rearrangement of 4,7-diallyloxycoumarin : 7-Hydroxy-6-allyl-2-methyl-2,3-dihydro-4-oxo-4H-furo (3,2-c) benzopyran (5) :

4,7-Diallyloxycoumarin (2 g.) was refluxed with dimethyl aniline (10 ml.) for 8 hr. The reaction mixture was poured into conc. hydrochloric acid containing crushed ice. The reaction mixture was extracted with ether and the etherial layer was shaken with sodium hydroxide solution. The alkaline layer was separated and acidified with cons. hydrochloric acid. The separated product was filtered and crystallised from alcohol, m.p. 222°. Yield 1.5 g.

Analysis : Found : C, 70.18 ; H, 5.17 %

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

The ether extract after evaporation of ether gave little amount of the compound 7-allyloxy-2-methyl-2,3-dihydro-4-oxo-4H-furo (3,2-c) benzopyran. (4), whose analysis is as follows :-

Analysis : Found : C, 69.60 ; H, 5.17 %.

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

I.R.Spectrum : 1710 cm^{-1} (lactonyl >C=O group), 1275 cm^{-1} (aromatic ether linkage) and at 875 cm^{-1} (furan).

Claisen rearrangement of 7-allyloxy-2-methyl-2,3-dihydro-4-oxo-4H-furo (3,2-c) benzopyran : 7-Hydroxy-6-allyl-2-methyl-2,3-dihydro-4-oxo-4H-furo (3,2-c) benzopyran (5) :

7-Allyloxy-2-methyl-2,3-dihydro-4-oxo-4H-furo (3,2-c) benzopyran (0.5 g.) was refluxed with dimethyl

aniline (4 ml.) for 8 hr. The reaction mixture was poured into conc. hydrochloric acid containing crushed ice. The separated product was filtered and treated with dilute sodium hydroxide solution. The product was soluble in sodium hydroxide solution. The solution was filtered, acidified and the product separated was filtered and crystallised from alcohol, m.p. 222°. Yield 0.3 g. The mixed m.p. with (5) was depressed.

Cyclisation of 7-hydroxy-6-allyl-2-methyl-2,3-dihydro-4-oxo-4H-furo (3,2-c) benzopyran : 2,7-Dimethyl-4-oxo-4H-2,3,6,7-tetrahydrodifuro (3,2-c : 2',3'-h) benzopyran (6) :

7-Hydroxy-6-allyl-2-methyl-2,3-dihydro-4-oxo-4H-furo (3,2-c) benzopyran (1 g.) was triturated with conc. sulphuric acid (5 ml.) for 15 minutes at room temperature. The mixture was poured into crushed ice. The separated product was filtered and washed with sodium hydroxide solution to remove unreacted compound. The compound was crystallised from benzene-petroleum ether, after drying, m.p. 147°. Yield 0.8 g.

Analysis : Found : C, 69.71 ; H, 5.47 %.

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

I.R.spectrum : 1720 $cm.^{-1}$ (lactonyl >C=O group), 840 $cm.^{-1}$ and 905 $cm.^{-1}$ (two furan rings).

Dehydrogenation of 2,7-dimethyl-4-oxo-4H-2,3,6,7-tetrahydrodifuro (3,2-c ; 2',3'-h) benzopyran : 2,7-Dimethyl-4-oxo-4H-difuro (3,2-c ; 2',3'-h) benzopyran (7) :

A mixture of 2,7-dimethyl-4-oxo-4H-2,3,6,7-tetrahydrodifuro (3,2-c ; 2',3'-h) benzopyran (0.5 g.) palladised charcoal (0.3 g.; 10 %) was refluxed with diphenyl ether 4 ml.) for 12 hr. The reaction mixture was filtered hot. After cooling, petroleum ether was added to the filtrate. The separated product was filtered and washed with petroleum ether several times. The product crystallised from benzene, m.p. 225°. Yield 0.3 g.

Analysis : Found : C, 71.06; H, 3.96 %.

$C_{15}H_{10}O_4$: requires : C, 70.89; H, 3.93 %.

I.R.spectrum : 1730 cm^{-1} (lactonyl >C=0 group), 800 cm^{-1} and 880 cm^{-1} (furan).

$\lambda_{max.}^{Chloroform}$ 255 nm (log e 4.50), 268 nm (log e 4.41), 305 nm (log e 4.19), 320 nm (log e 4.12), 330 nm (log e 4.05) and 336 nm (log e 4.01).

