CHAPTER II.

STUDIES IN THE SYNTHESIS OF FURO-BENZO-γ-PYRONES

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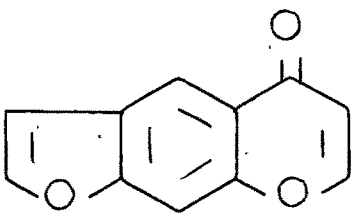
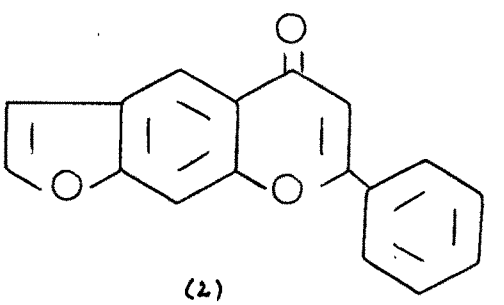
Studies in the synthesis of furobenzo-y-pyrones.

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

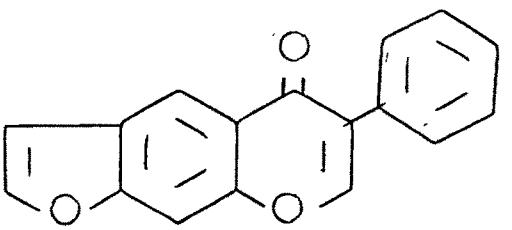
Furobenzo-y-pyrones are the compounds which are obtained either by constructing a furan ring on a suitably substituted benzo-y-pyrone derivatives or constructing a y-pyrone ring on a suitably substituted benzofuran derivatives. These are mainly grouped into furochromones (1), furoflavones (2), furoisoflavones (3) and furoxanthones (4). These may be linear or angular.



(1)



(2)



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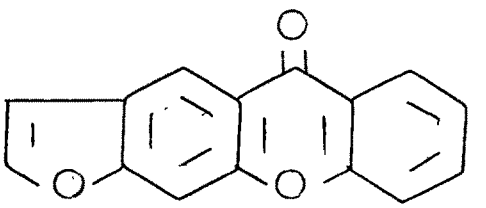
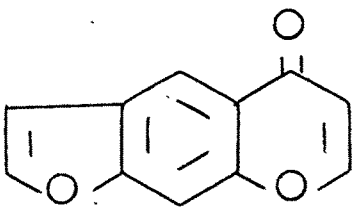


(4)

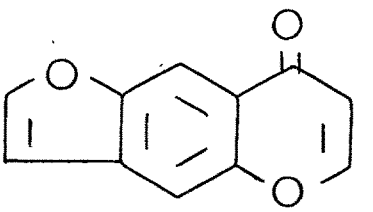
As the present work deals with the synthesis of compounds, which belong to furochromones and furoxanthones, the detailed description is also limited to these two groups only.

Furochromones :

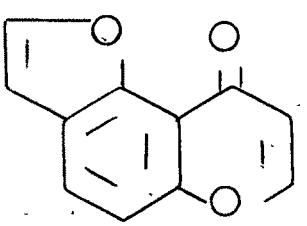
Five isomeric forms of furochromones are found in the literature.



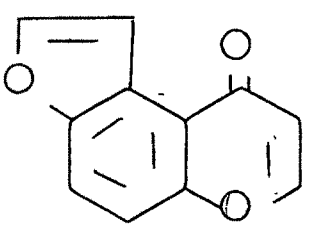
(A)



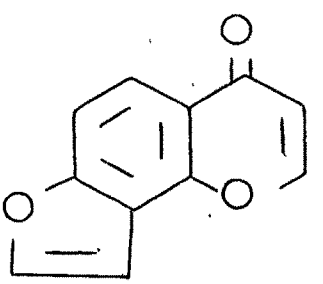
(B)



(C)



(D)



(E)

Furochromones occuring in nature are of the linear type (A) and are limited in number. Many linear and angular furochromones are obtained synthetically. Khellin, Visnagin, Khellinin, Ammiol, Khellinol and Visammiol are the important naturally occuring furochromones. Khellin is the most important member of this group. Many physiological activities of Khellin are known. It has selective antispasmodic effect upon ureter[1,2,3], gall bladder[4,5] and bile duct[6]. A bronchodilating action of Khellin has been reported[7,8,9]. Khellin has specific relaxing effect on the coronary vessles[10,11,12] and it can be used as potent coronary vasodilator[13-21]. It was also used in whooping cough. The inhibitory action of Khellin on gastric ulcers[22,23,24] human tumours[25] and intestinal activity[26] has also been studied. Synergism was observed between Khellin and barbiturate, since it shortened the interval before the hypnotic effect of the barbiturate appeared. Its antispasmodic effect was reinforced by small dose of papaverine. Khellin combined with barbiturate and papavarine produced a sustained hypotensive action.[27]

Khellol glucosides, khellinin, possesses a persistent and rather selective stimulating action on the heart, producing a more complete systol and diastole, with corresponding increase in cardiac output. It increases the coronary flow, and is not cumulative. Contrary to Khellin and Visnagin, it afforded no protection against poisoning by histamine aerosol. It is not converted into Khellin in

the digestive tract or in the body tissue[28].

By studying the chemical constitution and the antispasmodic activity of a number of furochromones, Schonberg and co-workers[29] formed the generallisation, which applies to the compounds of the Khellin and of the Visnagin type. The loss of the furan ring leads to a 70-90 % decrease in activity. Opening of the γ-pyrone ring results in a 75 % loss of activity. Removal of the 8-methoxyl group results in a 30-50 % loss of activity and removal of both 5 and 8-methoxyl groups reduces the activity by 90 %. Simultaneous replacement of both 5- and 8-methoxyl groups by hydroxyl groups reduces the activity by 90 %, but replacement by ethoxyl causes only 25 % loss of activity, whereas higher alkoxyl groups reduces the activity by 80-90 %. Replacement of the 2-methyl group by hydroxyl-methyl group reduces the activity more than 50 % but, on the other hand, replacement of the 2-methyl group by the glucose radical renders the compound almost inactive. Replacement of the 2-methyl group by hydrogen or by ethyl results in 45 % and 25 % loss of activity respectively.

Although among the naturally occuring furochromones, only linear type is known, but many linear as well as angular furochromones are prepared synthetically.

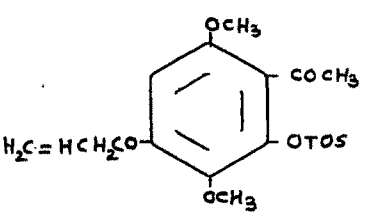
Synthesis of Khellin[30-35], Visnagin and other naturally occuring furochromones have been achieved by many workers by different routes, however, due to the limited space, a few synthesis of special interest are reviewed here.

Seshadri and co-workers[36,37] prepared Khellin (9) as follows :-

2-Tosyloxy-3,6-dimethoxy-4-hydroxy-5-allyl-res-acetophenone (6) was obtained when 2-tosyloxy-3,6-dimethoxy-4-allyloxy resacetophenone (5) was subjected to Claisen rearrangement. Ozonolysis followed by catalytic hydrogenation of (6) gave the corresponding acetaldehyde derivative (7), which on cylisation with polyphosphoric acid followed by hydrolysis gave 4,7-dimethoxy-5-acetyl-6-hydroxycoumarone (8). Kostanecki-Robinson acetylation of (8) gave Khellin (9).

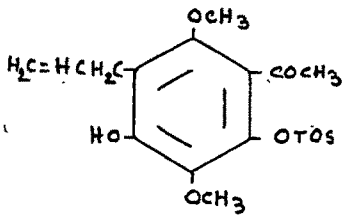
Fayez and Badami[38] synthesised 4-methoxy-7-methyl-5-oxo-5H-furo (3,2-g) benzopyran or visnagin by the condensation of 2-methyl-5-methoxy-6-formyl-7-hydroxychromone (10) with diethyl bromomalonate in acetone and potassium carbonate for 30 hr. to give ethyl-4-methoxy-7-methyl-5-oxo--5H-furo (3,2-g) benzopyran-2-carboxylate (11). Careful saponification of (11) with sulphuric acid in acetic acid solution gave the corresponding acid (12), which was decarboxylated with copper bronze in quinoline to Visnagin (13).

They also synthesised Visnagin starting with 2-methyl-5,7-dihydroxy-6-formylchromone (14), which was prepared from phloroglucinaldehyde through condensation with ethyl acetoacetate in diphenyl ether according to Desai, Trivedi and Sethna[39]. Condensation of (14) with diethyl bromomalonate in ethanolic alkali gave (15), which



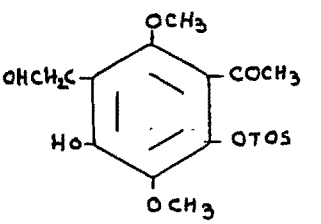
(5)

Claisen rearrangement



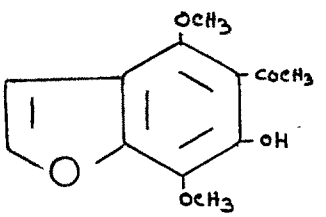
(6)

(i) O_3
(ii) Hydrogenation.



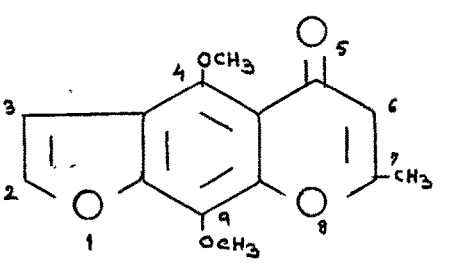
(7)

1. Cyclisation
2. Saponification

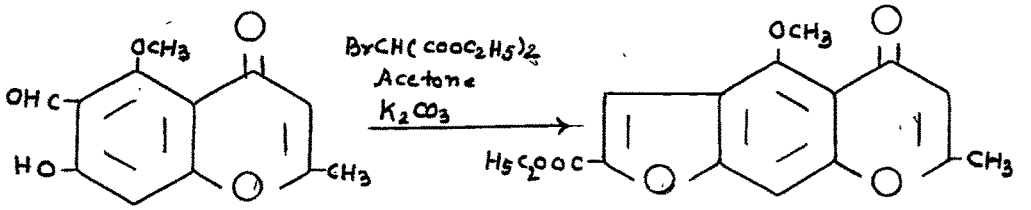


(8)

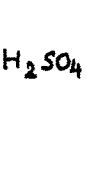
$(CH_3CO)_2O$
CH_3COONa

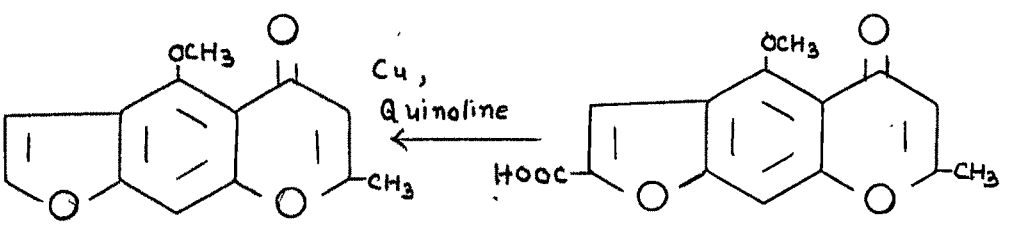


(9)



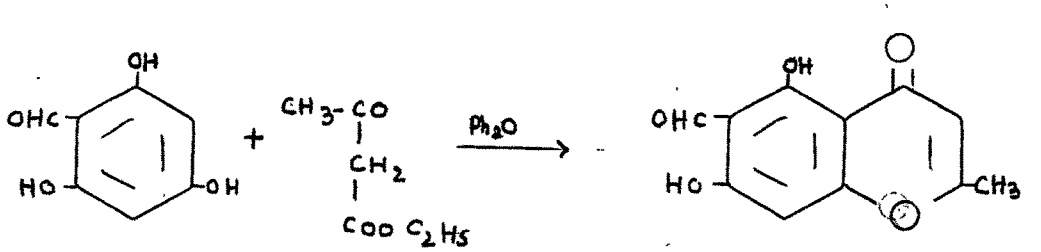
(10) (11)



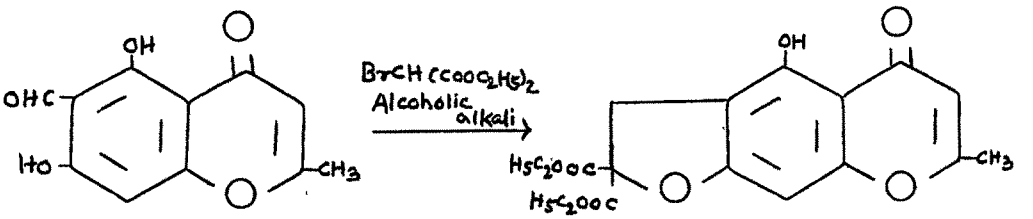


(13) (12)

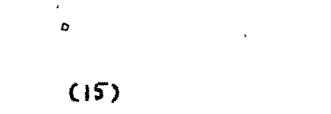
on saponification with potassium carbonate aor hydrochloric acid in acetone solution afforded a mixture comprising (16), which was then methylated to (17). (17) was transformed into visnagin as described before.

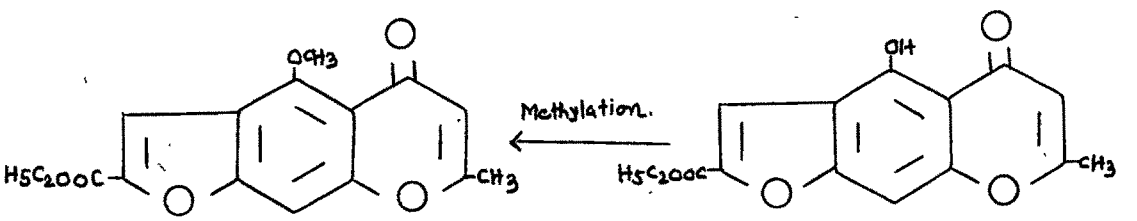


(14)

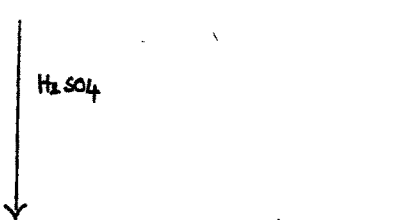

OH
OHC
HO
CH3
BrCH(COOC2H5)2
Alcoholic alkali
OH
H5C2OOC
H5C2OOC
CH3

(14) (15)


K2CO3 or
HCl, Acetone

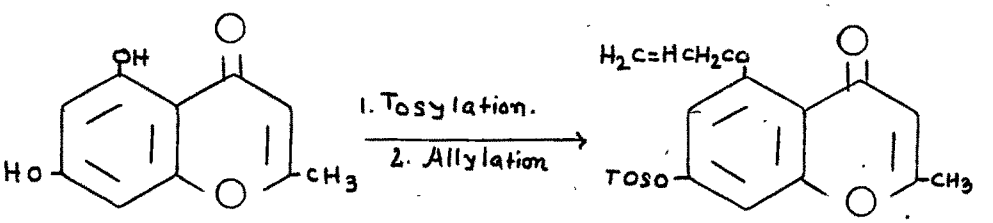

OCH3
H5C2OOC
CH3
Methylation.
OH
H5C2OOC
CH3

(17) (16)

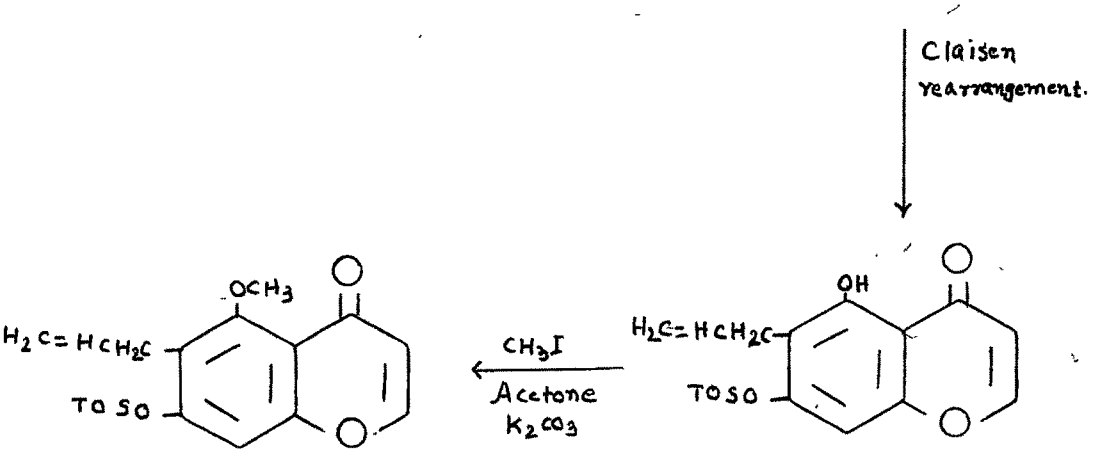

H2SO4
OCH3
HOOC
CH3
Cu,
Quinoline.
OCH3
CH3

(13)

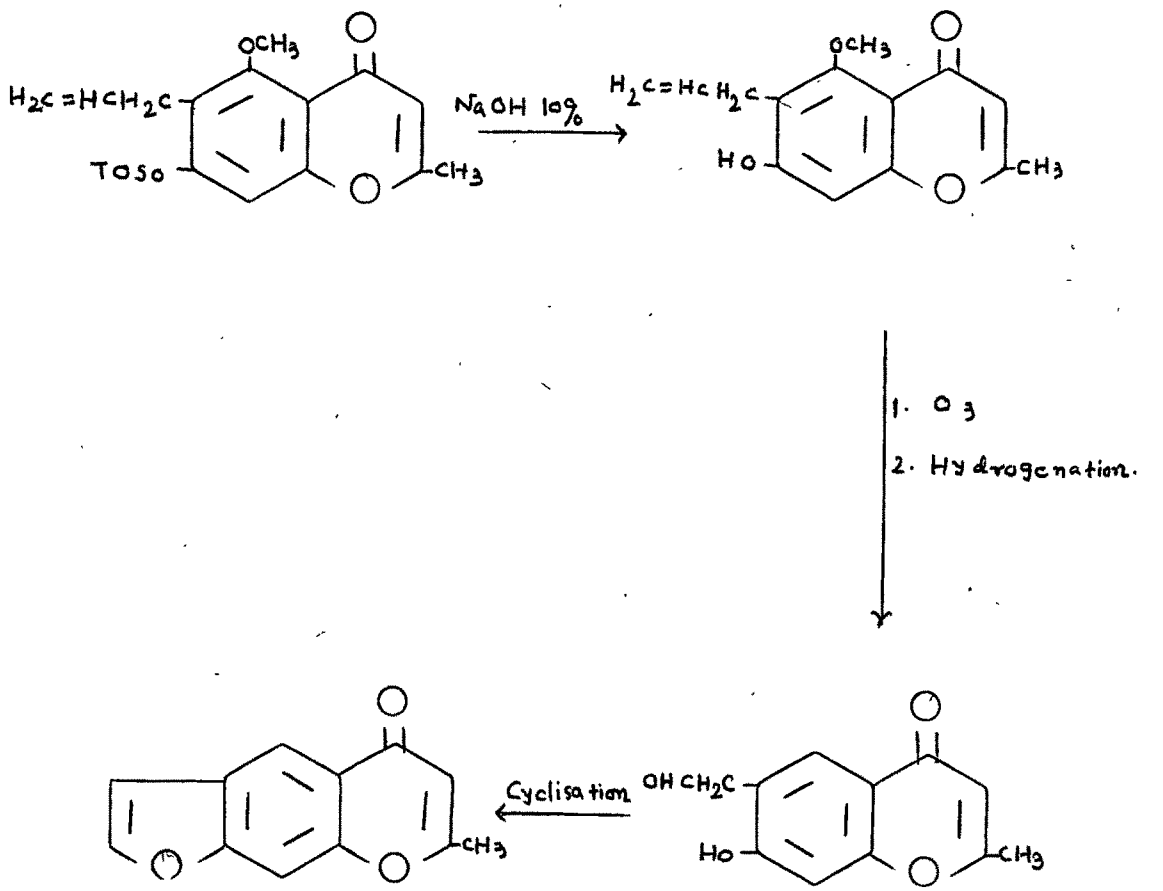
Seshadri and co-workers[40] had also synthesised Visnagin starting with 5,7-dihydroxy-2-methylchromone (18). They had introduced an allyl group into the 6-position (20) by Claisen migration of 5-allyl ether (19). The initial protection of the 7-hydroxyl group was affected by tosylation, which was then removed just before ozonolysis. The previous methylation of the 5-position was advantageous. This gave Visnagin in good yield.