Synthesis of 2,6,8-trimethyl-4-oxo-4H-difuro (3,2-c : 3',2'-g) benzopyran (12) : Allylation of 4-hydroxy-7-allyloxy-8-methylcoumarin : 4,7-Diallyloxy-8-methylcoumarin (9) : 4-Hydroxy-7-allyloxy-8-methylcoumarin (8) :

4-Hydroxy-7-allyloxy-8-methylcoumarin was prepared according to Dholakia and Trivedi[2].

4,7-Diallyloxy-8-methylcoumarin (9) :

A mixture of 4-hydroxy-7-allyloxy-8-methylcoumarin (5 g.), allyl bromide (3 g.) and anhydrous potassium carbonate (10 g.) was boiled under reflux for 8 hr. in dry acetone (200 ml.) on a water bath. After the evaporation of acetone, the residue was treated with water and the compound was filtered, washed with dilute sodium hydroxide solution to remove unreacted compound. It crystallised from alcohol, m.p. 156°. Yield 3.5 g.

Analysis : Found : C, 70.49 ; H, 5.89 %.

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

Claisen rearrangement of 4,7-di-allyloxy-8-methylcoumarin : 7-Hydroxy-8-allyl-2,6-dimethyl-2,3-dihydro-4-oxo-4H-furo (3,2-c) benzopyran (10) :

4,7-Diallyloxy-8-methylcoumarin (2 g.) was refluxed with dimethyl aniline (10 ml.) for 8 hr. The reaction mixture was poured into conc. hydrochloric acid containing crushed ice. The reaction mixture was extracted with ether and the etherial layer was shaken with sodium hydroxide solution. The alkaline layer was separated and acidified with conc. hydrochloric acid. The separated product was filtered and dried. It was purified by passing its chloroform solution over a short column of alumina and crystallised from benzene, m.p. 179°. Yield 1.5 g.

Analysis : Found : C, 71.01 ; H, 5.96 %

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

I.R. spectrum : 1780 $cm.^{-1}$ (lactonyl >C=O group), and a broad band at 3340 $cm.^{-1}$ (aromatic hydroxy group).

Evaporation of ether gave no products.

Cyclisation of 7-hydroxy-8-allyl-2',6-dimethyl-2,3-dihydro--4-oxo-4H-furo (3,2-c) benzopyran : 2,6,8-Trimethyl-4-oxo-4H-2,3,8,9-tetrahydro-difuro (3,2-c ; 3 ,2 -g) benzopyran (11):

7-Hydroxy-8-allyl-2',6-dimethyl-2,3-dihydro-4-oxo-4H-furo (3,2-c) benzopyran (1 g.) was triturated with conc. sulphuric acid (5 ml.) for 15 minutes at room temperature. The mixture was poured into crushed ice. The separated product was filtered and washed with dilute sodium hydroxide solution to remove unreacted compound. It crystallised from alcohol, m.p. 167°. Yield 0.8 g.

Analysis : Found : C, 70.08 ; H, 5.60 %.

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

I.R.spectrum : 1690 $cm.^{-1}$ (lactonyl >C=O group), 830 $cm.^{-1}$ and 890 $cm.^{-1}$ (two furan rings).

$\lambda_{max.}^{Methanol}$ 246 nm (log e 4.07), 294 nm (log e 3.93), 324 nm (log e 4.33), 338 nm (log e 4.29).

Dehydrogenation of 2,6,8-trimethyl-4-oxo-4H-2,3,8,9-tetra-hydrodifuro (3,2-c ; 3 ,2 -g) benzopyran : 2,6,8-Trimethyl--4-oxo-4H-difuro(3,2-c : 3',2'-g) benzopyran (12) :

A mixture of 2,6,8-trimethyl-4-oxo-4H-2,3,8,9-tetrahydrodifuro (3,2-c : 3',2'-g) benzopyran (0.5 g.) palladised charcoal (0.3 g.; 10 %) was refluxed with diphenyl ether (4 ml.) for 12 hr. The reaction mixture was filtered hot. After cooling petroleum ether was added to the filtrate. The separated product was filtered and washed with petroleum ether several times. The product was purified by passing its benzene solution over a short column of alumina. It crystallised from benzene, m,p. 218°. Yield 0.3 g.

Analysis : Found : C, 71.68 ; H, 4.72 %

$C_{16}H_{12}O_4$: requires : C, 71.65 ; H, 4.48 %.