(18) (19)

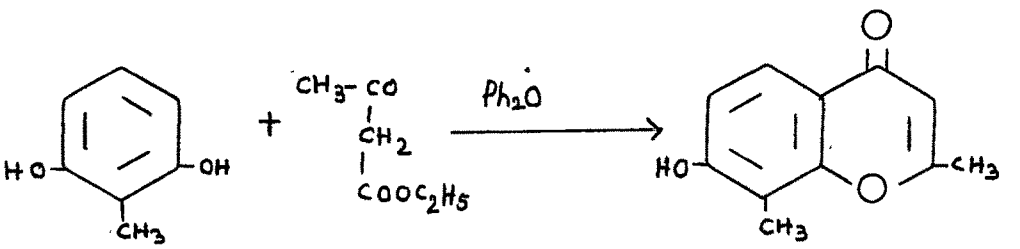


(20)

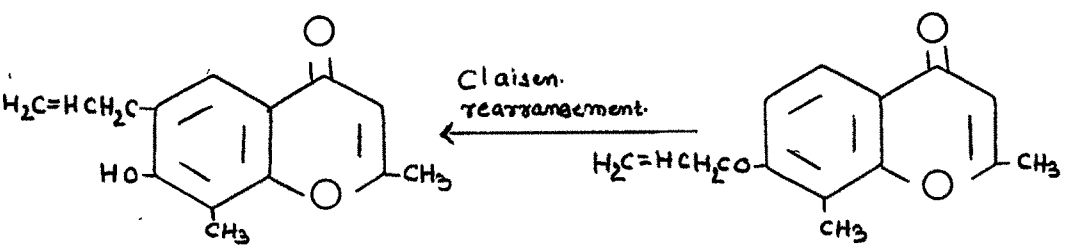


(13)

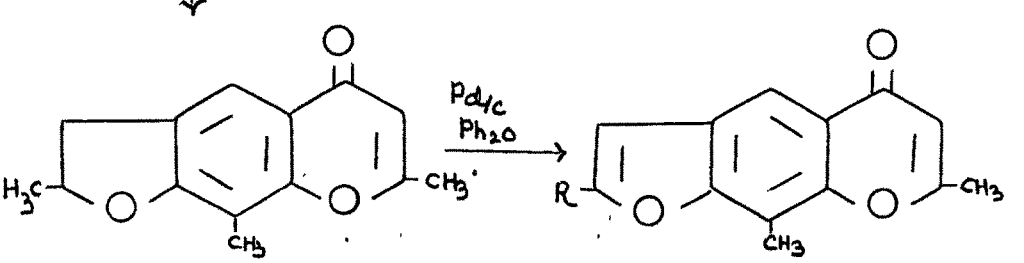
Pardanani and Trivedi[41] have recently synthesised furobenzo-γ-pyrones of the above type. Condensation of 2-methylresorcinol with ethyl acetoacetate in boiling diphenyl ether gave 2,8-dimethyl-7-hydroxychromone (21). This on allylation with allyl bromide afforded the allyl ether, which when subjected to Claisen rearrangement gave



(21)



(22)



(23)

23a, R=CH_3

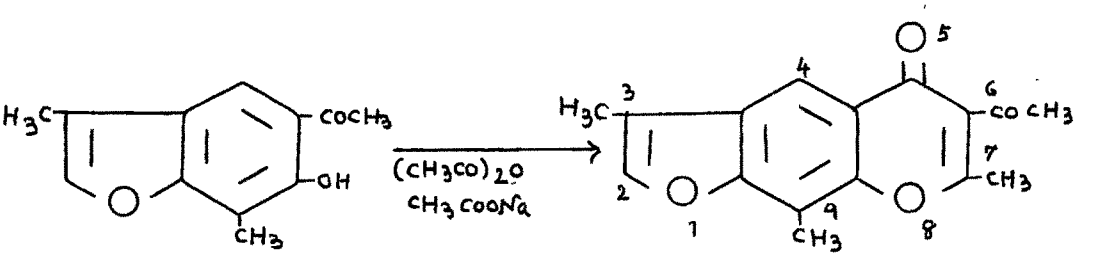
23 b, R=H

6-allyl-7-hydroxy-2,8-dimethylchromone (22). Cyclisation of (22) with conc. sulphuric acid gave the dihydrofuro-benzopyran derivative, which on dehydrogenation with palladised charcoal furnished 2,7,9-trimethyl-5-oxo-5H-furo (3,2-g) benzopyran (23).

Ozonolysis of (22) gave an acetaldehydo derivative, which was cyclised with o-phosphoric acid to give 7,9-dimethyl--5-oxo-5H-furo (3,2-g) benzopyran (23 b).

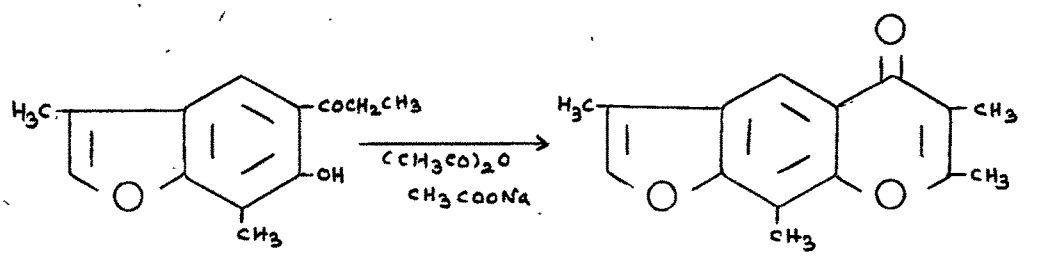
Shaikh and Trivedi[42] synthesised 6-acetyl-3,7,9-trimethyl-5-oxo-5H-furo (3,2-g) benzopyran (25) by the following method :-

Kostanecki-Robinson acetylation of 6-hydroxy-5-acetyl-3,7-dimethyl benzofuran (24) with acetic anhydride and freshly fused sodium acetate gave a product, which was insoluble in cold dilute alkali and did not develop any colouration with alcoholic ferric chloride solution. The compound has been assigned 6-acetyl-3,7,9-trimethyl-5-oxo-5H-furo (3,2-g) benzopyran (25) structure on the basis of I.R.Spectra. Attempts to deacetylate this, either by sodium carbonate or conc. sulphuric acid were unsuccessful.



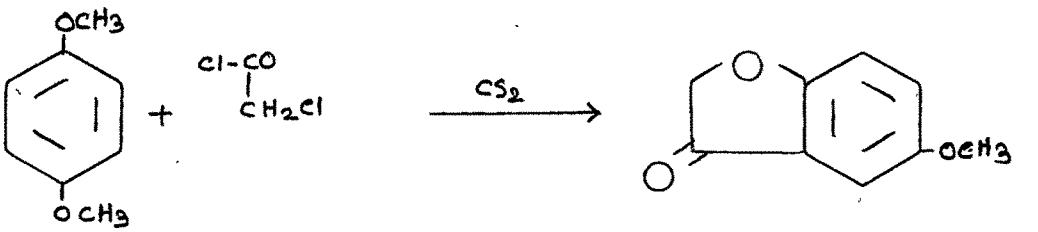
(24) (25)

They have also synthesised 3,6,7,9-tetramethyl-5-oxo-5H-furo (3,2-g) benzopyran (27) by Kostanecki-Robinson acetylation of 6-hydroxy-5-propionyl-3,7-dimethyl benzopyran (26).



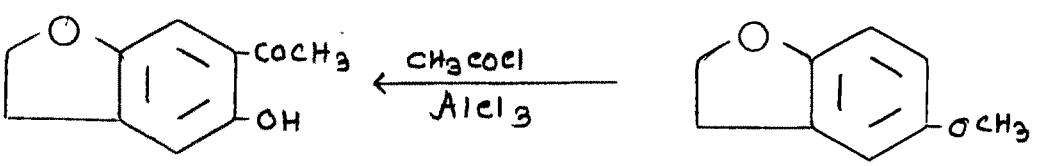
(26) (27)

Furochromones of type (B) where oxygen atoms which are involved in heterocyclic ring are para to one another, was synthesised by Ramage and Stead[43]. Quinol dimethyl ether (28) underwent reaction with chloracetyl chloride to give 2-hydroxy-5-methoxy-phenyl-acyl chloride which was cyclised to 5-methoxycoumaran-3-one (29). Hydrogenation of (29) with Raney nickel gave 5-methoxycoumaran (30), which when treated with acetyl chloride and aluminium chloride gave 5-hydroxy-6-acetylcoumaran (31), which on sublimation under reduced pressure was dehydrogenated to 5-hydroxy-6-acetylcoumarone (32). Claisen condensation of (32) with ethyl acetate in the presence of sodium, underwent simultaneous cyclisation and afforded 6-methyl-8-oxo-8H-furo (2,3-g) benzopyran (33).



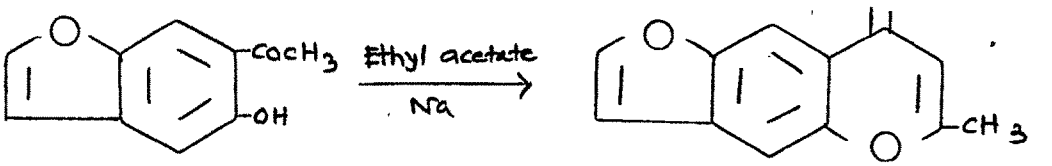
(28) (29)

Raney nickel



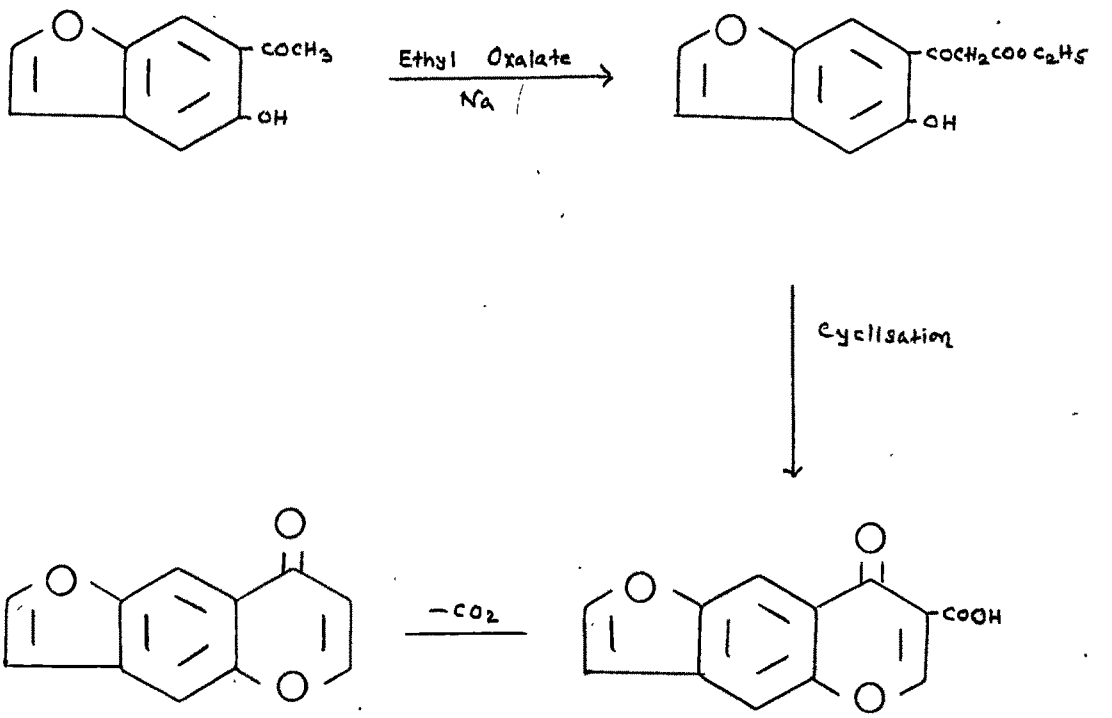
(31) (30)

(Dehydrogenation)
Sublimation



(32) (33)

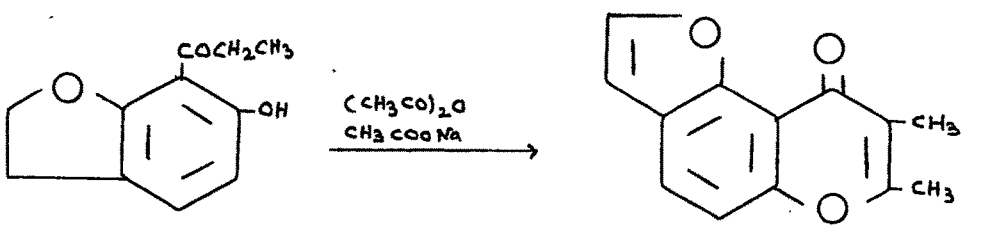
Use of ethyloxalate instead of ethyl acetate in Claisen condensation gave the diketo ester (34), which was cyclised to 8-oxo-8H-furo (2,3-g) benzopyran-2-carboxylic acid (35). This acid was smoothly decarboxylated in vacuo to 8-oxo-8H-furo (2,3-g) benzopyran (36).



Furochromone of type (C) was prepared by Clarke, Glaser and Robertson[44]. Application of Hoesch reaction with acetonitrile or of Friedel-Craft reaction with acetyl chloride on 2-carboethoxy-4-methoxy-6-hydroxycoumarone (37) where carbethoxy group served to protect the reaction in

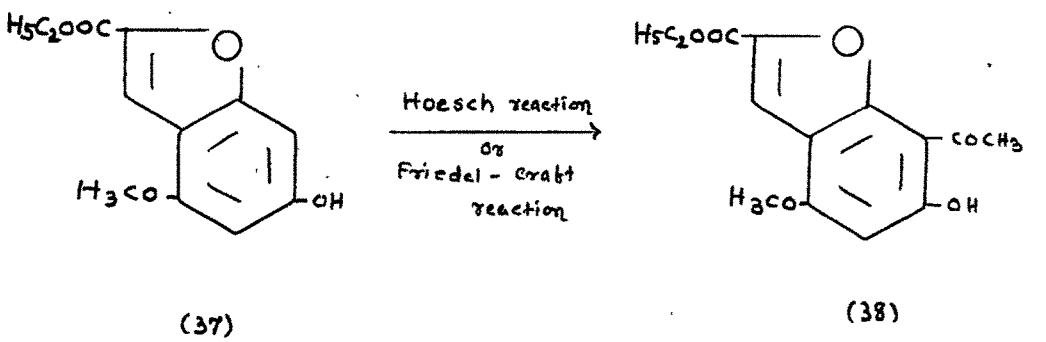
2-position, gave 7-acetyl derivative (38), which on hydrolysis and seubsequent decarboxylation afforded 4-methoxy-6-hydroxy--7-acetylcoumarone (39). Claisen condensation of (39) with ethyl acetate gave the diketone (40), which was cyclised to 4-methoxy-7-methyl-9-oxo-9H-furo (2,3-f) benzopyran (41).

Shaikh and Trivedi[42] synthesised 7,8-dimethyl-9-oxo-9-H-furo (2,3-f) benzopyran (43) from 6-hydroxy-7-propionyl-benzofuran (42) by Kostanecki-Robinson acetylation.



(42) (43)

They also synthesised 7-phenyl8-methyl-9-oxo-9H-furo (2,3-f) benzopyran (45), 3,7,8-trimethyl-9-oxo-9H-furo (2,3-f) benzopyran (47) from 6-hydroxy-7-propionyl benzofuran (44) and 6-hydroxy-7-propionyl-3-methylbenzofuran (46) by Kostanecki-Robinson acetylation.

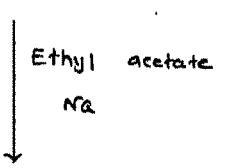

H5C2OOC
H3CO
OH
Hoesch reaction
or
Friedel - Crafft
reaction
COCH3

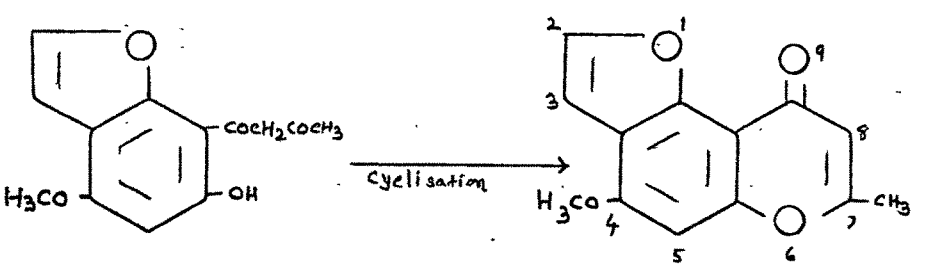
(37) (38)


Hydrolysis

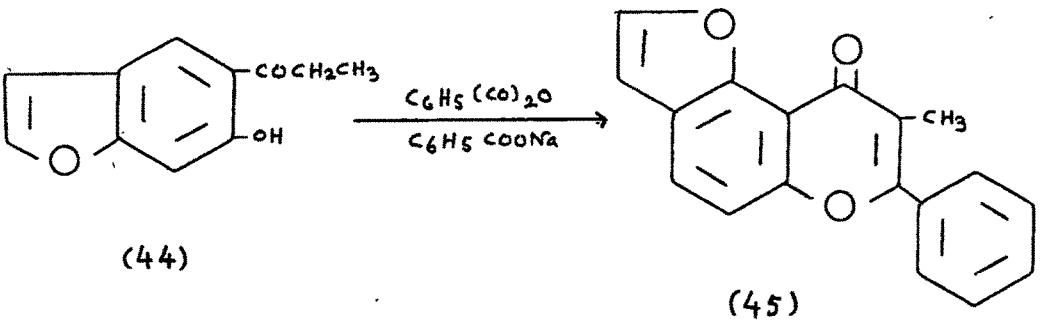
HOOC
COCH3
H3CO
OH
−CO2

(39)

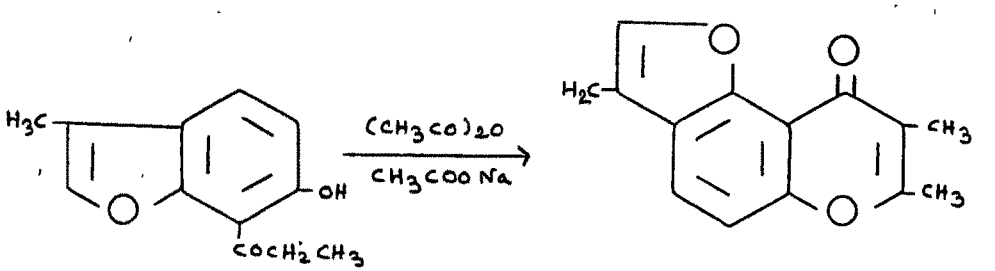

Ethyl acetate
Na


COCH2COCH3
H3CO
OH
Cyclisation
CH3

(40) (41)



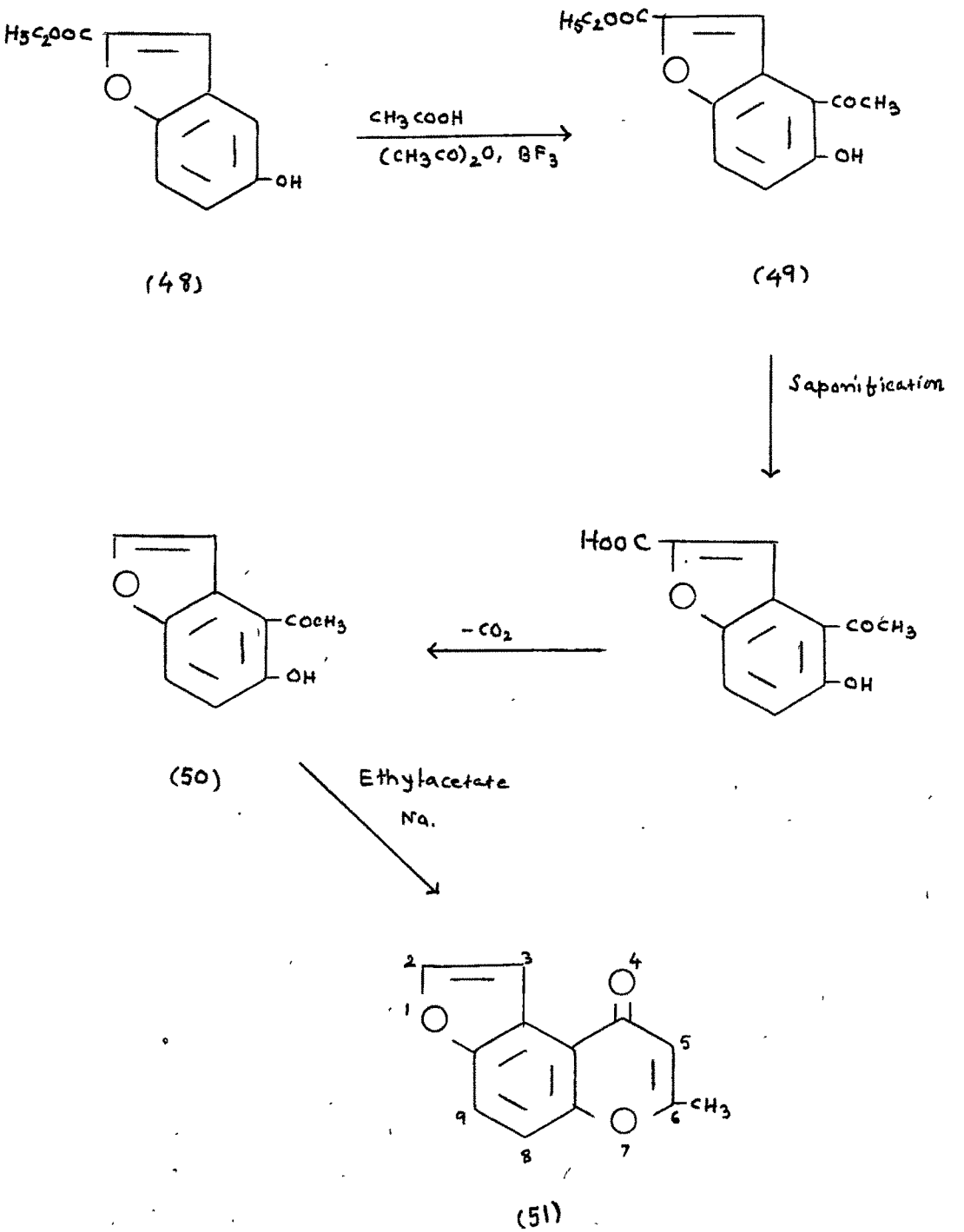
(44) (45)



(46) (47)

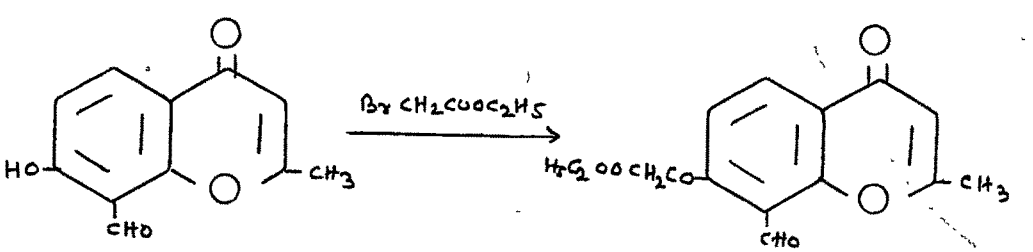
The synthesis of furochromone of type (D) was achieved by Ramchandran and co-workers[45]. Acetylation of 2-carbethoxy-5-methoxycoumarone (48) in boron trifluoride and acetic acid-acetic anhydride at room temperature for 80 hr. gave 2-carbethoxy-4-acetyl-5-hydroxycoumarone (49), which on saponification followed by decarboxylation gave 5-hydroxy-4-acetyl benzofuran (50). Claisen condensation of (50) with ethyl acetate directly gave 6-methyl-4-oxo-

-4H-furo (3,2-f) benzopyran (51). This represented the first example of the synthesis of furochromone of type(D).

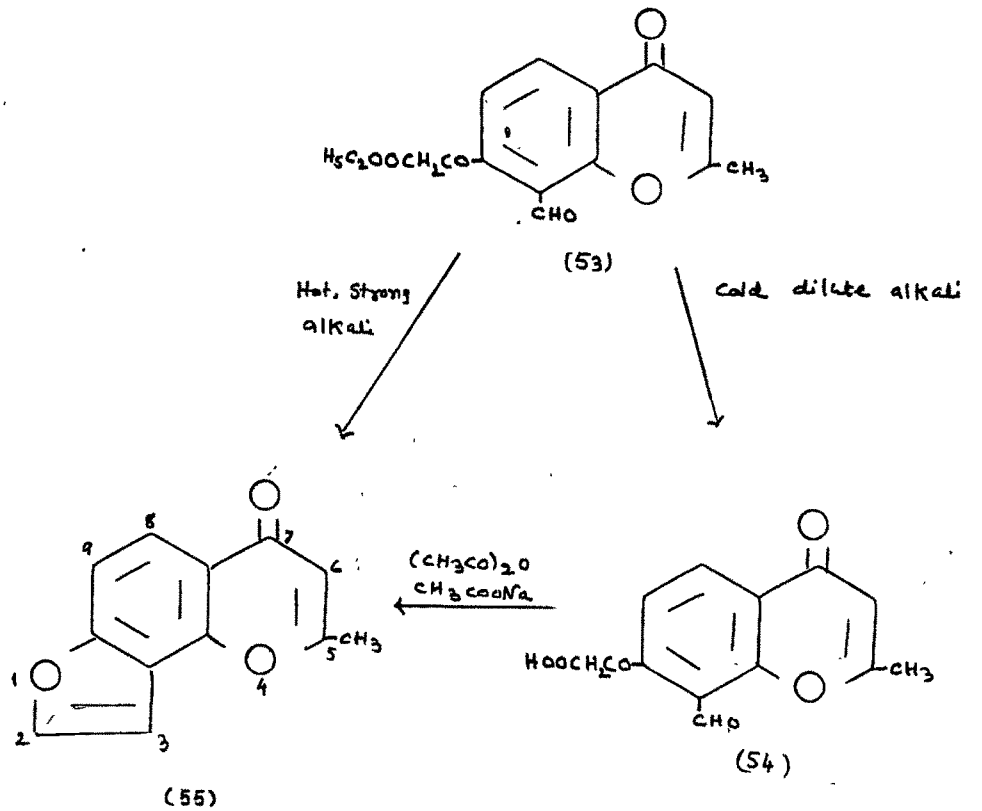


Synthesis of furochromone of type (E) was achieved by many workers.

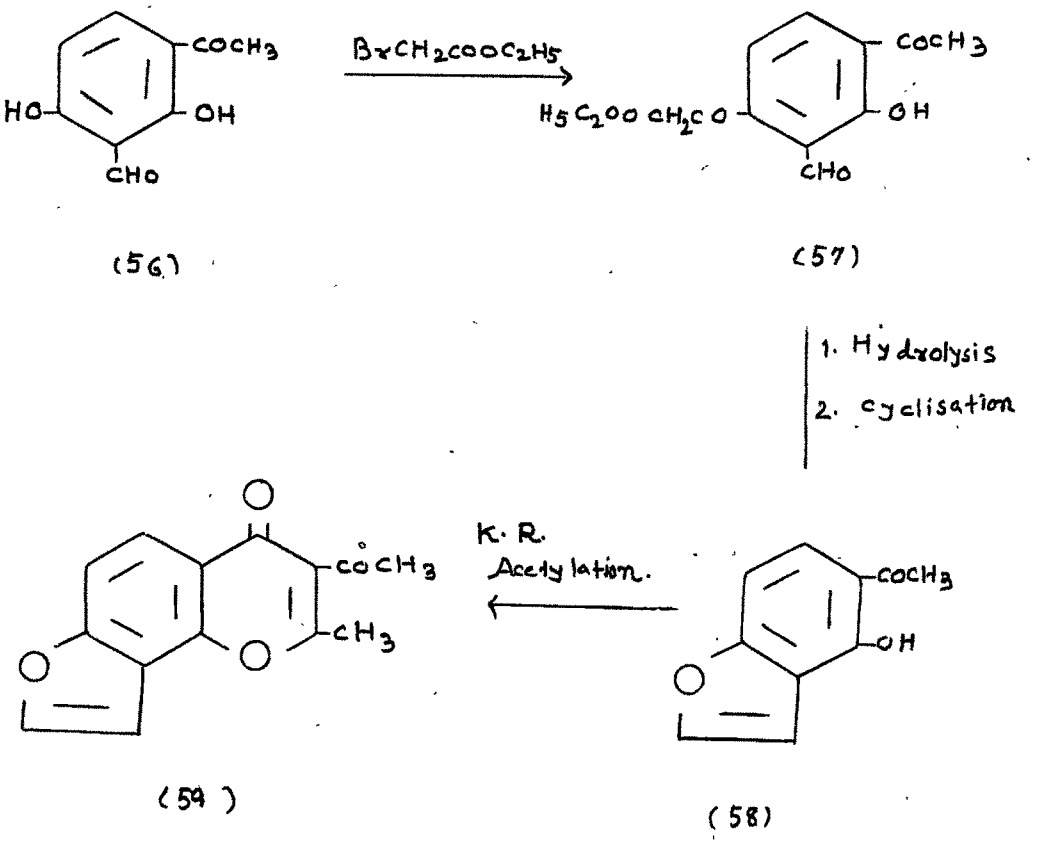
Rao, Subramanyam and Venkateswarlu[46] has synthesised this type of furochromone by constructing a furan ring on a suitably substituted chromone. 8-Formyl-7-hydroxy-2-methylchromone (52) was condensed with ethyl bromo acetate, yielding ethyl-8-formyl-2-methyl-7-chromonyloxy acetate (53), which on hydrolysis with cold dilute alkali gave the corresponding carboxylic acid (54), while hydrolysis using strong hot alkali gave the corresponding furochromone (55), decarboxylation and cyclisation taking place simultaneously during the course of the hydrolysis. Furochromone (55) could also be produced by cyclising the acid (54) using acetic anhydride and sodium acetate.



(52) (53)

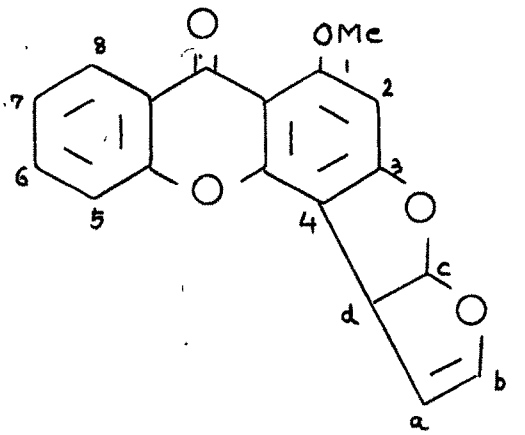


The same authors haye synthesised similar type of furochromone starting with 2,4-dihydroxy-3-formyl-res-acetophenone (56), which was condensed with ethyl bromo-acetate to give 4-O-carbethoxy-methyl-3-formyl-2-hydroxy acetophenone (57). Hydrolysis followed by cyclisation of (57) gave 5-acetyl-4-hydroxy benzofuran (58), which on Kostanecki-Robinson acetylation gave 5-methyl-6-acetyl-7-oxo-7H-furo (2,3-h) benzopyran (59). Deacetylation of this was a failure.



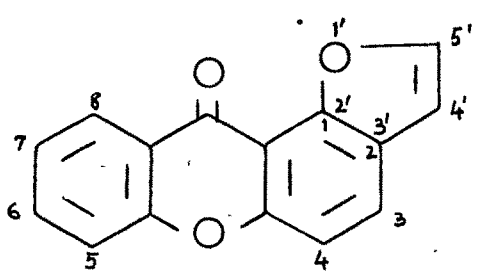
Furoxanthones :

Xanthones are naturally occuring compounds found in fungi and plants. A condensed furan nucleus occur in a number of related natural products, viz., furocoumarins, furochromones, furoflavones, etc. Furoxanthones are the condensed nucleus of furan with xanthones. Sterigmatocystin[47-54] (3a, 12a-dihydro-8-hydroxy-6-methoxy-7H-furo (3',2'-4,5) furo (2,3-c) xanthen-7-one) (60) is a naturally occuring furo-xanthone. Sterigmatocystin has no significant tuberculostatic or amoebicidal activity.

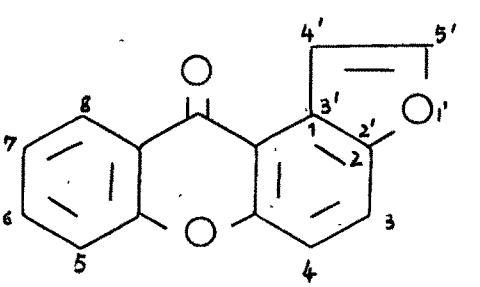


(60)

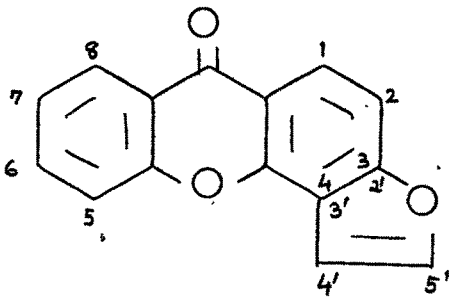
The parent pyrans, the furoxanthenes, are not known to occur in nature. Six isomeric forms of furoxanthones are found in literature.



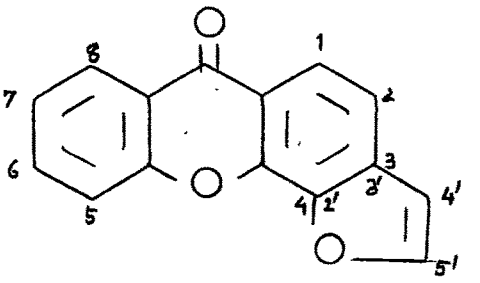
(A)



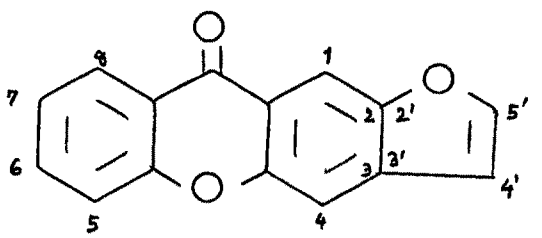
(B)



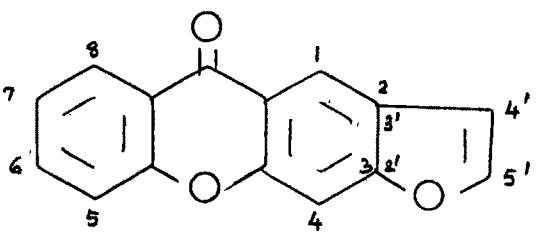
(C)



(D)



(F)



(E)

Furoxanthones of type (A) was synthesised by F. Scheinmann and H. Suschitzky[55], by the following methods.

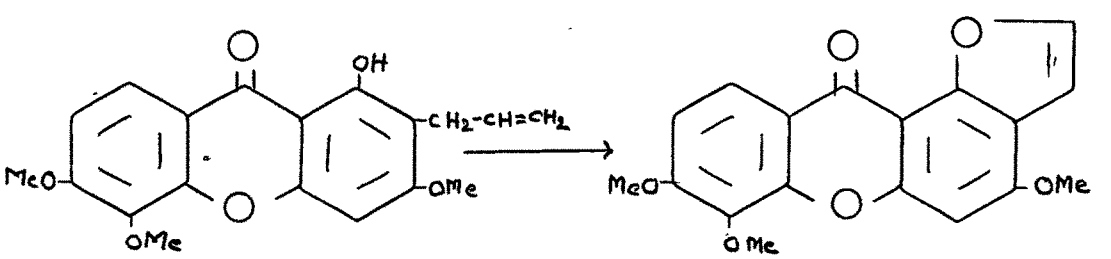
1-Allyloxyxanthone (61) on Claisen rearrangement by refluxing in dimethylaniline afforded 2-allyl-1-hydroxy-xanthone (62). Addition of bromine to 2-allyl-1-hydroxy-xanthone gave the dibromo adduct (63), from which two molecules of hydrogen bromide were eliminated by treatment with ethanolic sodium ethoxide to give a cyclic ether. By

analogy with the results of Adams and Rindfusz[56], who cyclised o-allylphenols by the same method, they assigned the furano structure (64) to above cyclic ether.

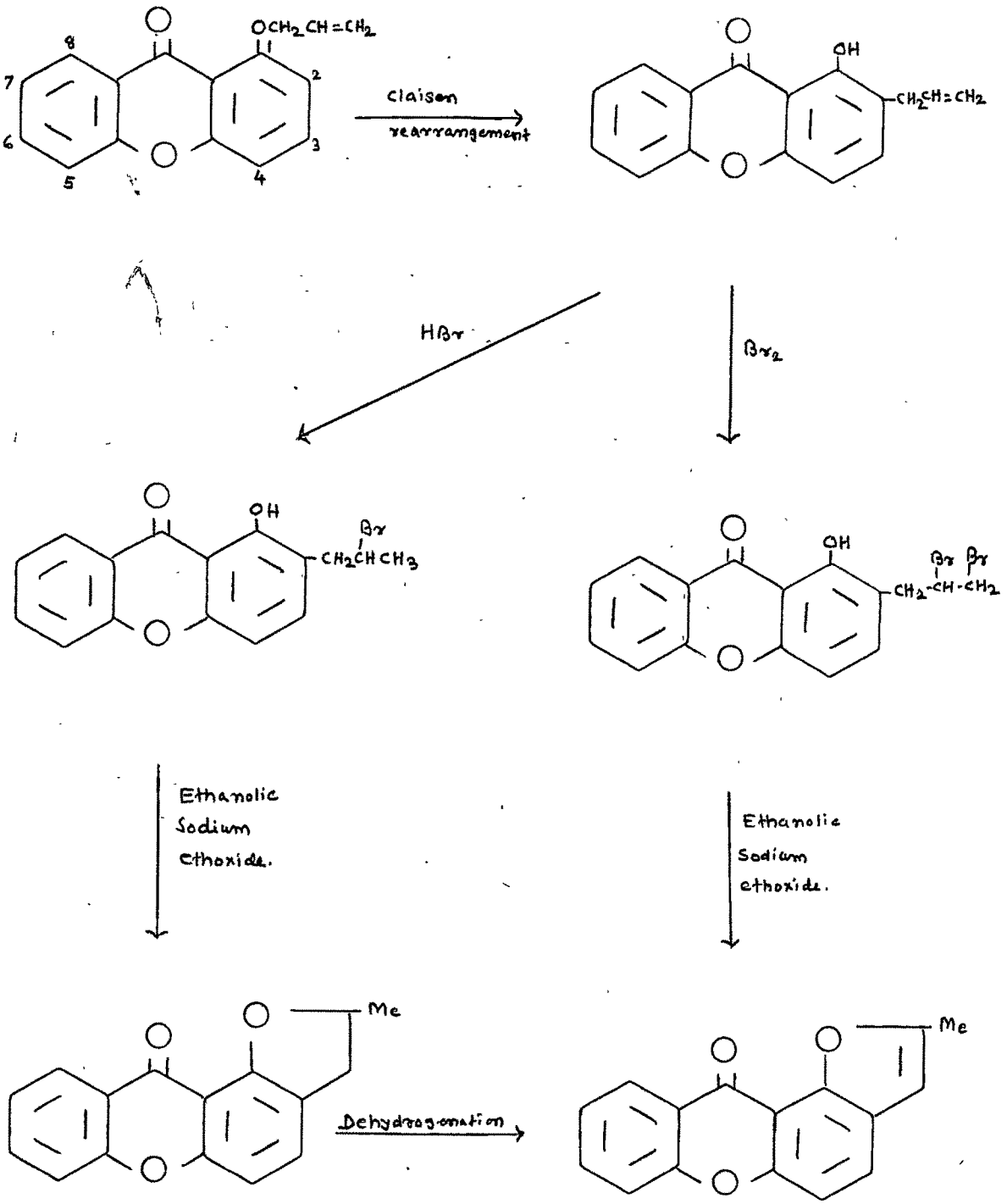
2-Allyl-1-hydroxyxanthone (62) was made to react with hydrogen bromide to give 2-B-bromopropyl-1-hydroxy-xanthone (65). Cyclisation of this bromo compound by refluxing in ethanolic sodium ethoxide gave, a furoxanthone 5'-methyl-4 ,5'-dihydrofuro (2',3'-1,2) xanthone (66) almost quantitatively. The attempts to convert the furoxanthone (66) by dehydrogenation into (64) failed.

Seshadri and co-workers' new method[57] on synthesing benzopyrono furans has recently been adopted by Scheinmann and co-workers[58,59], for the preparation of the furoxanthone.

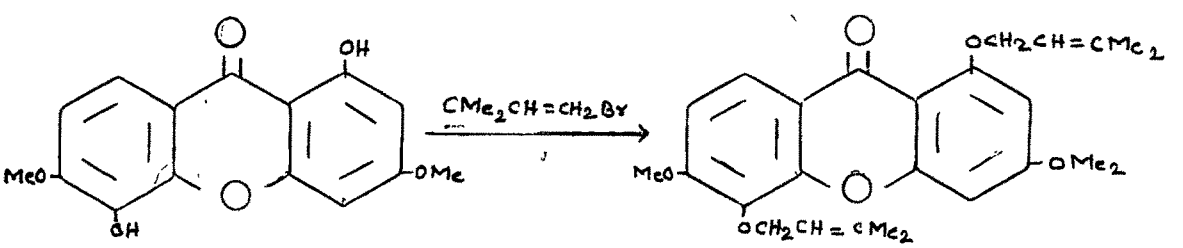
Ozonolysis of the allyl derivative (67), followed by cyclisation with polyphosphoric acid gave 3,5,6-trimethoxy-furo (2',3'-1,2) xanthone (68).



(67) (68)

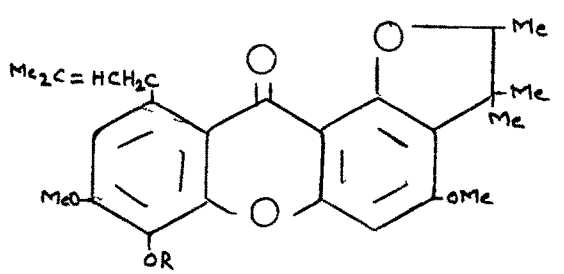

OCH2CH=CH2
8
7
6
5
4
3
2
Claisen rearrangement
OH
CH2CH=CH2
HBr
Br2
OH
Br
CH2CHCH3
OH
Br Br
CH2-CH-CH2
Ethanolic Sodium ethoxide.
Ethanolic Sodium ethoxide.
Me
Dehydrogenation
Me

The reaction of 1,5-dihydroxy-3,6-dimethoxy-xanthone (69) with 3,3-dimethyl allyl bromide gave the ether (70) which rearranged in dimethyl aniline to two xanthones (71 and 72a). Migration in the other ring occurs to yield the ortho product, 5-hydroxy-2,6-dimethoxy-8-(3',3'-dimethyl-allyl)-4',5'-dihydro-4',4',5'-trimethyl furo (2',3'-1,2) xanthone (72), and in addition the para isomer (71). Methylation of (72a) gave the trimethyl ether (72b)[59].



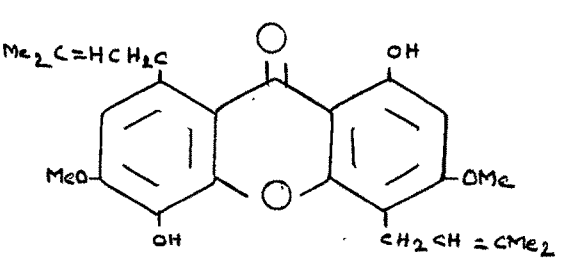
(69) (70)

Claisen rearrangement.



(72)

72 a, R=H ; 72 b, R=Me.