I.R.Spectrum : 1715 cm^{-1} (lactonyl >C=0 group), 825 cm^{-1} and 930 cm^{-1} (two furan ring).

$\lambda^{Methanol}_{Max.}$ 304 nm (log e 4.09), 332 nm (log e 4.19).

Synthesis of 2,9-dimethyl-4-oxo-4H-difuro (3,2-c : 3',2'-f) benzopyran (17) : Allylation of 4-hydroxy-6-allyloxycoumarin : 4,6-Diallyloxycoumarin (14) : 4-Hydroxy-6-allyloxycoumarin(13):

4-Hydroxy-6-allyloxycoumarin was prepared according to Dholakia and Trivedi[2].

4,6-Diallyloxycoumarin (14) :

A mixture of 4-hydroxy-6-allyloxycoumarin (5 g.), allyl bromide (3 g.) and anhydrous potassium carbonate (10 g.) was boiled under reflux for 8 hr. in dry acetone (200 ml.) on a water bath. After the evaporation of acetone, the residue

was treated with water and the compound was filtered, washed with dilute sodium hydroxide solution to remove unreacted compound. It crystallised from alcohol, m.p. 119°. Yield 3.5 g.

Analysis : Found : C, 70.01 ; H, 5.63 %

$C_{15}H_{14}O_4$: requires : C, 69.78 ; H, 5.43 %.

Claisen rearrangement of 4,6-diallyloxycoumarin : 8-Hydroxy-9-allyl-2-methyl-2,3-dihydro-4-oxo-4H-furo (3,2-c) benzopyran (15) :

4,6-Diallyloxycoumarin (2 g.) was refluxed with dimethyl aniline (10 ml.) for 8 hr. The reaction mixture was poured into conc. hydrochloric acid containing crushed ice. The reaction mixture was extracted with ether and the etherial layer was shaken with sodium hydroxide solution. The alkaline layer was separated and acidified with conc. hydrochloric acid. The separated product was filtered and crystallised from alcohol, m.p. 255°. Yield 1.5 g.

Analysis : Found : C, 69.71 ; H, 5.76 %.

$C_{15}H_{14}O_4$: requires: C, 69.78 ; H, 5.43 %.

Evaporation of ether gave no products.

Cyclisation of 8-hydroxy-9-allyl-2-methyl-2,3-dihydro-4-oxo-4H-furo (3,2-c) benzopyran : 2,9-Dimethyl-2,3,9,10-tetrahydro-4-oxo-4H-difuro (3,2-c : 3',2'-f) benzopyran (16) :

8-Hydroxy-9-allyl-2-methyl-2,3-dihydro-4-oxo-4H-furo (3,2-c) benzopyran (1 g.) was triturated with conc. sulphuric acid (5 ml.) for 15 minutes at room temperature.

The mixture was poured into crushed ice. The separated product was filtered and washed with sodium hydroxide solution to remove unreacted compound. The compound was purified by passing its benzene solution over a short column of alumina. It crystallised from benzene-petroleum ether, m.p. 180°. Yield 0.3 g.

Analysis : Found : C, 69.71 ; H, 5.54 %.

$C_{15}H_{14}O_4$: requires : C, 69.78 ; H, 5.42 %.

$\lambda^{\text{Methanol}}_{\text{Max.}}$ 296 nm (log e 4.13), 307 nm (log e 4.05), 342 nm (log e 3.63).

Dehydrogenation of 2.9-dimethyl-2,3,9,10-tetrahydro-4-oxo-4H-difuro (3,2-c : 3',2'-f) benzopyran : 2,9-Dimethyl-4-oxo-4H-difuro (3,2-c : 3',2'-f) benzopyran (17) :

A mixture of 2,9-dimethyl-2,3,9.10-tetrahydro-4-oxo-4H-difuro (3,2-c :3',2'-f) benzopyran (0.5 g.), palladised charcoal (0.3 g.; 10 %) was refluxed with diphenyl ether (4 ml.) for 12 hr. The reaction mixture was filtered hot. After cooling, petroleum ether was added to the filtrate. The separated product was filtered and washed several times with petroleum ether. The product was purified by passing its benzene solution over a short column of alumina. It crystallised from benzene, m.p. 228°. Yield 0.3 g.

Analysis : Found : C, 70.87 ; H, 3.60 %

$C_{15}H_{10}O_4$: requires : C, 70.88 ; H, 3.94 %.

$\lambda^{\text{Methanol}}_{\text{Max}}$ 326 nm (log e 4.50), 342 nm (log e 4.41).

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