(71)

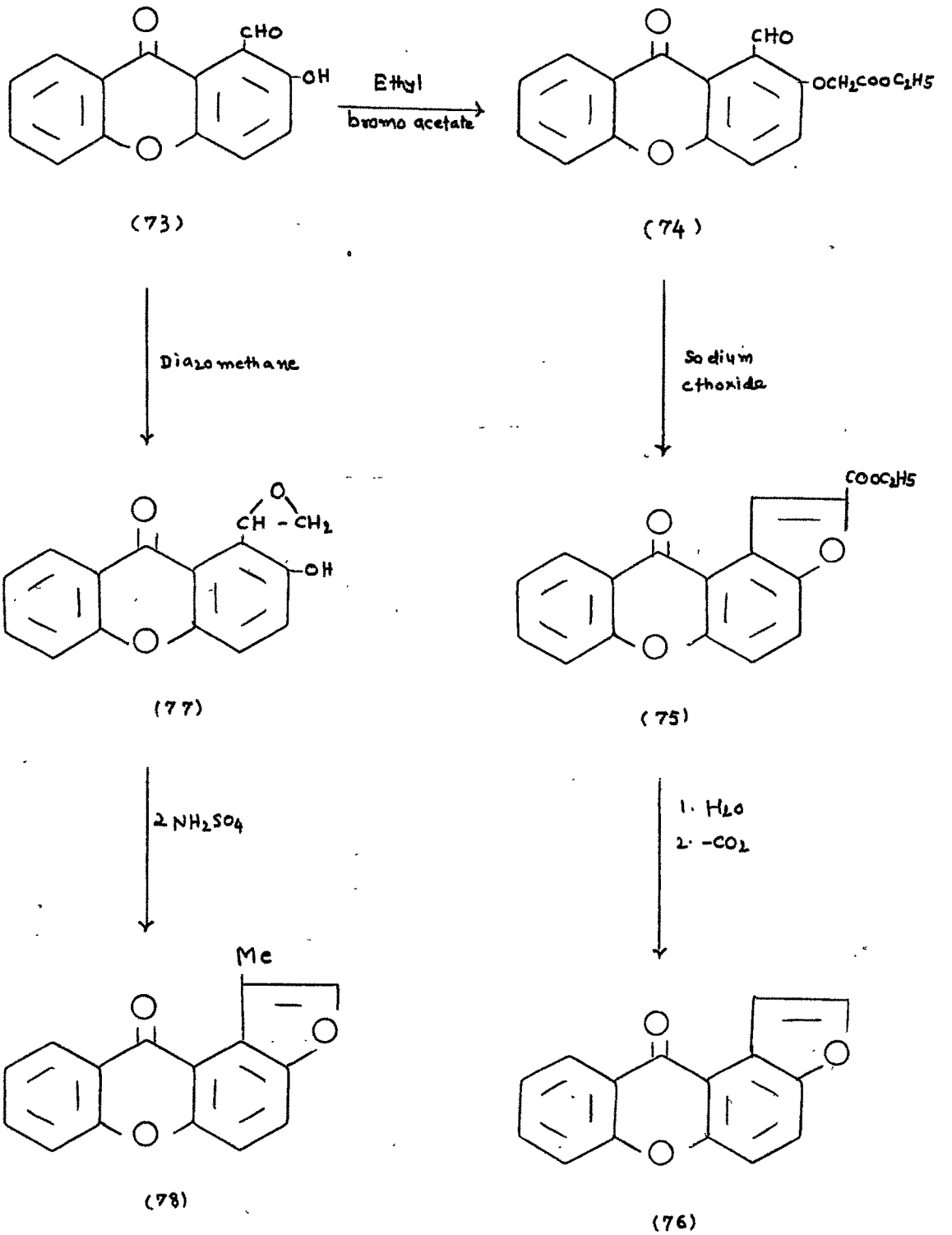
Furo xanthones of type (B) was synthesised by Davies and his co-workers[60].

This synthesis employs one of the typical methods for the preparation of benzofuran derivatives, viz., a mixed Claisen type condensation or internal aldol condensation using the appropriately substituted aldehyde or ketone and bromoacetic or bromomalonic ester.

2-Hydroxyxanthone was readily formylated by a Duff reaction to obtain 1-formyl-2-hydroxyxanthone (73). Cyclisation of 1-formyl-2-xanthyloxy acetate (74)(obtained by condensation of 1-formyl-2-hydroxyxanthone and ethyl bromo acetate) in ethanol with sodium ethoxide at room temperature gave 5'-carbethoxy-furo (3',2'-1,2) xanthone (75) in good yield. Hydrolysis of this ester followed by decarboxylation, gave the parent angular furoxanthone (76), which was also obtained by ring closure of 1-formyl-2-xanthyloxy acetic acid accompanied by decarboxylation.

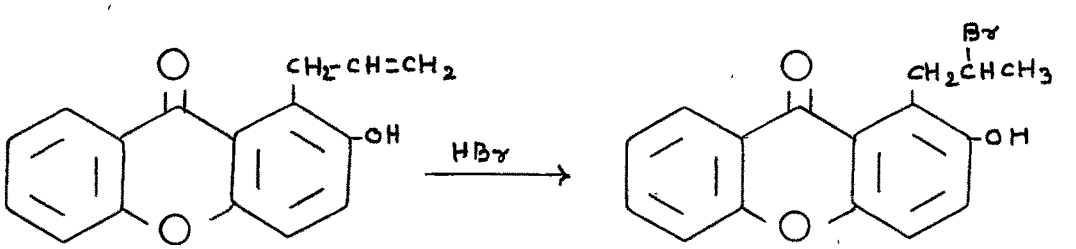
F. Lamb and H. Suschitzky[61] have prepared 4'-methylfuro (3',2'-1,2) xanthone (78) by the following :- method :-

1-Formyl-2-hydroxyxanthone (73) was made to react with diazomethane yielding 2-hydroxy-1-xanthylethylene oxide (77), which on treatment with 2-N-sulphuric acid gave the furoxanthone (78).

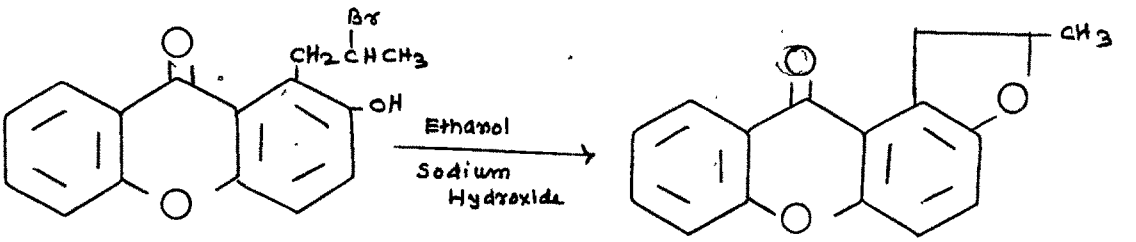

CHO
OH
Ethyl
bromo acetate
CHO
$OCH_2COOC_2H_5$
(73)
(74)
Diazomethane
Sodium
ethoxide
$CH-CH_2$
O
OH
$COOC_2H_5$
(77)
(75)
$2\ NH_2SO_4$
1. H_2O
2. $-CO_2$
Me
(78)
(76)

On the other hand, the corresponding ketone, viz., 2-acetyl-1-hydroxyxanthone, which can also be submitted to a similar internal condensation leading to the formation of a furan skeleton, can be more readily prepared and in better yield from the hydroxyxanthones by means of the Friedel-Crafts-Fries reactions. However, while aldehydo ester give rise to furo compounds, unsubstituted in the furan ring. The use of substituted ketones for such internal Claisen condensation results in the formation of furo compounds carrying a methyl substituent in the B-position.

Cyclisation of 1-β-bromopropyl-2-hydroxyxanthone (80), obtained by treatment of 1-allyl-2-hydroxyxanthone (79) with hydrogen bromide in ethanol with sodium hydroxide yields 5'-methyl-4',5'-dihydro furo (3',2'-1,2) xanthone(81).



(79) (80)

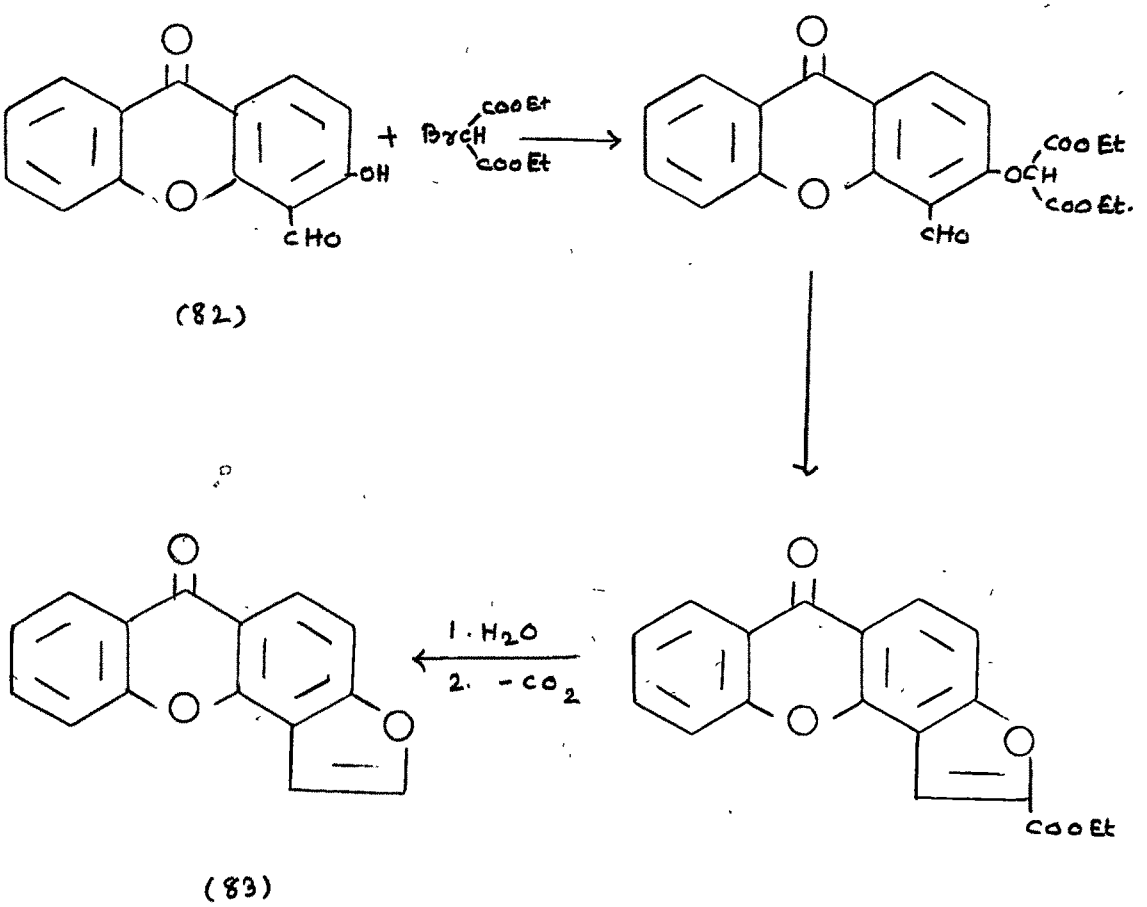


(80) (81)

Furoxanthone of type (C) was synthesised by G.S. Puranik and S. Rajopal[62]. 4-Formyl-3-hydroxyxanthone (82) when condensed with bromomalonic ester, which effected simultaneous esterification and internal aldol condensation followed by hydrolysis and decarboxylation of 5'-carbethoxy derivative formed, yielded furo (3',2'-4,3) xanthone (83).

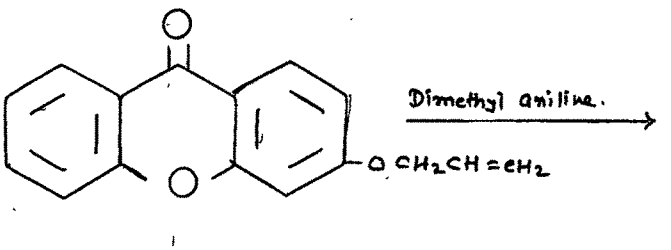
The same authors[63] have also synthesised 5'-methyl and 5',6-dimethyl furo (3',2'-4,5) xanthone.

3-Allyloxy xanthone (84) on Claisen rearrangement in dimethylaniline afforded 4-allyl-3-hydroxyxanthone (85). Two methods for the furan ring closure of 4-allyl-3-hydroxy-xanthones were adopted. The first based on Scheinmann and Suschitzky's work[55], which gives dihydro furo compounds, by the following route. 4-Allyl-3-hydroxyxanthone was treated with hydrogen bromide gas in the presence of traces

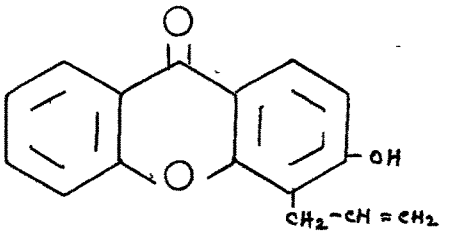


of diphenylamine gave 4-β-bromopropyl-3-hydroxyxanthone (86), which on treatment with acetone and potassium carbonate gave 4',5'-dihydro-5'-methyl-furo (3',2'-4,3) xanthone (87). Dihydrofuro xanthone was dehydrogenated by treatment with N-bromo succinimide in the presence of benzoyl peroxide, followed by dehydro bromination with pyridine[64] to 5'-methyl furo (3',2'-4,3) xanthone (88a).

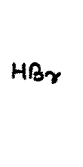
The second route is an adaption of Adams and Rindfusz's[56] method, involving addition of bromide to 3-acetoxy-

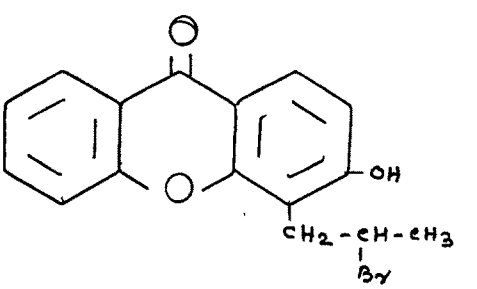

Dimethyl aniline.
O CH2CH=CH2

(84)


OH
CH2-CH=CH2

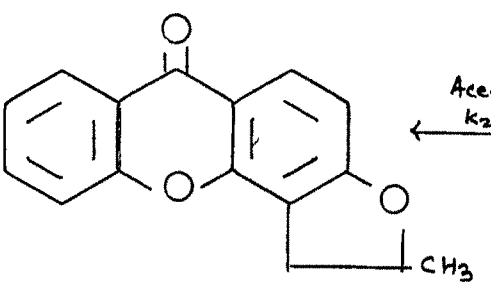
(85)


HBr

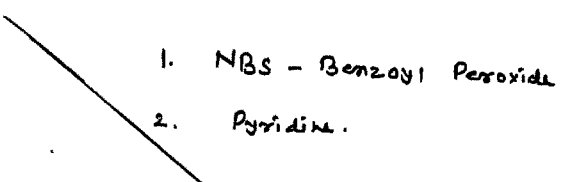

OH
CH2-CH-CH3
Br

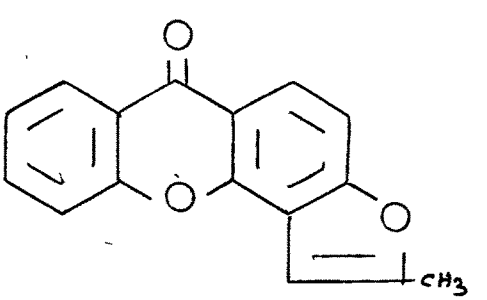
(86)

Acetone
K2CO3


CH3

(87)


1. NBS - Benzoyl Peroxide
2. Pyridine.

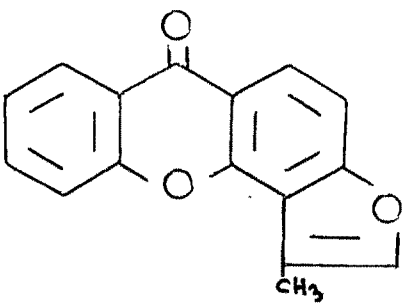

CH3

(88)

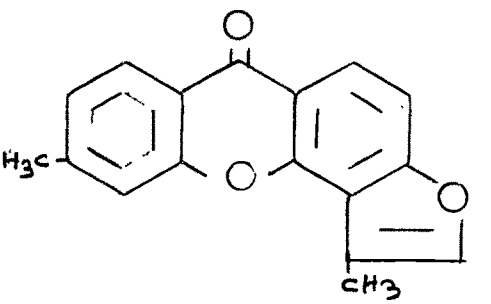
-4-allyl derivatives followed by cyclisation and dehydro bromination by reaction with alcoholic potassium hydroxide.

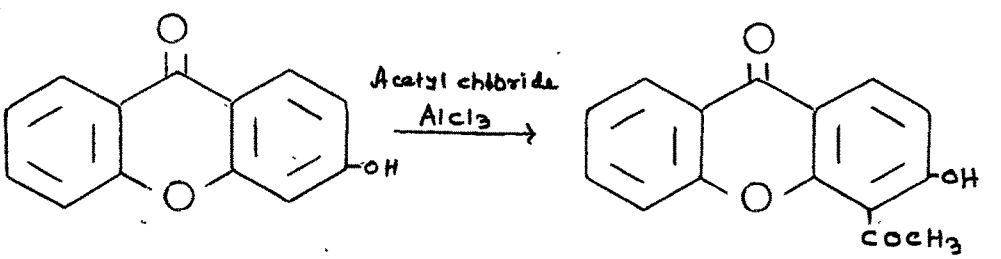
3-Allyloxy-6-methyl xanthone, by the same series of reaction gave 5',6-dimethyl furo (3',2'-4,3) xanthone (88b).

They[64] also synthesised 4'-methyl-furo (3',2'-4,3) xanthone (92) and 4',6-dimethyl-furo (3',2'-4,3)xanthone (95) starting from 3-hydroxy and 3-hydroxy-6-methylxanthone by the following route :-



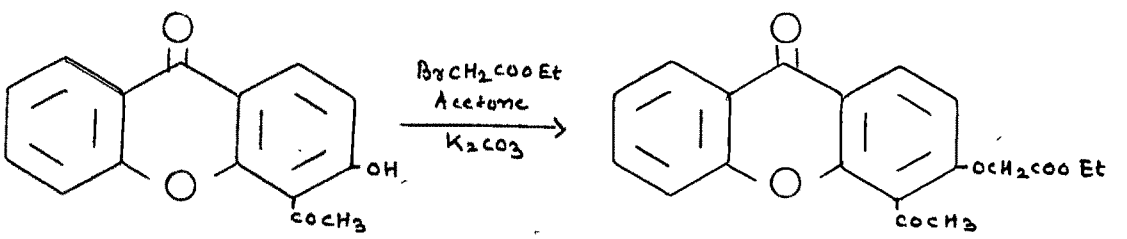
(92)



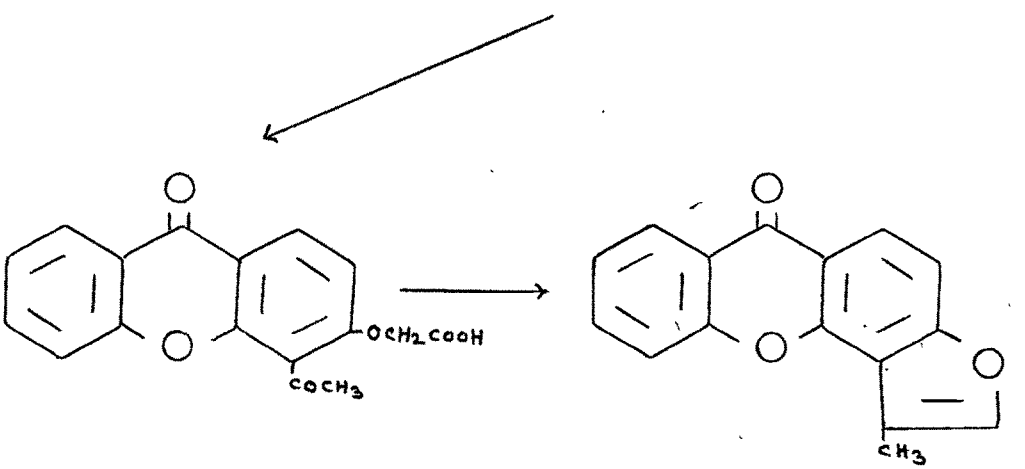


(89)

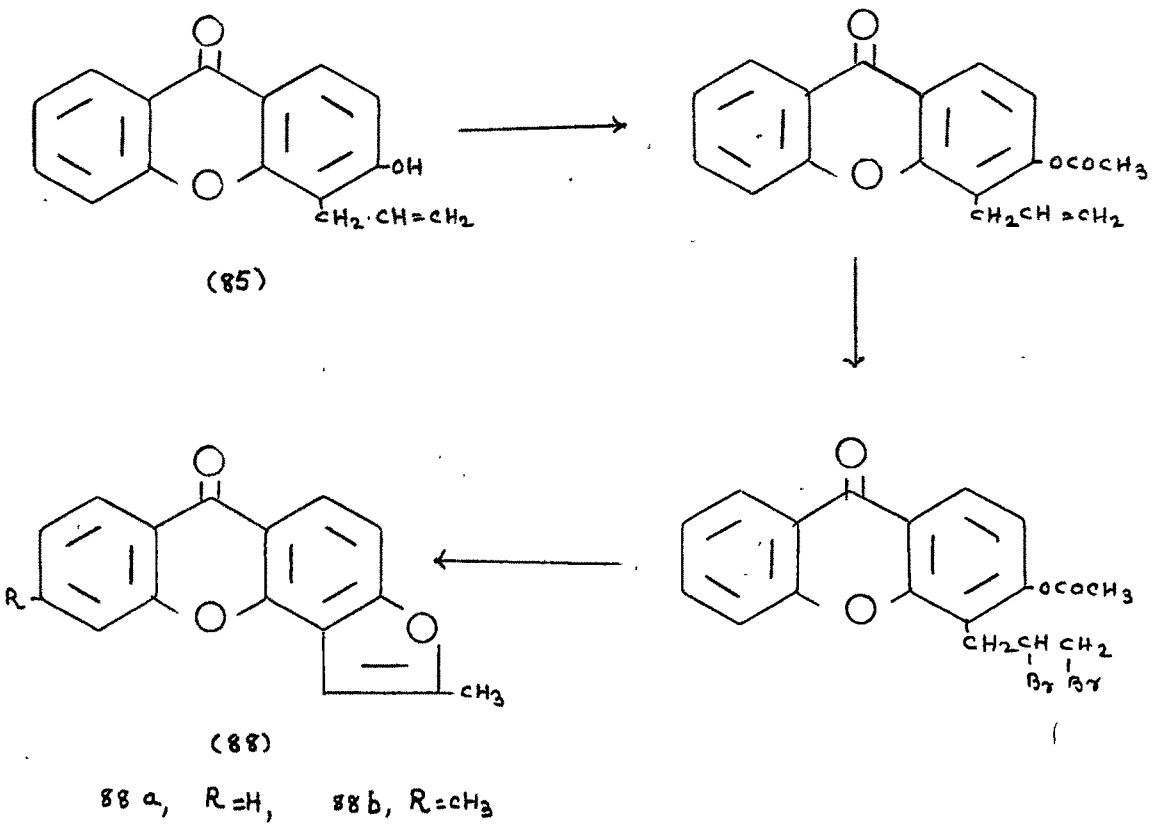
3-Hydroxyxanthone on treatment with acetyl chloride in the presence of aluminium chloride yielded 4-acetyl-3-hydroxyxanthone (89). 4-Acetyl-3-hydroxyxanthone (90) condensed with bromo acetic ester in the presence of potassium carbonate and acetone to yield Ethyl-4-acetyl-9-oxo-3-xanthyloxy acetate (90), which on hydrolysis with aqueous potassium hydroxide gave 4-acetyl-9-oxo-3-xanthyloxy acetic acid (91). The internal Claisen condensation of the acid (91) with sodium acetate and acetic anhydride yielded 4'-methyl-furo (3',2'-4,3) xanthone (92).



(89) (90)



(91) (92)



(85)

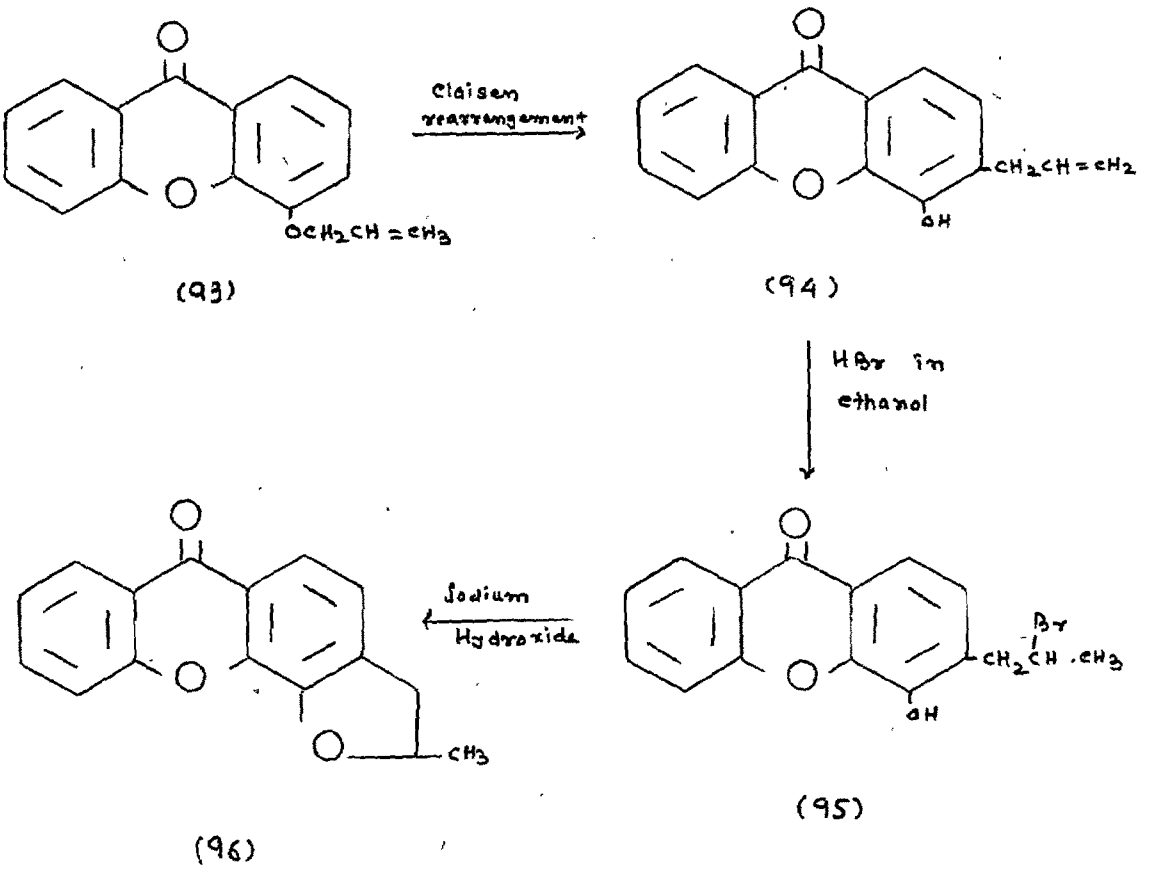
(88)

88 a, R=H, 88 b, R=CH3

3-Hydroxy-6-methylxanthone on similar series of reactions gave 4',6-dimethylfuro (3',2'-4,3) xanthone.

Furoxanthone of type (D) was synthesised by A. Mustafa and his co-workers[65].

4-Allyloxy-xanthone (93) on Claisen rearrangement gave 2-allyl-4-hydroxyxanthone (94). Cyclisation of 3-β-bromopropyl-4-hydroxyxanthone (95), obtained by treatment of 3-allyl-4-hydroxyxanthone (94) with hydrogen bromide in ethanol with sodium hydroxide, yields 4',5'-dihydro-5'-methyl-furo (2',3'-4,3) xanthone (96).



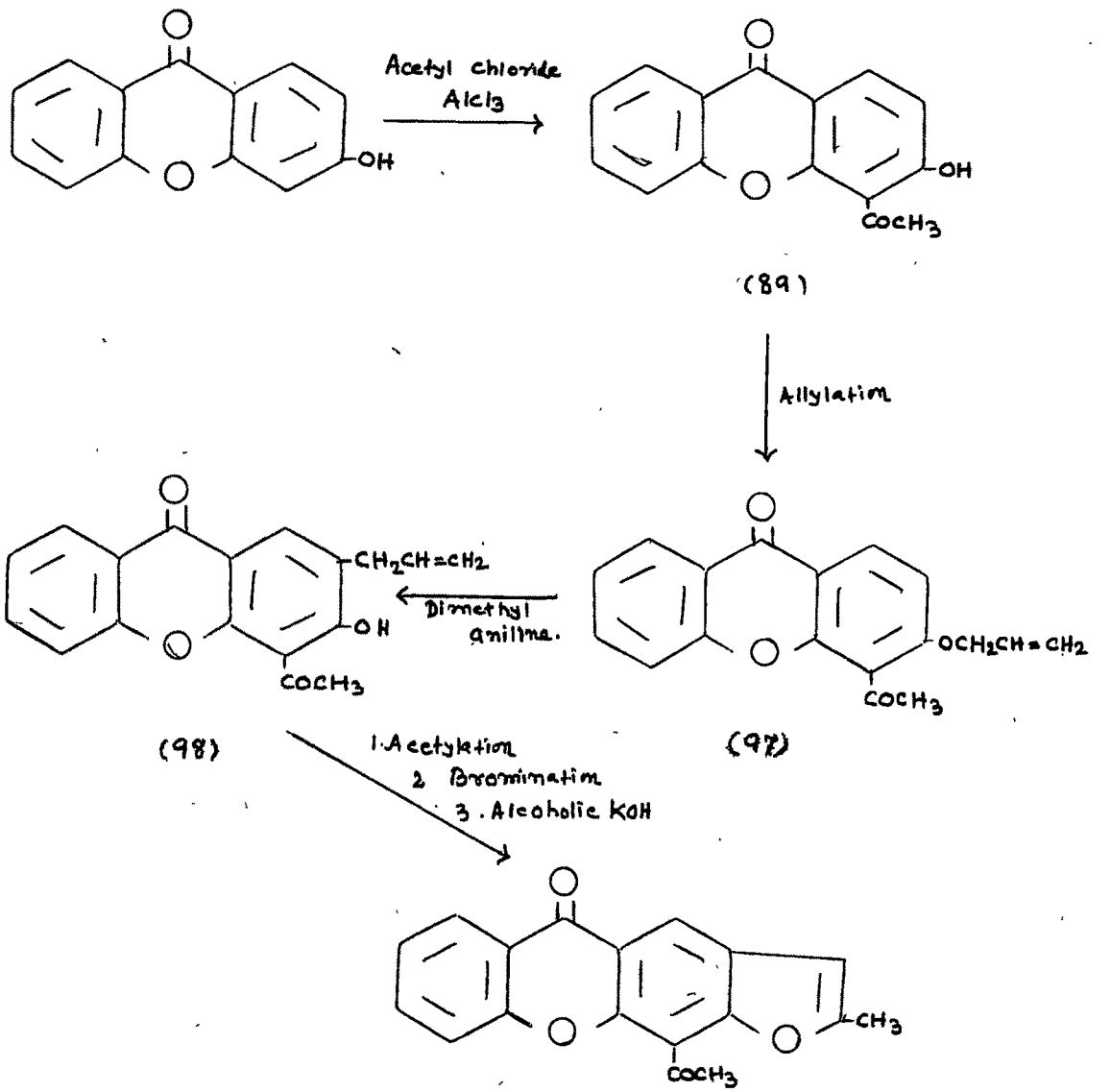
(93) (94) (95) (96)

Linear furoxanthone of type (E) was synthesised by Agasimudin and S. Rajopal[66].

4-Acetyl-3-hydroxyxanthone (89) obtained by treatment of 3-hydroxyxanthone with acetyl chloride in the presence of aluminuum chloride have been allylated to 4-acetyl-3-allyloxy-xanthone (97). 4-Acetyl-3-allyloxyxanthone on Claisen rearrangement in dimethyl aniline gave 4-acetyl-2-allyl-3-hydroxyxanthone (98), which after acetylation and bromination, treated with potassium hydroxide in ethanol to bring about

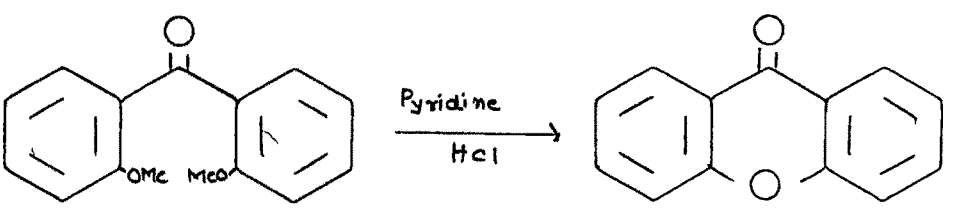
simultaneous dehalogenation and cyclisation with the formation of 4-acetyl-5'-methyl-furo (4',5'-2,3) xanthone (99).

4-Acetyl-3-hydroxy-6-methylxanthone on similar series of reactions gave 4-acetyl-5',7-dimethyl-furo (4',5'-2,3) xanthone.



Linear furo xanthone of type (F) was prepared recently by Royer Rene and his co-workers[67].

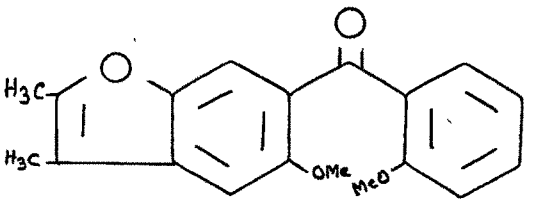
They observed that 2,2'-dimethoxy benzophenone derivative (100) when heated with pyridine-hydrochloric acid for 24-48 hr., it gave xanthones (101). The weight ratio of pyridine-hydrochloric acid to (100) is five.



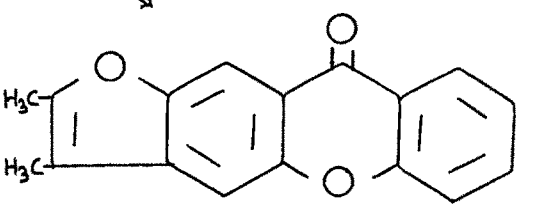
(100) (101)

By using this method, furo (2',3'-2,3) xanthone derivative was synthesised. 2,3-Dimethyl-5-methoxy-6--(o-methoxy-benzoyl) benzufuran (102) on treatment with pyridine-hydrochloric acid gave 4',5'-dimethyl-furo (2',3'-2,3) xanthone (103).

Substitution in benzoyl ring of (102) gave the furoxanthone (103) with the substitution in the benzene nucleus.



(102)



(103)

PRESENT WORK

In recent years furobenzo-γ-pyrones have received considerably attention as they not only occur in nature but also possess therapeutic properties. It was, therefore, though of interest to synthesise Khellin and Visnagin type of compounds which are likely to be physiologically active and in an attempt to prepare physiologically active molecules of simple structure, analogus to biologically active molecules Khellin, the synthesis of furo xanthones has been also achieved. The synthesis of furochromones and furoxanthones is described here. The following furochromones were synthesised

1. 9-Methyl-1,2,3,4-tetrahydrocyclopenta (b) furo (3,2-g) benzopyran-4-one (108).

2. 7,9-Dimethyl-1,2,3,4-tetrahydrocyclopenta (b) furo (3,2-g) benzopyran-4-one (110).
3. 8-Methyl-1,2,3,4,8,9-hexahydrocyclopenta (b) furo (2,3-h) benzopyran-4-one (114).
4. 9-Methyl-1,2,3,4-tetrahydrocyclopenta (b) furo (2,3-h) benzopyran-4-one (119).

The following furo xanthones were synthesised.

1. 5-Methyl-1,2,3,4-tetrahydro-furo (2',3'-6,7) xanthone (124).
2. 5',5-Dimethyl-1,2,3,4-tetrahydro furo (2',3'-6,7) xanthone (127).
3. 5',4-Dimethyl-furo (3',2'-2,3) xanthone (129).
4. 1,2,3,4-Tetrahydro-furo (3',2'-5,6) xanthone (133).
5. 5'-Methyl-furo (2',3'-3,4) xanthone (135).
6. 4'-Methyl-furo (2',3'-3,4) xanthone (141).

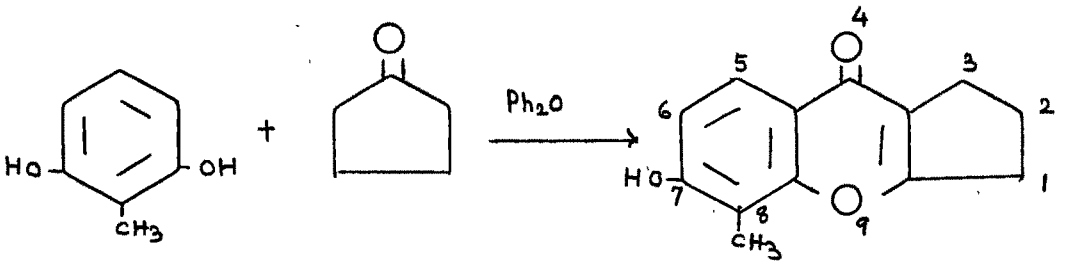
Synthesis of 9-methyl-1,2,3,4-tetrahydrocyclopenta (b) furo (3,2-g) benzopyran-4-one (108) :

Condensation of 2-methyl-resorcinol with ethyl cyclopentanone 2-carboxylate in the presence of diphenyl ether according to Desai, Trivedi and Sethna[38] gave 7-hydroxy-8-methyl-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (104). This on allylation with allyl bromide in dry acetone and anhydrous potassium carbonate afforded 7-allyloxy-8-methyl-1,2,3,4-tetrahydrocyclopenta (b) benzo-

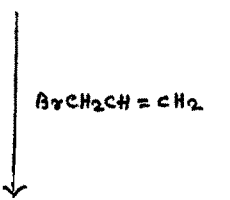
pyran-4-one (105), which was subjected to Claisen rearrangement by refluxing it with dimethyl aniline to give 7-hydroxy-6-allyl-8-methyl-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (106). The structure of (106) was assigned on the basis of I.R. spectrum (fig. 1), which showed a sharp band at 1630 cm^{-1} (γ-pyronyl >C=O group) and a broad band at 3300 cm^{-1} (aromatic hydroxy group). 7-Hydroxy-6-allyl-8-methyl-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (106) on treatment with osmium tetroxide, potassium periodate[68], in ethyl acetate-water medium afforded, 7-hydroxy-8-methyl-6-acetaldehydo-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (107), the I.R. spectrum of which showed a broad band at 3180 cm^{-1} (aromatic hydroxyl group) a sharp band at 1630 cm^{-1} (γ-pyronyl >C=O group) and at 1700 cm^{-1} (aldehyde, >C=O group). (Fig.2) Cyclisation of (107) with polyphosphoric acid gave 9-methyl-1,2,3,4-tetrahydrocyclopenta (b) furo (3,2-g) benzopyran-4-one (108), the I.R. spectrum of which showed a band at 875 cm^{-1} (furan ring) and at 1615 cm^{-1} (γ-pyronyl >C=O group). (Fig.3)

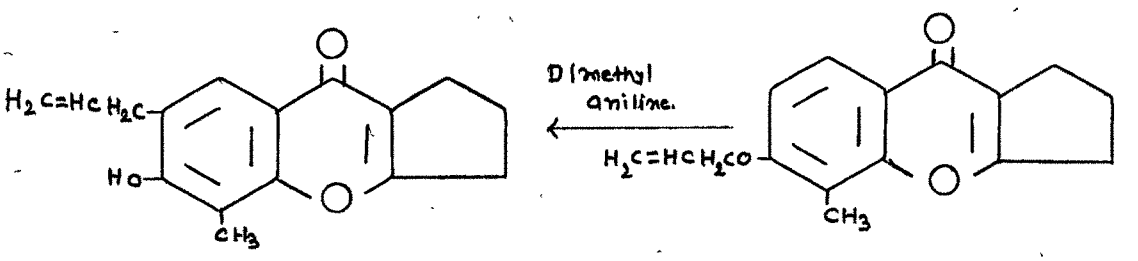
Synthesis of 7,9-dimethyl-1,2,3,4-tetrahydrocyclopenta (b) furo (3,2-g) benzopyran-4-one (110):

Cyclisation of (106) by trituration with conc. sulphuric acid according to Shaikh and Trigedi[69] afforded 7,9-dimethyl-1,2,3,4,6,7-hexahydrocyclopenta (b) benzopyran-4-one (109), the I.R. spectrum of which showed a sharp band at 1630 cm^{-1} (γ-pyronyl >C=O group). (Fig.4) Dehydrogenation of (109) with palladised charcoal in boiling diphenyl ether

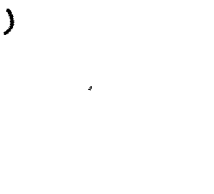


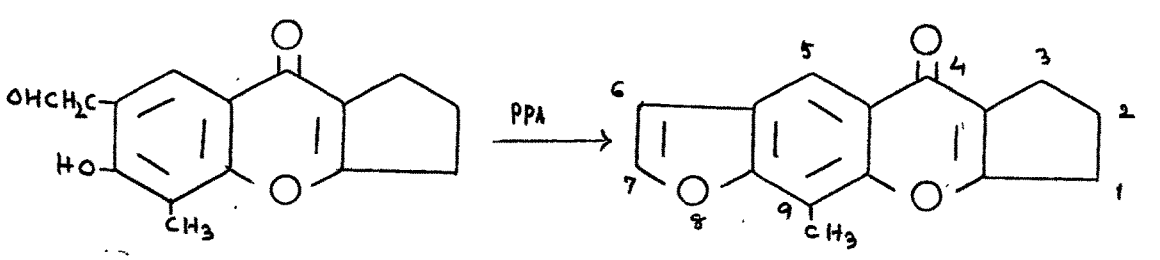
(104)





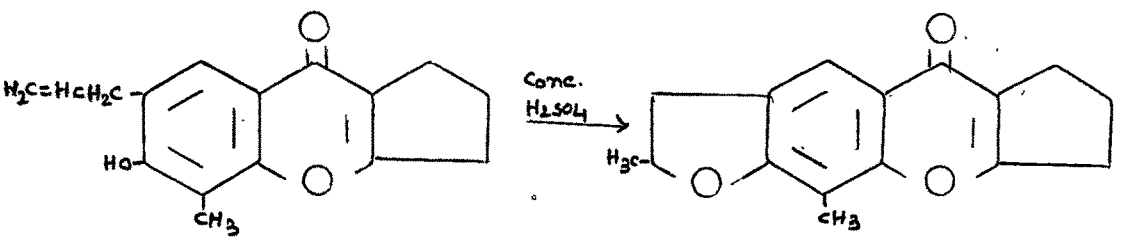
(106) (105)



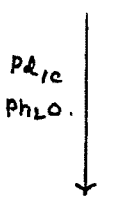


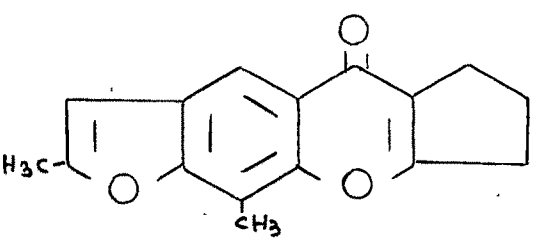
(107) (108)

furnished 7,9-dimethyl-1,2,3,4-tetrahydrocyclopenta (b) furo (3,2-g) benzopyran-4-one (110), the I. R. spectrum of which showed a band at 835 cm^{-1} (furan), 1630 cm^{-1} (γ-pyronyl > C=O group). (Fig. 5)



(106) (109)





(110)

Synthesis of 8-methyl-1,2,3,4,8,9-hexahydrocyclopenta (b) furo (2,3-h) benzopyran-4-one (114) :

Condensation of resorcinol with ethyl cyclopentanone -2-carboxylate in the presence of diphenyl ether according to

Desai, Trivedi and Sethna[39] gave 7-hydroxy-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (111). This on allylation with allyl bromide in dry acetone and anhydrous potassium carbonate afforded 7-allyloxy-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one, which was subjected to Claisen rearrangement by refluxing it with dimethyl aniline to give 7-hydroxy-8-allyl-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (113). Two ortho position are free for Claisen migration, the migration took place at 8-position, was supported by the NMR spectrum of (113). The NMR of (113) showed the following signals (Fig.6) :-

Chemical shift (δ) ppm.	Coupling constant J (Cps)	Signals	Assignments
2.68	-	Doublet	2H, $\underline{CH_2}$ group of allyl group at position 7. Ar-o-$\underline{CH_2}$CH=CH_2
6.1	-	Multiplet	1H, 1H of allyl group at position 7. Ar-o-$CH_2\underline{CH}$=CH_2
5.22	-	Doublet	2H, =CH_2 group of allyl group at position 7. Ar-o-CH_2CH=$\underline{CH_2}$
3.3-4.0	-	Multiplet	6H, protons of cyclopentane.
7.42	6Hz	Doublet	Aromatic proton at 6-position.
8.3	6Hz	Doublet,	Aromatic proton at 5-position.

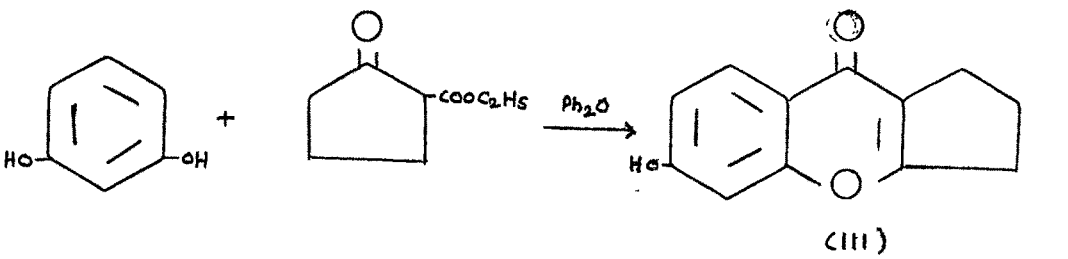
The migrated compound (113) was insoluble in ethyl acetate and tetrahydrofuran hence the reaction with osmium tetroxide was not possible.

Cyclisation of(113) by trituration with conc. sulphuric acid according to Shaikh and Trivedi[69] afforded 8-methyl-1,2,3,4,8,9-hexahydrocyclopenta (b) furo (2,3-h) benzopyran-4-one (114). Attempts to dehydrogenate (114) either with palladised charcoal in diphenyl ether or DDQ in benzene met with failure.

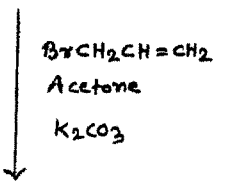
As the above method to build up the furan ring on 7-hydroxy-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one did not succeed, the following route was tried with success.

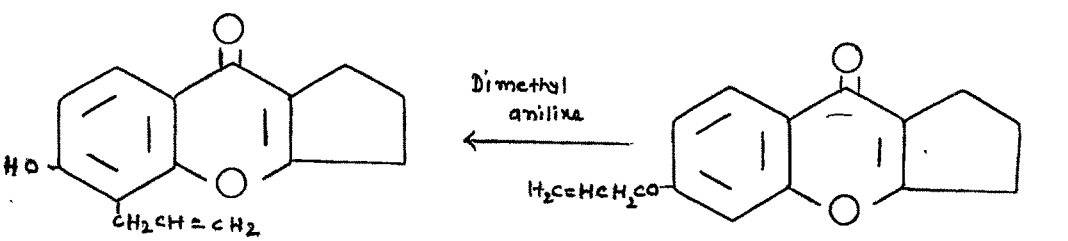
Synthesis of 9-methyl-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (119) :

7-Hydroxy-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (111), on acetylation with acetic anhydride and fused sodium acetate, gave 7-acetoxy-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (115). Fries migration of 7-acetoxy-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (115) afforded 7-hydroxy-8-acetyl-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (116). Two ortho position are free for migration. Migration took place at 8-position. The structure of (116) was supported by its NMR spectrum (Fig. 7) which showed the following signals :-



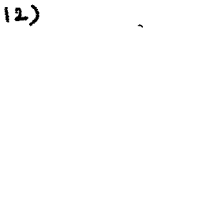
(111)

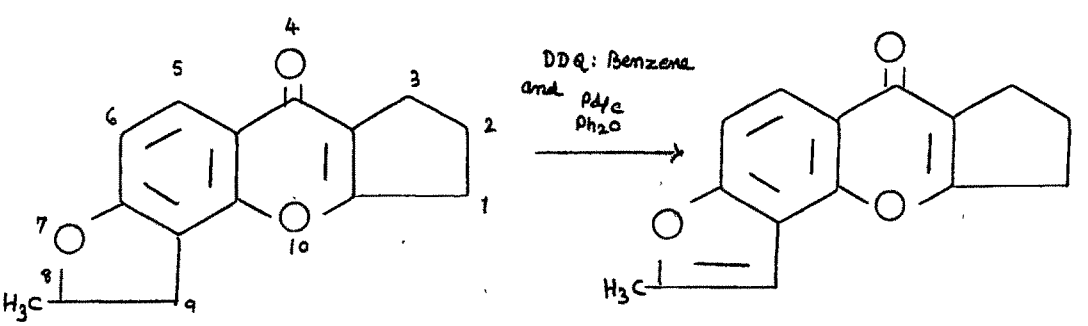




(113)

(112)





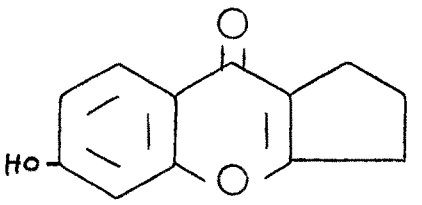
(114)

Chemical Shift (δ) ppm.	Coupling constant J (Cps.).	Signals	Assignments.
2.8	-	Singlet	3H, $-COCH_3$ group at position 8.
7.0	9Hz	Doublet	1H, Aromatic proton at position 6.
8133	9Hz	Doublet	1H, Aromatic proton at position 5.
2.2-3.2	-	Multiplet	6H, proton of cyclopentane ring.

7-Hydroxy-8-acetyl-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (116) condensed with ethyl bromo acetate in the presence of anhydrous potassium carbonate and dry acetone gave ethyl-8-acetyl-4-oxo-1,2,3,4-tetrahydrocyclopenta (b) benzopyranyloxy-7-acetate (117), which was hydrolysied by refluxing it with acetic acid-hydrochloric acid (1 : 1) to give corresponding carboxylic acid, 8-acetyl--4-oxo-1,2,3,4-tetrahydrocyclopenta (b) benzopyranyloxy-7-acetic acid (118). (118) was cyclised to 9-methyl-1,2,3,4-tetrahydrocyclopenta (b) furo (2,3-h) benzopyran-4-one (119), when refluxed with acetic anhydride and sodium acetate.

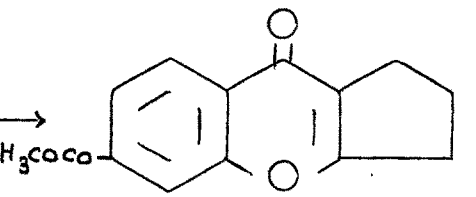
Synthesis of 5-methyl-1,2,3,4-tetrahydro furo (2',3'-6,7) Xanthone (124) :

Condensation of 2-methyl-resorcinol with ethyl cyclohexanone-2-carboxylate in the presence of diphenyl ether



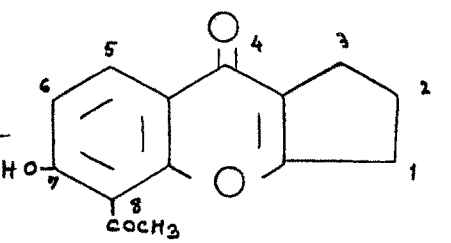
(111)

$(CH_3CO)_2O$
CH_3COONa



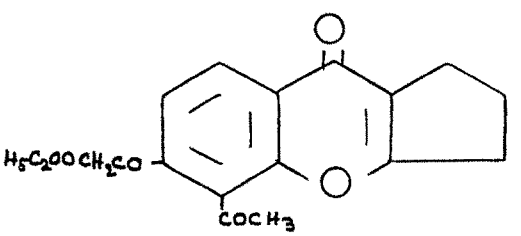
(115)

Fries migration



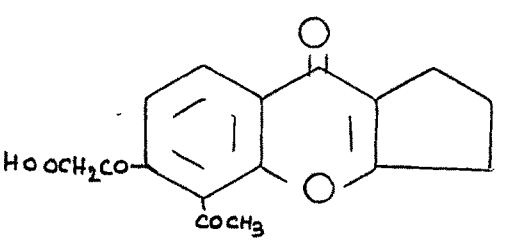
(116)

$BrCH_2COOC_2H_5$
Acetone, K_2CO_3



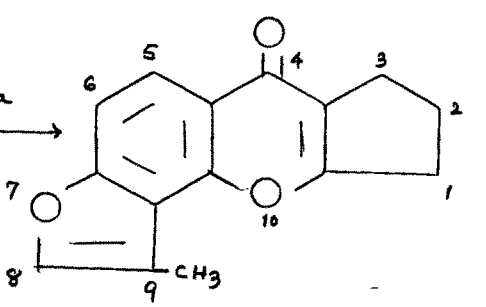
(117)

$CH_3COOH - HCl$



(118)

$(CH_3CO)_2O$
CH_3COONa

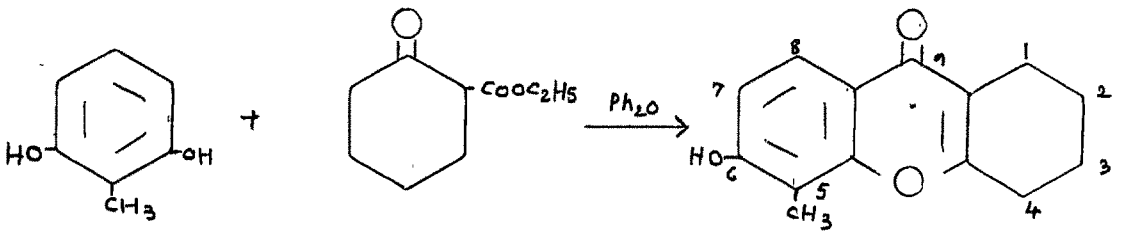


(119)

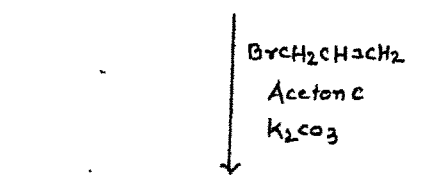
according to Desai, Trivedi and Sethna[39], gave 6-hydroxy-5-methyl-1,2,3,4-tetrahydroxanthone (120). This on allylation with allyl bromide in dry acetone and anhydrous potassium carbonate afforded 6-allyloxy-5-methyl-1,2,3,4-tetrahydroxanthone (121), which was subjected to Claisen rearrangement by refluxing it with dimethyl aniline to give 6-hydroxy-7-allyl-5-methyl-1,2,3,4-tetrahydro xanthone (122). 6-Hydroxy-7-allyl-5-methyl-1,2,3,4-tetrahydroxanthone (122) on treatment with osmium tetroxide, potassium per iodate in ethyl acetate - water medium afforded 6-hydroxy-5-methyl-7-acetaldehydo-1,2,3,4-tetrahydroxanthone (123), cyclisation of which with polyphosphoric acid gave 5-methyl-1,2,3,4-tetrahydro-furo (2',3'-6,7) xanthone (124), the I.R. spectrum of which showed a sharp band at 870 $cm.^{-1}$ (furan), 1640 $cm.^{-1}$ (γ-pyronyl >C=O group). (Fig.8)

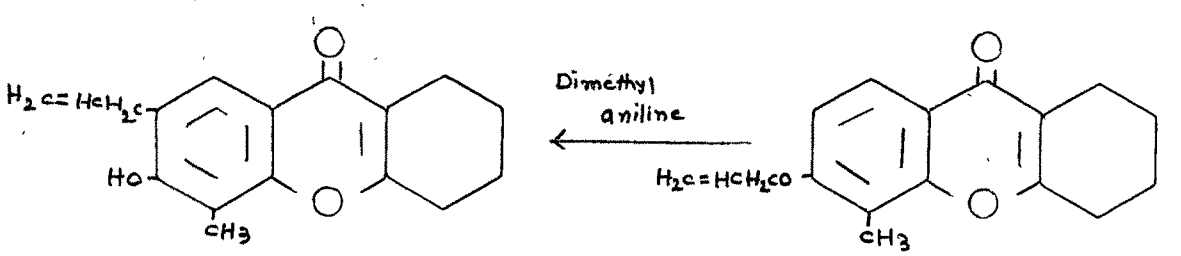
Synthesis of 5',5-dimethyl-1,2,3,4-tetrahydro-furo (2',3'-6,7) xanthone (127) :

5',5-Dimethyl-1,2,3,4-tetrahydro furo (2',3'-6,7) xanthone (124) was prepared according to the method developed by Kaufmann[70]. 6-Hydroxy-7-allyl-5-methyl-1,2,3,4-tetrahydro-xanthone (122) on acetylation with acetic anhydride and fused sodium acetate, gave 7-allyl-5-methyl-6-acetoxy-1,2,3,4-tetrahydroxanthone (125), which on bromination with bromine in acetic acid afforded 7-(2',3'-dibromopropyl)-5-methyl-6-acetoxy-1,2,3,4-tetrahydroxanthone (126). (126) When refluxed

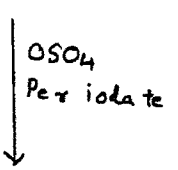

HO
OH
CH3
+
COOC2H5
Ph2O
HO
CH3

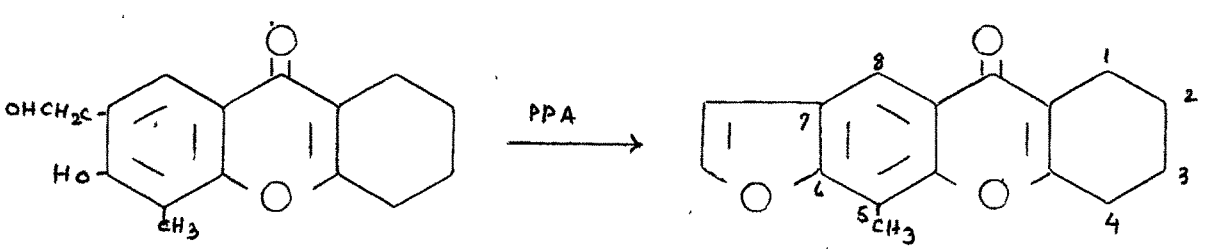
(120)


BrCH2CH=CH2
Acetone
K2CO3


H2C=HCH2C
HO
CH3
Dimethyl
aniline
H2C=HCH2CO
CH3

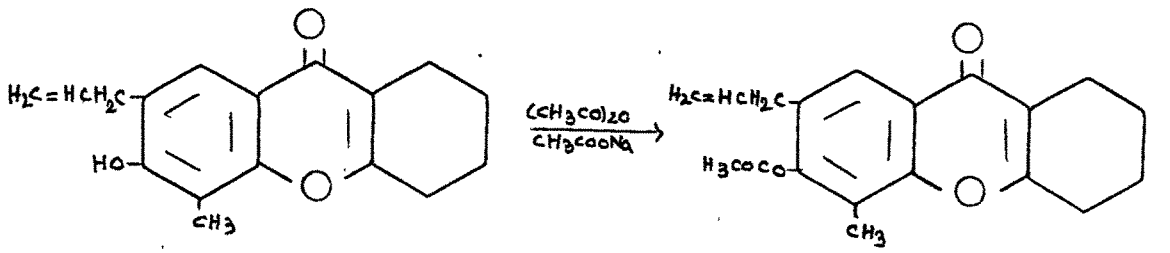
(122)


OSO4
Periodate

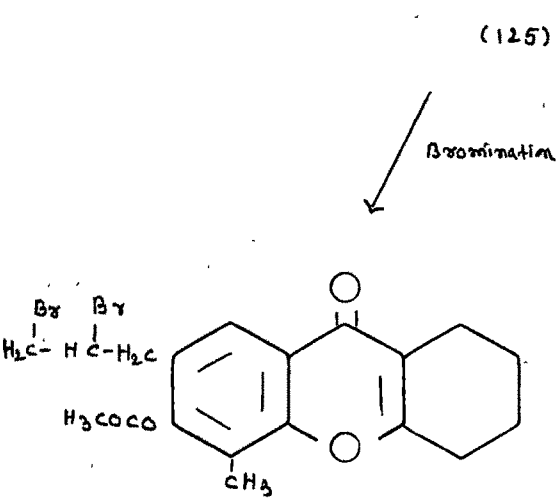

OHCH2C
HO
CH3
PPA
CH3

(124)

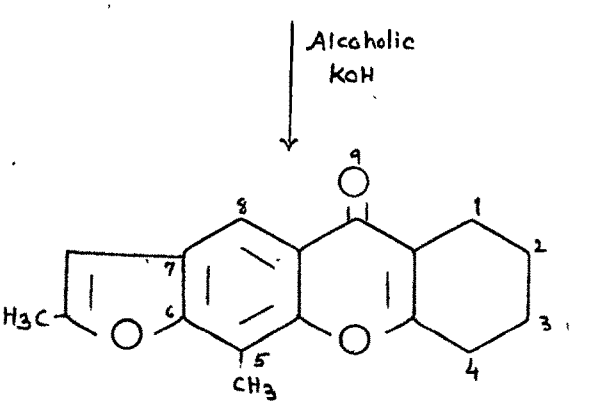
with alcoholic potassium hydroxide furnished 5',5-dimethyl-1,2,3,4-tetrahydro furo (2',3'-6,7) xanthone (127).



(122) (125)



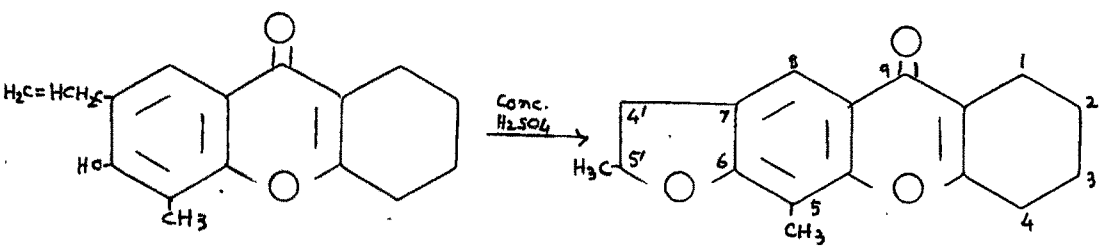
(126)



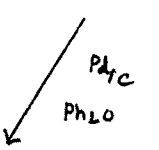
(127)

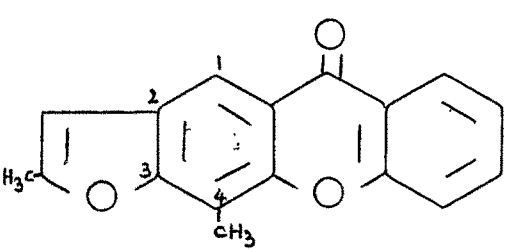
Synthesis of 5',4-dimethyl-furo (3',2'2,3) xanthone (129) :

6-Hydroxy-7-allyl-5-methyl-1,2,3,4-tetrahydro-xanthone (122) was triturated with conc. sulphuric acid to give 5',5-dimethyl-1,2,3,4,4',5'-hexahydro furo (2',3'-6,7) xanthone (128), which was dehydrogenated with palladised charcoal in boiling diphenyl ether to 5',4-dimethyl-furo (3',2'-2,3) xanthone (129).



(122) (128)





(129)

Synthesis of 1,2,3,4-tetrahydro furo (3',2'-5,6) xanthone (133) :

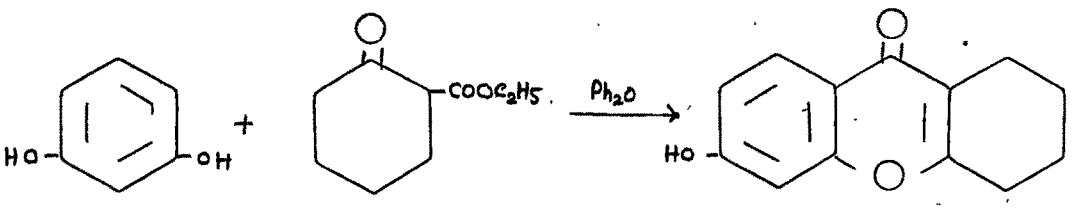
Resorcinol was condensed with ethyl cyclo hexanone-2-carboxylate in diphenyl ether to give 6-hydroxy-1,2,3,4-tetrahydroxanthone (130), which was previously prepared by Charles, Mentzer and his co-workers[71]. (130) on allylation with allyl bromide in the presence of anhydrous potassium carbonate and dry acetone afforded 6-allyloxy-1,2,3,4-tetrahydroxanthone (131), which was subjected to Claisen rearrangement by refluxing it with dimethyl aniline to give 6-hydroxy-5-allyl-1,2,3,4-tetrahydroxanthone (132). (132) on treatment with osmium tetroxide, potassium periodate in ethyl acetate-water medium afforded 6-hydroxy-5-acetaldehydo-1,2,3,4-tetrahydroxanthone, which was directly cyclised with polyphosphoric acid to give 1,2,3,4-tetrahydro furo (3',2'-5,6) xanthone (133).

Synthesis of 5'-methyl-furo (2',3'-3,4) xanthone (135) :

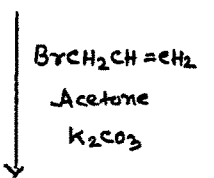
Cyclisation of 6-hydroxy-5-allyl-1,2,3,4-tetrahydroxanthone (132) by trituration with conc. sulphuric acid afforded 5'-methyl-1,2,3,4,4',5'-hexahydro (3',2'-5,6) xanthone (134), which was dehydrogenated with palladised charcoal in boiling diphenyl ether to 5'-methyl furo (2',3'-3,4) xanthone (135).

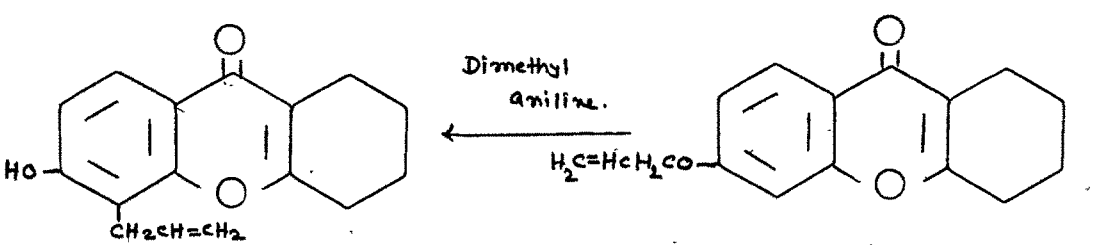
Synthesis of 4'-methyl-furo (2',3'-3,4) xanthone (141) :

6-Hydroxy-1,2,3,4-tetrahydro xanthone (130) on acetylation with acetic anhydride and fused sodium acetate



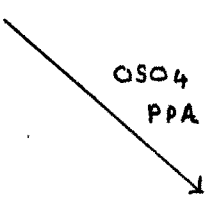
(130)

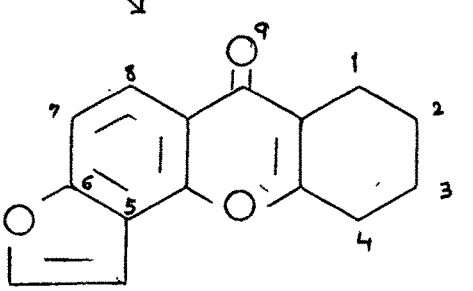




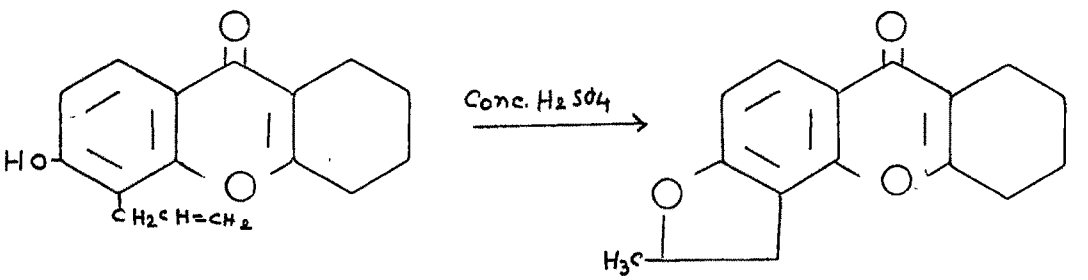
(131)

(132)

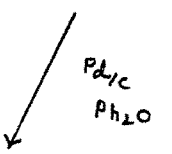


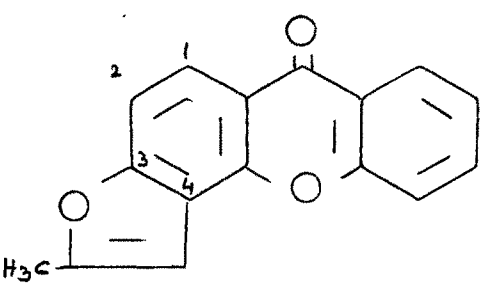


(133)



(132) (134)

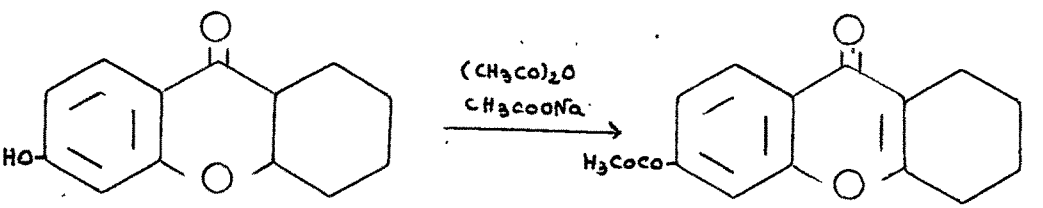




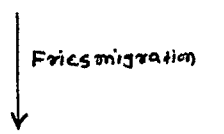
(135)

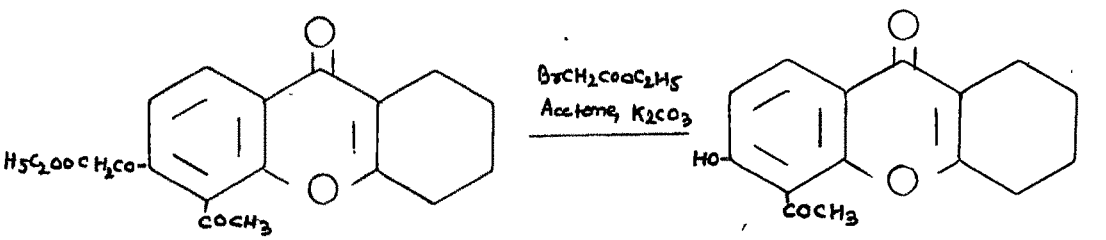
gave 6-acetoxy-1,2,3,4-tetrahydroxanthone. Fries migration of 6-acetoxy-1,2,3,4-tetrahydroxanthone (136) afforded 6-hydjoxy-5-acetyl-1,2,3,4-tetrahydroxanthone (137), which was condensed with ethyl bromo acetate in the presence of anhydrous potassium carbonate and dry acetone gave ethyl--5-acetyl-1,2,3,4-tetrahydro-6-xanthonyloxy acetate (138). (138), was hydrolysed by refluxing it with acetic acid, hydrochloric acid (1 : 1) to give corresponding carboxylic acid, 5-acetyl-1,2,3,4-tetrahydro-6-xanthonyloxy acetic acid (139).

(139), when refluxed with sodium acetate and acetic anhydride gave 4'-methyl-1,2,3,4-tetrahydro-furo (3',2'-5,6) xanthone (140). (140) was dehydrogenated with palladised charcoal in boiling diphenyl ether to give 4'-methyl-furo (2',3'-3,4) xanthone (141).

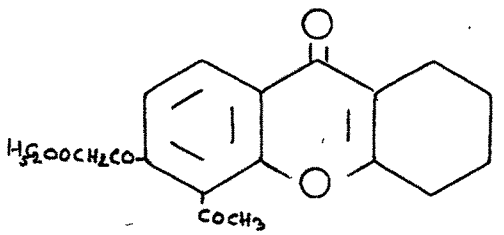


(130) (136)



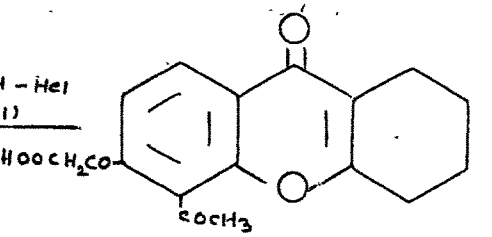


(138) (137)



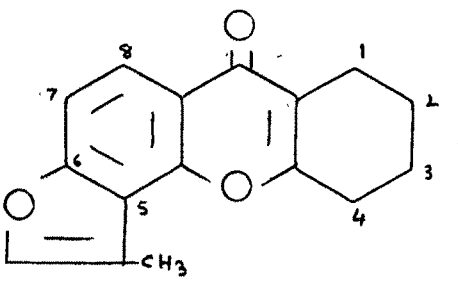
(138)

$CH_3COOH - HCl$
(1:1)



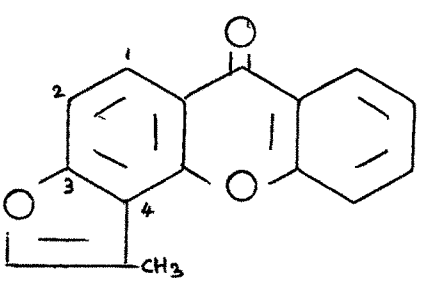
(139)

$(CH_3CO)_2O$
CH_3COONa



(140)

Pd/c
Ph_2O



(141)

EXPERIMENTAL.

I.R. spectra were determined with Perkin-Elmer 457 grating spectrophotometer in nujol.

NMR spectra were recorded on Varian A-60 spectrophotometer using TMS as internal standard. Solvent CF_3COOH (Fig. 6) $CDCl_3$ (Fig. 7)

The ultra-violet absorption spectra were measured with Beckmann DU Spectrophotometer.

Synthesis of 9-methyl-1,2,3,4-tetrahydrocyclopenta (b) furo (3,2-g) benzopyran-4-one (108) : 7-Hydroxy-8-methyl-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (104) :

A mixture of 2-methylresorcinol (3 g.) and ethyl cyclopentanone-2-carboxylate (4 ml.) was refluxed with diphenyl ether (10 ml.) for three hrs. with a short condenser to facilitate the removal of alcohol formed. After cooling the separated product was filtered and washed several times with petroleum ether. It crystallised from dimethyl formamide, m.p. 309°. Yield 2.0 g.

Analysis : Found : C, 71.54 ; H, 5.47 %.

$C_{13}H_{12}O_3$: requires : C, 72.21 ; H, 5.55 %.

Allylation of 7-hydroxy-8-methyl-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one : 7-Allyloxy-8-methyl-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (105) :

A mixture of 7-hydroxy-8-methyl-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (2 g.), allyl bromide

(1.2 g.) and anhydrous potassium carbonate (8 g.) was refluxed in dry dimethyl formamide (150 ml.) in a water bath for 10 hr. The reaction mixture was poured into water. The separated product was filtered, washed with very dilute sodium hydroxide solution to remove unreacted compound and crystallised from alcohol, m.p. 137°. Yield 1.3 g.

Analysis : Found : C, 74.86 ; H, 5.95 %

$C_{16}H_{16}O_3$: requires : C, 75.00 ; H, 6.25 %.

Claisen rearrangement of 7-allyloxy-8-methyl-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one : 7-Hydroxy-6-allyl--8-methyl-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (106) :

7-Allyloxy-8-methyl-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (2 g.) was refluxed with dimethyl aniline (10 ml.) for 8 hr. After cooling, the reaction mixture was poured into conc. hydrochloric acid (50 ml.) containing pieces of ice. The separated product was filtered and dissolved in sodium hydroxide solution. The solution was filtered. The filtrate on acidification with conc. hydrochloric acid gave the product which was filtered and crystallised from acetic acid, m.p. 222°. Yield 1.5 g.

Analysis : Found : C, 74.74 ; H, 6.28 %.

$C_{16}H_{16}O_3$: requires : C, 75.00 ; H, 6.25 %.

I.R.spectrum :- 1630 cm^{-1} (γ-pyronyl > C=O group) and a broad band at 3300 cm^{-1} (aromatic hydroxy group).

7-Hydroxy-8-methyl-6-acetaldehydo-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (107) :

7-Hydroxy-6-allyl-8-methyl-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (106) (500 mg.) was vigorously shaken with osmium tetroxide (50 mg.) and water (100 ml.). To the dark solution was added potassium periodate (2 g.) in 100 ml. water) dropwise over a period of 3 hr. The ethyl acetate layer was separated, dried and evaporated. The residue was dissolved in chloroform and the clear solution was percolated through a short column of alumina. The residue left after evaporation of chloroform crystallised from alcohol, m.p. 260° (decomp.). Yield 0.3 g.

Analysis : Found : C, 69.76 ; H, 5.51 %

$C_{15}H_{14}O_4$: requires : C, 69.69 ; H, 5.42 %.

Cyclisation of 7-hydroxy-8-methyl-6-acetaldehydo-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one : 9-Methyl--1,2,3,4-tetrahydrocyclopenta (b) furo (3,2-g) benzopyran--4-one (108) :

7-Hydroxy-8-methyl-6-acetaldehydo-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (107) (250 mg.) was heated with polyphosphoric acid (10 ml.) in a water bath for 1 1/2 hr. and then poured into ice water. The solid separated was filtered and washed with dilute sodium hydroxide solution to remove uncyclised compound. A chloroform extract of the dried residue was passed over a short column of

alumina. Evaporation of solvent left a product which crystallised from benzene, m.p. 266°. Yield 100 mg.

Analysis : Found : C, 74.84 ; H, 5.01 %

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

I.R. spectrum 875 cm^{-1} (furan ring) and at 1615 cm^{-1} (lactonyl >C=0 group).

$\lambda^{Chloroform}_{max.}$ 246 nm (log e 4.76), 278 nm (log e 4.17), 314 nm (log e 3.99).

Synthesis of 7,9-dimethyl-1,2,3,4-tetrahydrocyclopenta (b) furo (3,2-g) benzopyran-4-one (110) : Cyclisation of 7-hydroxy-6-allyl-8-methyl-1,2,3,4-tetrahydrocyclopenta (b) furo (3,2-g) benzopyran-4-one : 7,9-Dimethyl-1,2,3,4,6,7-hexahydrocyclopenta (b) benzopyran-4-one (109) :

7-Hydroxy-6-allyl-8-methyl-1,2,3,4-tetrahydrocyclopenta (b) furo (3,2-g) benzopyran-4-one (1 g.) was triturated with conc. sulphuric acid (5 ml.) in a water bath for 10 minutes. The contents were poured into crushed ice. The separated product was filtered and washed with dilute sodium hydroxide solution to remove uncyclised compound. It crystallised from benzene, m.p. 154° Yie.d 0.8 g.

Analysis : Found : C, 75.01 ; H, 6.45 %.

$C_{16}H_{16}O_3$: requires : C, 75.00 ; H, 6.25 %.

I.R. spectrum 1630 cm^{-1} (y-pyronyl >C=0 group).

$\lambda^{Methanol}_{Max.}$ 249 nm (log e 4.19), 256 nm (log e 4.23) and at 300 nm (log e 4.18).

Dehydrogenation of 7,9-dimethyl-1,2,3,4,6,7-hexahydrocyclopenta (b) benzopyran-4-one : 7,9-Dimethyl-1,2,3,4-tetrahydrocyclopenta (b) furo (3,2-g) benzopyran-4-one (110) :

A mixture of 7,9-dimethyl-1,2,3,4,6,7-hexahydrocyclopenta (b) benzopyran-4-one (0.5 g.) and palladised charcoal (10 % ; 0.3 g.) and diphenyl ether (4 ml.) was refluxed for 10 hr. The reaction mixture was filtered hot and after cooling, petroleum ether was added to the filtrate. The separated product was filtered and washed several times with petroleum ether. The benzene solution of the product was passed over a short column of alumina. Evaporation of solvent left a product, which crystallised from benzene, M.p. . Yield 0.2 g.

Analysis : Found : C, 76.17 ; H, 5.53 %

$C_{16}H_{14}O_3$: requires : C, 76.00 ; H, 5.51 %.

I.R. spectrum : 835 cm^{-1} (furan), 1630 cm^{-1} (γ-pyronyl >C=O group).

$\lambda^{Methanol}_{Max.}$ 246 nm (log e 4.82), 290 nm (log e 4.19), 298 nm (log e 4.11) and at 320 nm (log e 4.03).

Synthesis of 8-methyl-1,2,3,4,8,9-hexahydrocyclopenta (b) furo (2,3-h) benzopyran-4-one (114) : 7-Hydroxy-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (111) :

A mixture of resorcinol (3 g.) and ethyl cyclo-

pentanone-2-carboxylate (4.5 ml.) was refluxed with diphenyl ether (10 ml.) for 3 hr. with a short condenser to facilitate the removal of alcohol formed. After cooling, the separated product was filtered and washed several times with petroleum ether. It crystallised from alcohol, m.p. 288°. Yield 2 g.

Analysis : Found : C, 71.52 ; H, 5.35 %

$C_{12}H_{10}O_3$: requires : C, 71.29 ; H, 4.95 %.

Allylation of 7-hydroxy-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one : 7-Allyloxy-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (112) :

A mixture of 7-hydroxy-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (2 g.), allyl bromide (1.2 g.) and hy anhydrous potassium carbonate (8.0 g.) was refluxed in dry acetone (200 ml.) in a water bath for 10 hr. The reaction mixture was worked up as described earlier. The product crystallised from benzene-petroleum ether, m.p. 112°. Yield 1.5 g.

A nalysis : Found : C, 74.33 ; H, 5.76 %

$C_{15}H_{14}O_3$: requires : C, 74.39 ; H, 5.78 %.

Claisen rearrangement of 7-allyloxy-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one : 7-Hydroxy-8-allyl-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (113) :

7-Allyloxy-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (2 g.) was refluxed with dimethyl aniline (10 ml.) for 8 hr. The reaction mixture was worked up as

described earlier. The product crystallised from alcohol, m.p. 267°. Yield 1.5 g.

Analysis : Found : C, 73.92 ; H, 5.84 %

$C_{15}H_{14}O_3$: requires : C, 74.39 ; H, 5.78 %.

I.R. spectrum: 1620 cm^{-1} (γ-pyronyl >C=O group) and a broad band at 3400 cm^{-1} (aromatic hydroxy group).

Cyclisation of 7-hydroxy-6-allyl-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one : 8-Methyl-1,2,3,4,8,9-hexahydrocyclopenta (b) furo (2,3-h) benzopyran-4-one (114) :

7-Hydroxy-6-allyl-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (1 g.) was triturated with conc. sulphuric acid (5 ml.) in water bath for 15 minutes. The reaction mixture was worked up as described earlier. The product crystallised from alcohol, m.p. 190°. Yield 0.8 g.

Analysis : Found : C, 74.06 ; H, 5.79 %

$C_{15}H_{14}O_3$: requires : C, 74.39 ; H, 5.78 %.

I.R. spectrum : 1635 cm^{-1} (γ-pyronyl >C=O group).

$\lambda^{\text{Methanol}}_{\text{Max.}}$ 248 nm (log e 4.29), 256 nm (log e 4.32), 300 nm (log e 4.12).

Attempted synthesis of 8-methyl-1,2,3,4-tetrahydrocyclopenta (b) furo (2,3-h) benzopyran-4-one : Attempted dehydrogenation of 8-methyl-1,2,3,4,8,9-hexahydrocyclopenta (b) furo (2,3-h) benzopyran-4-one :

(1) A solution of 8-methyl-1,2,3,4,8,9-hexahydro-

cyclopenta (b) furo (2,3-h) benzopyran-4-one (114) (0.5 g) in diphenyl ether (6 ml.) was refluxed with palladised charcoal (0.4 g.; 10 %) for 6 hr. to 30 hr. The reaction mixture was filtered hot and the filtrate was allowed to cool. The separated product was filtered and crystallised from alcohol, m.p. 190°. It was found to be original compound. Mixed m.p. with (114) did not depress.

(2) A solution of 8-methyl-1,2,3,4,8,9-hexahydrocyclopenta (b) furo (2,3-h) benzopyran-4-one (0.5 g.) in dry benzene (50 ml.) was refluxed with DDQ (0.5 g.) for 35 hr. The reaction mixture was filtered hot and benzene was evaporated. Evaporation of solvent left a red colour residue, which was dissolved in chloroform and passed over a short column of alumina. Evaporation of solvent left a colourless product which was crystallised from alcohol, m.p. 190°. Yield 0.3 g. It was found to be original compound. Mixed m.p. with (114) did not depress.

Synthesis of 9-methyl-1,2,3,4-tetrahydrocyclopenta (b) furo (2,3-h) benzopyran-4-one (119) : Acetylation of 7-hydroxy-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one : 7-Acetoxy-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (115) :

A mixture of 7-hydroxy-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (2 g.), acetic anhydride (10 ml.) and a few crystals of sodium acetate was heated gently on a wire gauze with a low flame for 2 hr. The reaction mixture

was poured into crushed ice. The product was filtered and washed with dilute sodium hydroxide solution to remove unreacted compound. It crystallised from alcohol, m.p. 141°. Yield 1.6 g.

Analysis : Found : C, 68.98 ; H, 4.73 %.

$C_{14}H_{12}O_4$: requires : C, 68.85 ; H, 4.92 %.

Fries migration of 7-acetoxy-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one : 7-Hydroxy-8-acetyl-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (116) :

An intimate mixture of 7-acetoxy-1,2,3,4-tetrahydrocyclopenta (b) benzopyran-4-one (2 g.) and powdered anhydrous aluminium chloride (6 g.) was heated in an oil bath at 140° for 3hr. After cooling, it was decomposed with ice and conc. hydrochloric acid. The product was filtered and treated with sodium hydroxide solution. The product is soluble in sodium hydroxide solution, it was filtered, acidified with hydrochloric acid and crystallised from acetic acid, m.p. 215°. Yield 1.5 g.

The compound was soluble in alkali and developed red colouration with alcoholic ferric chloride solution.

Analysis : Found : C, 68.80 ; H, 5.89 %.

$C_{14}H_{12}O_4$: requires : C, 68.85 ; H, 4.92 %.

Ethyl-8-acetyl-4-oxo-1,2,3,4-tetrahydrocyclopenta (b) benzopyranyloxy-7-acetate (117) :

A mixture of 7-hydroxy-8-acetyl-1,2,3,4-tetra-

hydrocyclopenta (b) benzopyran-4-one (1 g.), ethyl bromo acetate (1 ml.) and anhydrous potassium carbonate (5 g.) was refluxed in dry acetone (100 ml.) for 6 hr. in a water bath. The acetone was evaporated and the residue was treated with water. The separated product was filtered and washed with dilute sodium hydroxide solution to remove unreacted compound. It crystallised from alcohol, m.p. 163°. Yield 0.7 g.

Analysis : Found : C, 65.00 ; H, 5.46 %

$C_{18}H_{18}O_6$: requires : C, 65.45 ; H, 5.45 %.

Hydrolysis of ethyl-8-acetyl-4-oxo-1,2,3,4,-tetrahydro-cyclopenta (b) benzopyranyloxy-7-acetate : 8-Acetyl-4-oxo--1,2,3,4-tetrahydrocyclopenta (b) benzopyranyloxy-7-acetic acid (118) :

A mixture of ethyl-8-acetyl-4-oxo-1,2,3,4-tetra-hydrocyclopenta (b) benzopyranyloxy-7-acetate (1 g.), distilled acetic acid (20 ml.) and A.R. Hydrochloric acid (20 ml.) was refluxed for 4 hr. The reaction mixture was diluted with water and allowed to stand. The product which separated was filtered and dissolved in sodium bicarbonate solution and filtered. The filtrate was acidified and the separated product was filtered. It crystallised from alcohol, m.p. 245° (decomp.). Yield 0.7 g.

Analysis : Found : C, 63.54 ; H, 4.47 %

$C_{16}H_{14}O_6$: required : C, 63.57 ; H, 4.63 %.

Cyclisation of 8-acetyl-4-oxo-1,2,3,4-tetrahydrocyclopenta (b) benzopyranoloxy-7-acetic acid : 9-Methyl-1,2,3,4-tetrahydrocyclopenta (b) furo (2,3-h) benzopyran-4-one (119) :

8-Acetyl-4-oxo-1,2,3,4-tetrahydrocyclopenta (b) benzopyranyloxy-7-acetic acid (0.5 g.) was cyclised by refluxing it with acetic anhydride (6 ml.) and freshly fused sodium acetate (1 g.) on a sand bath for 4 hr. After cooling, the mixture was poured into crushed ice. The separated product was filtered and washed with sodium bicarbonate solution to remove uncyclised acid. It crystallised from acetic acid, m.p. 281°. Yield 0.3 g.

Analysis : Found : C, 74.52 ; H, 4.95 %.

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

I.R. spectrum : 1625 cm^{-1} (γ-pyronyl >C=0 group), 825 cm^{-1} (furan).

$\lambda^{\text{Chloroform}}_{\text{Max.}}$ 245 nm (log e 4.60), 304 nm (log e 3.85), 340 nm (log e 2.87).

Synthesis of 5-methyl-1,2,3,4-tetrahydro-furo (2',3'-6,7) xanthone (124) : 6-Hydroxy-5-methyl-1,2,3,4-tetrahydroxanthone (120) :

A mixture of 2-methylresorcinol (3 g.) and ethyl-cyclohexanone-2-carboxylate (4 ml) was refluxed with diphenyl ether (10 ml.) for three hrs. with a short condenser to facilitate the removal of alcohol formed. After cooling, the separated product was filtered and washed

several times with petroleum ether. It crystallised from dimethyl formamide, m.p. 270°. Yield 2 g.

Analysis : Found : C, 72.90 ; H, 6.07 %.

$C_{14}H_{14}O_3$: requires : C, 73.05 ; H, 6.08 %.

Allylation of 6-hydroxy-5-methyl-1,2,3,4-tetrahydroxanthone : 6-Allyloxy-5-methyl-1,2,3,4-tetrahydroxanthone (121) :

A mixture of 6-hydroxy-5-methyl-1,2,3,4-tetrahydroxanthone (2 g.), allyl bromine (1 g.) and anhydrous potassium carbonate (8 g.) was refluxed in dry acetone (200 ml.) in a water bath for 10 hr. The reaction mixture was worked up as described earlier. The product crystallised from benzene-petroleum ether, m.p. 110°. Yield 1.5 g.

Analysis : Found : C, 75.68 ; H, 6.34 %

$C_{17}H_{18}O_3$: requires : C, 75.53 ; H, 6.66 %.

Claisen rearrangement of 6-allyloxy-5-methyl-1,2,3,4-tetrahydroxanthone : 6-Hydroxy-7-allyl-5-methyl-1,2,3,4-tetrahydroxanthone (122) :

6-Allyloxy-5-methyl-1,2,3,4-tetrahydroxanthone (2 g.) was refluxed with dimethyl aniline (10 ml.) for 8 hr. The reaction mixture was worked up as usual. The product crystallised from alcohol, m.p. 221°. Yield 1.5 g.

Analysis : Found : C, 75.26 ; H, 6.20 %

$C_{17}H_{18}O_3$: requires : C, 75.53 ; H, 6.66 %.

I.R. spectrum : 1625 cm^{-1} (γ-pyronyl >C=O group), and a broad band at 3500 cm^{-1} (aromatic hydroxy group).

6-Hydroxy-7-acetaldehydo-5-methyl-1,2,3,4-tetrahydro-xanthone (123) :

6-Hydroxy-7-allyl-5-methyl-1,2,3,4-tetrahydro-xanthone (500 mg.) was vigorously shaken with osmium tetroxide (50 mg.) and water (100 ml.). To the dark solution was added potassium periodate (2 g. in 100 ml. water) dropwise over a period of 3 hr. The ethyl acetate layer was separated, The residue was dissolved in chloroform and the clear solution was percolated through a short column of alumina. The residue left after evaporation of chloroform crystallised from acetic acid, m.p. 267°. Yield 300 mg.

Analysis : Found : C, 70.71 ; H, 6.18 %

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

I.R. spectrum : 1630 $cm.^{-1}$ (γ-pyronyl >C=O group), 1700 $cm.^{-1}$ (aldehyde >C=O group), a broad band at 3350 $cm.^{-1}$ (aromatic hydroxy group).

Cyclisation of 6-hydroxy-7-acetaldehydo-5-methyl-1,2,3,4-tetrahydroxanthone : 5-Methyl-1,2,3,4-tetrahydro furo (2',3'-6,7) xanthone (124) :

6-Hydroxy-7-acetaldehydo-5-methyl-1,2,3,4-tetra-hydroxanthone (250 mg.) was treated with polyphosphoric acid (10 ml.) in a water bath for 1 1/2 hr. and poured into ice water. The solid separated was filtered and washed with dilute sodium hydroxide solution to remove uncyclised compound. A chloroform extract of the dried residue was passed

over a short column of alumina. Evaporation of solvent left a product, which was crystallised from alcohol, m.p. 198°. Yield 100 mg.

Analysis : Found : C, 75.15 ; H, 5.37 %

$C_{16}H_{14}O_3$: requires : C, 75.55 ; H, 5.50 %.

I.R. spectrum : 870 cm^{-1} (furan), 1640 cm^{-1} (γ-pyronyl >C=0 group).

$\lambda^{\text{Chloroform}}_{\text{Max.}}$ 246 nm (log ε 4.74), 278 nm (log ε 4.60).

Synthesis of 5'-5-Dimethyl-1,2,3,4-tetrahydro furo (2',3'-6,7) xanthone (127) : Acetylation of 6-hydroxy-7-allyl--5-methyl-1,2,3,4-tetrahydro xanthone : 6-Acetoxy-7-allyl-5-methyl-1,2,3,4-tetrahydroxanthone (125) :

A mixture of 6-hydroxy-7-allyl-5-methyl-1,2,3,4-tetrahydroxanthone (2 g.) and acetic anhydride (10 ml.) containing a few crystals of fused sodium acetate was heated under reflux for 5 hr. The reaction mixture was poured into crushed ice and was shaken for about 15 minutes. The compound which separated on standing was filtered and crystallised from alcohol, m.p. 128°. Yield 1.8 g.

Analysis : Found : C, 72.64 ; H, 6.40 %

$C_{19}H_{20}O_4$: requires : C, 73.07 ; H, 6.41 %.

Bromination of 6-acetoxy-7-allyl-5-methyl-1,2,3,4,-tetrahydroxanthone : 7-(2 ,3 -Dibromopropyl)-5-methyl-6-acetoxy-

-1,2,3,4-tetrahydroxanthone (126) :

A solution of bromine (1.6 g.; 0.01 M) in acetic acid (25 ml.) was added dropwise to a well stirred solution of 6-acetoxy-7-allyl-5-methyl-1,2,3,4-tetrahydroxanthone (3.1 g.; 0.01 M) in acetic acid, (35 ml.) during a period of 1 hr. The solution was poured into crushed ice and allowed to stand. The product which separated was collected by filtration. A solution in chloroform of the dried product was run over a short column of alumina. Evaporation of solvent left a residue which crystallised from methanol, m.p. 146°. Yield 2 g.

Analysis : Found : C, 48.29 ; H, 4.08; Br, 33.53 %

$C_{19}H_{20}O_4Br_2$: requires : C, 48.31 ; H, 4.24; Br, 33.90 %.

Cyclisation of 7-(2',3'-dibromopropyl)-5-methyl-6-acetoxy--1,2,3,4-tetrahydroxanthone : 5',5-Dimethyl-1,2,3,4-tetrahydrofuro (2',3'-6,7) xanthone (127) :

7-(2',3'-Dibromopropyl)-5-methyl-6-acetoxy-1,2,3,4-tetrahydroxanthone (2 g.) was heated under reflux for 2 hr. with a solution of potassium hydroxide (2.6 g.) in absolute alcohol (75 ml.). The reaction mixture was concentrated to one-third of its volume, diluted with water (25 ml.) and was immediately acidified with dilute hydrochloric acid and was ether extracted. Evaporation of ether left a pasty product which was washed with liquid ammonia (10 ml.; 10 %) and then with water. A chloroform solution of the dried

solid product was run over a short column of alumina. Evaporation of the solvent gave the product which crystallised from acetic acid, m.p. 223°. Yield 0.7 g.

Analysis : Found : C, 76.07 ; H, 5.52 %

$C_{17}H_{16}O_3$: requires : C, 76.12 ; H, 5.97 %.

I.R. spectrum : 850 cm^{-1} (furan), 1630 cm^{-1} (γ-pyronyl >C=O group).

$\lambda^{\text{Chloroform}}_{\text{Max.}}$ 252 nm (log e 4.94), 290 nm (log e 4.26), 326 nm (log e 4.38).

<u>Synthesis of 5',4-dimethyl furo (3',2'-2,3) xanthone</u> (129) : <u>Cyclisation of 6-hydroxy-7-allyl-5- methyl-1,2,3,4-tetra-hydroxanthone</u> : <u>5',5-Dimethyl-1,2,3,4,4',5'-hexahydro-furo (2',3'-6,7) xanthone</u> (128) :

6-Hydroxy-7-allyl-5-methyl-1,2,3,4-tetrahydro-xanthone (122) (1 g.) was triturated with conc. sulphuric acid (5 ml.) in a water bath for 15 minutes. The contents were poured into crushed ice. The separated product was filtered and washed with dilute sodium hydroxide solution to remove uncyclised compound. It crystallised from alcohol, m.p. 210°. Yield 0.8 g.

Analysis : Found : C, 75.18 ; H, 6.35 %.

$C_{17}H_{18}O_3$: requires : C, 75.53 ; H, 6.66 %.

I.R. spectrum : 1635 cm^{-1} (γ-pyronyl >C=O group).

$\lambda^{\text{Chloroform}}_{\text{Max.}}$ 248 nm (log e 4.22), 255 nm (log e 4.24), 304 nm (log e 4.18).

Dehydrogenation of 5',5-dimethyl-1,2,3,4,4',5'-hexahydrofuro (2',3'-6,7) xanthone : 5',4'-Dimethyl-furo (3',2'-2,3) xanthone (129) :

A mixture of 5',5-dimethyl-1,2,3,4,4',5'-hexahydrofuro (2',3'-6,7) xanthone (0.5 g.) and palladised charcoal (10 % ; 0.3 g.) and diphenyl ether (5 ml.) was refluxed for 10 hr. The reaction mixture was filtered hot and after cooling, petroleum ether was added to the filtrate. The separated product was filtered and washed several times with petroleum ether. It crystallised from acetic acid, m.p. 245°. Yield 0.25 g.

Analysis : Found : C, 77.00 ; H, 4.34 %

$C_{17}H_{12}O_3$: requires : C, 77.27 ; H, 4.55 %.

I.R. spectrum : 1640 cm^{-1} (γ-pyronyl >C=O group), 880 cm^{-1} (furan).

$\lambda^{\text{Methanol}}_{\text{Max.}}$ 256 nm (log e 3.90), 290 nm (log e 3.10), 300 nm (log e 3.12), 360 nm (log e 2.84).

Synthesis of 1,2,3,4-tetrahydro-furo (3',2'-5,6) xanthone (133) : 7-Hydroxy-1,2,3,4-tetrahydroxanthone (130) :

A mixture of resorcinol (3 g.) and ethyl cyclohexanone-2-carboxylate (4 ml.) was refluxed with diphenyl

ether (10 ml.) for 3 hr. with a short condenser to facilitate the removal of alcohol formed. After cooling, the separated product was filtered and washed several times with petroleum ether. It crystallised from alcohol, m.p. 278°. Yield 2.0 g.

Analysis : Found : C, 72.38 ; H, 5.79 %

$C_{13}H_{12}O_3$: requires : C, 72.21 ; H, 5.55 %.

Allylation of 6-hydroxy-1,2,3,4-tetrahydroxanthone : 7-Allyloxy-1,2,3,4-tetrahydroxanthone (131) :

A mixture of 7-hydroxy-1,2,3,4-tetrahydroxanthone (2 g.), allyl bromide (1 g.) and anhydrous potassium carbonate (8 g.) was refluxed in dry acetone (200 ml.) in a water bath for 10 hr. The reaction mixture was worked up as described earlier. The product crystallised from petroleum ether, m.p. 88°. Yield 1.5 g.

Analysis : Found : C, 74.98 ; H, 6.24 %

$C_{16}H_{16}O_3$: requires : C, 75.00 ; H, 6.25 %.

Claisen rearrangement of 6-allyloxy-1,2,3,4-tetrahydroxanthone : 6-Hydroxy-5-allyl-1,2,3,4-tetrahydroxanthone (132) :

6-Allyloxy-1,2,3,4-tetrahydroxanthone (2 g.) was refluxed with dimethyl aniline (10 ml.) for 8 hr. The reaction mixture was worked up as described earlier. The product crystallised from alcohol, m.p. 236°. Yield 1.5 g.

Analysis : Found : C, 74.54 ; H, 6.47 %.

$C_{16}H_{16}O_3$: requires : C, 75.00 ; H, 6.25 %.

I.R. Spectrum : 1620 $cm.^{-1}$ (γ-pyronyl >C=O group), and a broad band at 3400 $cm.^{-1}$ (aromatic hydroxy group).

1,2,3,4-Tetrahydro furo (3',2'-5,6) xanthone (133) :

6-Hydroxy-5-allyl-1,2,3,4-tetrahydroxanthone (500 mg.) was vigorously shaken with osmium tetroxide (50 mg.) and water (100 ml.). To the dark solution was added potassium periodate (2 g. in 100 ml. water) dropwise over a period of 3 hr. The ethyl acetate layer was separated, dried and evaporated. The residue was dissolved in chloroform and the clear solution was percolated through a short column of alumina. The residue left after evaporation of chloroform was used for further reaction.

The pasty product was heated with polyphosphoric acid (10 ml.) in a water bath for 3 2 hrs. The reaction mixture was poured into ice-water. The solid separated was filtered and washed with dilute sodium hydroxide solution to remove uncyclised compound. A benzene solution of the dried product was passed over a short column of alumina. Evaporation of solvent left a product which was crystallised from benzene, m.p. 205°. Yield 50 mg.

Analysis : Found : C, 74.85 ; H, 4.82 %.

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

I.R. spectrum : 840 $cm.^{-1}$ (furan). 1615 $cm.^{-1}$ (γ-pyronyl >C=O group).

Synthesis of 5'-methyl-furo (2',3'-3,4) xanthone (135) :

Cyclisation of 6-hydroxy-5-allyl-1,2,3,4-tetrahydro xanthone :

5'-Methyl-1,2,3,4,4',5'-hexahydro (3',2'-5,6) xanthone(134) :

6-Hydroxy-5-allyl-1,2,3,4-tetrahydroxanthone (1 g.) was triturated with conc. sulphuric acid (5 ml.) in a water bath for 15 minutes. The reaction mixture was worked up as described earlier. It crystallised from alcohol, m.p. 180°. Yield 0.8 g.

Analysis : Found : C, 75.23 ; H, 6.40 %.

$C_{16}H_{16}O_3$: requires : C, 75.00 ; H, 6.25 %.

I.R. spectrum : 1635 cm^{-1} (γ-pyronyl >C=O group).

$\lambda^{Methanol}_{Max.}$ 248 nm (log e 4.32), 255 nm (log e 4.35), 302 nm (log e 4.12).

Dehydrogenation of 5'-methyl-1,2,3,4,4',5'-hexahydro (3',2'-5,6) xanthone : 5'-Methyl-furo (2',3'-3,4) xanthone (135):

A mixture of 5'-methyl-1,2,3,4,4',5'-hexahydro xanthone (0.5 g.) and palladised charcoal (10 % ; 0.3 g.) and diphenyl ether (4 ml.) was refluxed for 10 hr. The reaction mixture was filtered hot and after cooling, petroleum ether was added to the filtrate. The separated product was filtered and washed several times with petroleum ether. The benzene solution of the product was run over a short column of alumina. Evaporation of solvent left a product which crystallised from benzene-petroleum ether, m.p. 172°.

Yield 0.3 g. The mixed m.p. with (134) was depressed by 25°. The m.p. of (135) previously prepared by Puranik and Rajopal[68] is 170°.

Analysis : Found : C, 76.81 ; H, 3.95 %

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

I.R.Spectrum . 1645 cm^{-1} (γ- pyronyl >C=O group), and at 825 cm^{-1} (furan).

$\lambda^{Methanol}_{Max.}$ 255 nm (log e 4.77), 282 nm (log e 3.46), 293 nm (log e 3.46), 340 nm (log e 3.43).

Synthesis of 4'-methyl-furo (2',3'-4,3) xanthone (141) :

Acetylation of 6-hydroxy-1,2,3,4-tetrahydroxanthone : 6-Acetoxy--1,2,3,4,-tetrahydroxanthone (136) :

6-Hydroxy-1,2,3,4-tetrahydroxanthone (2 g.), acetic anhydride (10 ml.) and a few crystals of sodium acetate was heated gently on a wire gauze with a low flame for two hours. The reaction mixture was worked up as described earlier. The product crystallised from alcohol, m.p. 106°, Yield 1.6 g.

Analysis : Found : C, 69.72 ; H, 5.45 %

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

I.R. spectrum : 1750 cm^{-1} (acetoxy group), 1630 cm^{-1} (γ-pyronyl >C=O group).

Fries migration of 6-acetoxy-1,2,3,4-tetrahydroxanthone : 6-Hydroxy-5-acetyl-1,2,3,4-tetrahydroxanthone (137) :

An intimate mixture of 6-acetoxy-1,2,3,4-tetra-

hydroxanthone (2 g.) and powdered anhydrous aluminium chloride (6 g.) was heated in an oil bath at 140° for 3 hr. After cooling, it was decomposed with ice and conc. hydrochloric acid. The product was filtered and treated with sodium hydroxide solution. The product is soluble. It was filtered, acidified with hydrochloric acid and crystallised from alcohol, m.p. 218°. Yield 1.5 g. The compound was soluble in alkali and developed red colouration with alcoholic ferric chloride solution.

Analysis : Found : C, 69.58 ; H, 5.17 %.

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

I.R. spectrum: 1715 cm^{-1} (ketonic >C=O group), 1615 cm^{-1} (γ-pyronyl >C=O group), and a broad band at 3500 cm^{-1} (aromatic hydroxy group).

Ethyl-5-acetyl-1,2,3,4-tetrahydro-6-xanthonyloxy acetate (138) :

A mixture of 6-hydroxy-5-acetyl-1,2,3,4-tetrahydroxanthone (1 g.), ethyl bromo acetate (1 ml.) and anhydrous potassium carbonate (5 g.) was refluxed in dry acetone (100 ml.) for 6 hr. in a water bath. The acetone was evaporated and the residue was treated with water. The separated product was filtered and washed with dilute sodium hydroxide solution to remove unreacted compound. It crystallised from alcohol, m.p. 155°. Yield 0.7 g.

Analysis : Found : C, 65.80 ; H, 5.67 %.

$C_{19}H_{20}O_6$: requires : C, 66.26 ; H, 5.81 %.

I.R. spectrum : 1630 $cm.^{-1}$ (γ-pyronyl >C=O group), 1695 $cm.^{-1}$ (ketonic >C=O group), 1730 $cm.^{-1}$ (ester > C=O group).

Hydrolysis of ethyl-5-acetyl-1,2,3,4-tetrahydro-xanthonyloxy-acetate : 5-Acetyl-1,2,3,4-tetrahydro-6-xanthonyloxy acetic acid (139) :

A mixture of ethyl-5-acetyl-1,2,3,4-tetrahydro-6-xanthonyloxy acetate (1 g.), distilled acetic acid (20 ml.) and conc. hydrochloric acid (20 ml.) was refluxed for 4 hr. The reaction mixture was diluted with water and allowed to stand. The product which separated was filtered, dissolved in sodium bicarbonate solution and filtered. The filtrate was acidified and the separated product was filtered . It crystallised from alcohol, m.p. 216°. (melt with effervescence). Yield 0.7 g.

Analysis : Found :C:64.97; H, 4.67 %
(After heating in vacuum at 110°).

$C_{17}H_{16}O_6$: requires : C,64.55 ; H, 5.06 %.

I.R. spectrum : 1620 $cm.^{-1}$ (γ-pyronyl >C=O group), 1700 $cm.^{-1}$ (ketonic >C=O group).

Cyclisation of 5-acetyl-1,2,3,4-tetrahydro-6-xanthonyloxy-acetic acid : 4'-Methyl-1,2,3,4-tetrahydro furo (3', 2'-5,6) xanthone (140) :

5-Acetyl-1,2,3,4-tetrahydro-6-xanthonyloxy acetic

Acid (0.5 g.) was cyclised by refluxing it with acetic anhydride (6 ml.) and freshly fused sodium acetate (1 g.) on a sand bath for 4 hr. After cooling, the mixture was poured into crushed ice. The separated product was filtered and washed with sodium bicarbonate solution to remove uncyclised acid. It crystallised from acetic acid, m.p. 226°. Yield 0.3 g.

Analysis : Found : C, 75.61 ; H, 5.47 %

$C_{16}H_{14}O_3$: requires : C, 75.60 ; H, 5.51 %.

I.R. spectrum : 1620 cm^{-1} (γ-pyronyl >C=O group), 815 cm^{-1} (furan).

$\lambda^{\text{Chloroform}}_{\text{Max.}}$ 244 nm (log e 4.64).

Dehydrogenation of 4'methyl-1,2,3,4-tetrahydro furo (3',2'-5,6) xanthone : 4'-Methyl-furo (3',2'-4,3) xanthone (141) :

4'-Methyl-1,2,3,4-tetrahydro furo (3',2'-5,6) xanthone (0.3 g.) and palladised charcoal (10 % ; 0.2 g.), and diphenyl ether (3 ml.) was refluxed for 10 hr. The reaction mixture was filtered hot and after cooling, petroleum ether was add to the filtrate and washed several times with petroleum ether. The chloroform solution of the product was passed over a short column of alumina. It crystallised from acetic acid, m.p. 215°. Yield 0.1 g. The m.p. of (141)

previously prepared by Puranik and Rajopal[64] is 216°.

Analysis : Found : C, 76.35 ; H, 3.75 %

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

I.R. spectrum : 885 $cm.^{-1}$ (furan).

λ Chloroform Max. 256 nm (log e 4.79), 338 nm (log e 4.87).

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